



KADIN HASTALIKLARI VE DOĞUM ALANINDA GELİŞMELER

EDİTÖRLER

PROF. DR. SALIM GÜNGÖR

DOÇ. DR. MEHMET UYSAL

Kadın Hastalıkları ve Doğum Alanında Gelişmeler

Editörler

Prof. Dr. Salim Güngör

Doç. Dr. Mehmet Uysal

İmtiyaz Sahibi
Platanus Publishing®

Editör
Prof. Dr. Salim Güngör & Doç. Dr. Mehmet Uysal

Kapak & Mizanpaj & Sosyal Medya
Platanus Yayın Grubu

Birinci Basım
Aralık, 2024

Yayımcı Sertifika No
45813

Matbaa Sertifika No
47381

ISBN
978-625-6723-85-3

©copyright
Bu kitabın yayım hakkı Platanus Publishing'e aittir.
Kaynak gösterilmeden alıntı yapılamaz, izin
alınmadan hiçbir yolla çoğaltılamaz.

Adres:Natoyolu Cad. Fahri Korutürk Mah. 157/B,
06480, Mamak, Ankara, Türkiye.
Telefon: +90 312 390 1 118
web: www.platanuskita.com
e-mail: platanuskita@gmail.com



PLATANUS PUBLISHING®

İÇİNDEKİLER

Bölüm 1	5
Preeklampside Masif Proteinüri Seröz Retina Dekolmanı ile İlişkili midir?- Nurcan Yörük-	
Bölüm 2	11
Preterm Eylemin Göz Ardı Edilen Nedeni: Akut Vajinit- Bilge Akay Çolak-	
Bölüm 3	33
Myoma Uteri ile İlişkili Kanamalarda ve Myomektomide Hemostaz Teknikleri- Yakup Baykuş & .Rulin Deniz-	
Bölüm 4	49
Fetal Development and Maternal Physiological Changes in Pregnancy- Nihan Erdoğan Atalay-	
Bölüm 5	65
"From Ultrasound to Mri: Advances in Gynecological Imagng" Samet Kirat	
Bölüm 6	81
The Rate of Subclinic Intraamniotic Infection in Preterm Labour and the Role of Amniotic Fluid Analyses in Determining Infection Gonul Ozer & Gokhan Bayhan	
Bölüm 7	95
From Ultrasound to MRI: Advances in Gynecological Imaging Samet Kirat	
Bölüm 8	111
Pelvic Girdle Pain in Pregnancy and Pelvic Region Anatomy Nihan Erdoğan Atalay	



Bölüm 1

Preeklampside Masif Proteinüri Seröz Retina Dekolmanı ile İlişkili midir?

Nurcan Yörük¹

¹ Dr. Öğretim Üyesi, Sağlık Bilimleri Üniversitesi Erzurum Şehir Hastanesi, ORCID: 0000 0002 8330 2551

Giriş

Preeklampsi gebeliğin 20. haftasından sonra görülen hipertansiyon, proteinüri ve yaygın ödemle karakterize olan, gebeliklerin %5-7 'sinde görülen, gebelik spesifik sendrom olarak update edilen ve tüm sistemik organları etkileyen bir hastalıktır (Abimanyu B., 2014). Preeklampsi patogenezi tam olarak anlaşılmamakla beraber plasental mikrodolaşımdaki değişikliklerle ilişkili olduğu düşünülmektedir. Preeklampsi tanısı koyabilmek için her zaman proteinüri varlığı şart değildir. Proteinüri yokken hipertansiyona karaciğer disfonksiyonu, böbrek yetmezliği, pulmoner ödem, hemoliz, trombositopeni, görsel ve serebral bulgular eşlik ediyorsa yine preeklampsi tanısı konulabilir. Masif proteinüri şiddetli preklampsi kriterlerinden çıkarılmış olsa da preeklampsinin tedavisine başlanması açısından hala önemli olduğu düşünülmektedir (Kim M.J. ve diğerleri, 2017).

Preeklampsi görsel sistem dahil olmak üzere tüm organ ve sistemleri etkiler. Maternal sistemik inflamasyon ve endotel disfonksiyonuna yol açarak iskemik hasara neden olur (Baflo, Uzun, N.D., Uzun, F., Kale ve Terzi, 2018; Weel ve diğerleri, 2017). Preeklampsinin nadir bir komplikasyonu olan retina dekolmanı ağır preeklampitik hastaların %1-2'sinde görülebilmektedir. Preeklampside görme sistemi farklı düzeylerde etkilenebilir. Hastalarda retina, optik sinir ve serebral korteksteki çeşitli altta yatan patolojiler oküler semptomlara sebep olabilir. En sık görülen oküler patolojik değişiklik arteriyollerin vazokonstriksiyonudur. Seröz retina dekolmanı koroidal vaskülarizasyon sonucu oluşan, preeklampside görme kaybı yapabilen nadir görülen bir durumdur. Patofizyolojisi tam olarak bilinmemekle beraber hipertansiyon, koroid iskemisi ve retina pigment epitelinin (RPE) iskemik yaralanması nedeniyle oluşan vazokonstriksiyonun rol alabileceği düşünülmektedir (Mackensen, Paulus, Max ve Ness, 2014).

Bu olguda Hellp sendromu gelişen preeklampitik bir hastadaki seröz retina dekolmanının spontan iyileşmesi anlatılmaktadır.

Olgu

G(1) P(0) A(0) Y(0) olan hasta 30 yaşında idi. 31 haftalık IVF (invitro fertilization) ikiz gebelik ve erken doğum tehdidi tanılarıyla kliniğimize yatırıldı. Hasta daha önce hiç gebe kalmamış, infertilite nedeniyle tedavi görmüş ve dış merkezde yapılan IVF tedavisi ile gebe kalmıştı. Hastanın yattığı anda yoğun idrar yolu enfeksiyonu mevcuttu. Hct:%42.1, Hb:15,1 gr/dl, Plt: 183×10^3 / μ l, SGOT: 42 U/I, SGPT: 43 U/I, idrar tetkikinde bakteri 994, protein (+++++) olarak saptandı. Hastaneye başvurduğunda sistemik kan basıncı 120/80 mmHg olan

hastanın hastaneye yatışından sonraki iki gün boyunca hiç tansiyon yüksekliği olmadı. Hastaneye yatışından iki gün sonra fizik muayenesinde bilateral pretibial ve periorbital ödemi tespit edildi. 24 saatlik idrarda protein 9.26 g/L saptandı. Kontrol Plt: $128 \times 10^3 / \mu\text{l}$, SGOT: 57 U/I, SGPT: 60 U/I LDH 409 U/I saptandı. Yapılan obstetrik ultrasonda her iki fetus ölçüleri 31 hafta ile uyumluydu. Günlük muayene, NST ve biokimyasal tetkiklerle takip edilen hastanın yatışının 3. gününde sistemik kan basıncının yükselmesi (170/110 mmHg), trombosit değerinin düşmeye başlaması ($120 \times 10^3 / \mu\text{l}$) üzerine ağır preeklampsisi tanısıyla gebeliğin sonlandırılmasına karar verilerek hasta sezaryene alındı. 1.Bebek 1575 gr, makad geliş, APGAR skoru 1.dk 6, 5.dk. 8 canlı kız ve 2. Bebek 2010 gr, APGAR skoru 1.dk 6, 5.dk. 9, transvers geliş, canlı kız bebek sezaryen ile doğurtuldu. Postoperative Hellp sendromu gelişen hastanın Plt: $106 \times 10^3 / \mu\text{l}$, SGOT: 92 U/I, SGPT: 128 U/I LDH >750 U/I olarak saptandı. Postoperatif sistemik kan basıncı 160/100 mmHg civarında seyreden hastaya sistemik kan basıncı kontrolü sağlamak amacı ile alfamet tablet 3x1 ve MgSO_4 iv infüzyon başlandı. Postpartum 10. saatte görme bulanıklığı gelişen hastaya göz konsültasyonu istendi. Yapılan oftalmolojik muayenede görme keskinliği her iki gözde 1/10 olarak saptandı. Göz dibi muayenesinde makula ve periferik retinada total eksudatif retina dekolmanı tespit edildi. Ön segmentte sıvı birikimi izlenmedi. Göz içi basıncı normaldi. Hipertansif retinopati bulguları (disk ödemi, retinal hemoraji) izlenmedi. Hastanın göz polikliniği tarafından yapılan takiplerinde subretinal sıvı postpartum 4. gününde gerilemeye başladı. Görme keskinliği her iki gözde parmak sayma şeklinde açılmaya başladı. Hasta bebeklerine süt verdiği için etyolojik değerlendirmede flöresein angiografi kullanılmadı. Hastanın takipleri OCT(optical coherence tomography) ve fundus fotoğrafları ile yapıldı. Postpartum dört hafta sonra görme keskinliği her iki gözde 10/10 olarak saptandı. Herhangi bir cerrahi müdahaleye gerek kalmadan subretinal bölgedeki sıvı tamamen geriledi.

Tartışma

Preeklampside %1-2 oranında rastlanan seröz retina dekolmanı doğum öncesi veya sonrasında görülebilir. Preeklampsisi hastalarının %10-15'inde Hellp sendromu (trombositopeni, hemoliz ve karaciğer enzimlerinde artış) gelişebilir. Preeklampsisi ile ilişkili olarak Hellp sendromu gelişen hastalarda seröz retina dekolmanı yedi kat daha fazla görülebilir (Sánchez Zamora, Mejía Arnaud, Saz Castro, Gómez Del Pulgar Vázquez, ve Correa Barrera, 2022). Bu olguda da preeklampsisi Hellp sendromu ile komplike olunca sezaryen kararı verildi ve sezaryen sonrası postpartum 10. saatte görme bulanıklığı başladı.

Preeklampsiye baęlı gelişen seröz retina dekolmanı patofizyolojisi kesin olarak bilinmemekle beraber çeşitli teoriler öne sürölmüştür. Önceleri retina ve koroid dolaşım bozukluęunun birlikte sebep olduęu düşünölse de yapılan çalışmalarda koroid iskemisine baęlı olarak seröz retina dekolmanı geliştięi düşünölmektedir. Yapılan çalışmalarda FFA ve İndosiyanın yeşil anjiyografi incelemeleri ile koroid dolaşım bozukluęunun yol açtıęı vasküler geçirgenlik sonucu subretinal boşluęa sıvı ve protein geçişinin sorumlu olduęu gösterilmiştir (Iida, 2002). Literatürde Hellp sendromundaki oftalmolojik bulguların deęerlendirildięi 107 olguluk bir çalışmada hastaların % 16'sında hipertansiyona baęlı deęişiklikler, % 3.7'sinde seröz retina dekolmanı, % 2.7'sinde ise kortikal körlük tespit edilmiştir. HELLP sendromuna ikincil gelişen seröz retina dekolmanı doğum sırasında ya da doğum sonrasında görme azalması veya kaybı ile ortaya çıkabilir (Erbagci, Karaca, Ugur, Okumus ve Bekir, 2008).

Radha Bai Prabhu yaptıęı çalışmada, retina dekolmanı ve görme kaybının şiddetli preeklampsi hastalarında daha sık olduęunu göstermiştir. Retinopati derecesi, preeklampsinin derecesi ile pozitif korelasyon gösterir (Radha Bai Prabhu, 2017). Bizim çalışmamızda da retina bulgularının şiddetli preeklampside daha sık olması ve retina dekolmanının aęırlıklı olarak şiddetli preeklampsi hastalarında daha sık gözlenmesi bu çalışma ile uyumludur. Kim JM ve arkadaşları 233 hasta ile yaptıkları bir çalışmada, 24 saatlik idrarda 24 saatte 5 gr ya da üzerinde masif proteinürisi olan 10 hastada, 2-5gr/24h olan orta proteinürisi olan 2 hastada, 24 saatte 2 gr'ın altında hafif proteinürisi olan 1 hastada retina dekolmanı ile karşılaşmışlar. Bu olguda ise (+++++) masif proteinüri mevcuttu (Kim, M.J. ve dięerleri, 2017). Masif proteinürisi olan hastalarda daha yüksek oranda retina dekolmanı gelişmesi de bu olgu ile uyumludur.

Son çalışmalar preeklampsi öyküsü olan kadınların, antepartum, intrapartum ve postpartum dönemde saęlıklı gebelerden daha yüksek oküler komplikasyon riski altında olduęunu göstermiştir (Murphy, Casselman, ve Smith, 2013). Gebelikte, oküler deęişikliklerin çoęu fizyolojiktir. Göz içi basıncında düşme, miyopide artış, hipofiz bezinde fizyolojik büyümeye baęlı görme alanında bitemporal ve konsantrik defektler normal gebelikte olabilir. Preeklampside papilla ödemi, optik atrofi, retina kanamaları, maköla ödemi, retina dekolmanı gibi patolojik problemler olabilir. Bunun yanı sıra preeklampsiye baęlı olarak gelişen retinopati, altta yatan diyabet, kronik hipertansiyon ve böbrek hastalığı varsa daha şiddetli seyredebilir (Kalaycı ve Şahin 2020). Bu olguda diyabet, kronik hipertansiyon, böbrek hastalığı gibi altta yatan bir problem yoktu.

Görsel semptomlar fotopsi, hemianopsi, odaklanmada zorluk, bulanık görme, görme keskinliği azalması ve aęır vakalarda tamamen körlük şeklinde

olabilmektedir (Garg ve diğeri 2014). Bu olguda da hasta hiç görmediğini ifade etmişti. Ancak 4 hafta sonra hasta tamamen görmeye başladı. Literatür incelendiğinde seröz retina dekolmanı gelişen hastaların çoğu doğumdan sonraki 2-12 hafta içinde tamamen iyileşmektedirler. Bu vakada da hasta 4 hafta içinde tamamen iyileşti (Atış ve diğeri 2009).

Sonuç

Görme kaybı tarifleyen preeklampsi hastalarında retroorbital değerlendirmelerin mutlaka yapılması gerekmektedir. Bu yüzden görme kaybı gelişen preeklampsili gebeler için direkt oftalmoskop dışında optik sinir ve oksipital korteks kökenli lezyonlar için MRI (manyetik rezonans görüntüleme) ve VEP (görsel uyarılmış potansiyel) cihazlarıyla değerlendirmenin yapılması faydalı olabilir. Preeklampsi olan gebelerde retina dekolmanı, pigment epitel dekolmanı, maküla ödemi ve papilla ödemi gibi nadir fakat ciddi komplikasyonlar da ortaya çıkabilir. Preeklampsik gebelerin göz dibi muayenesinde hipertansif retinopati ve diğer retinal hastalıklar da akılda bulundurulmalıdır. Klinisyenler bu oküler belirtilerin varlığında göz konsültasyonu isteyip işbirliği içinde çalışmalıdır. Görme kaybı gelişen preeklampsik gebelerde, gebeliğin sonlandırılması görmenin yeniden kazanılmasında etkili görünmektedir. Görme kaybı preeklampsi ya da Hellp sendromu gelişen hastalarda özellikle masif proteinüri varlığında doğum yaptırdıldıktan sonra da gelişebilir. Eğer seröz retina dekolmanı tespit edilirse bunun 4-6 hafta içinde düzeleceği akılda bulundurulmalı ve hastaya zamanla bu durumun düzeleceği anlatılmalıdır.

References

- Abimanyu, B. (2014). The role of angiogenic factors in preeclampsia. *Pregnancy Hypertens*, 4, 246.
- Atış, A., Ciftci, F., Tutuman, T., Turker, C., Goker, N. ve Balcıoğlu N. (2009). Ağır preeklampside nadir görülen bir bilateral seroz retina dekolmanı. *Şişli Etfal Tıp Bülteni*, 43, 51-2.
- Baflol, G., Uzun, N.D., Uzun, F., Kale, A. ve Terzi, H. (2018). Retrospective analysis of the preeclampsia cases delivered in our clinic between 2013 and 2017. *Perinatal Journal*, 26, 135–40.
- Erbagci, I., Karaca, M., Ugur, M.G., Okumus, S. ve Bekir N.A. (2008). Ophthalmic manifestations of 107 cases with hemolysis, elevated liver enzymes and low platelet count syndrome. *Saudi Med J*, 29, 1160-3.
- Garg, A., Wapner, R.J., Ananth, C.V., Dale, E., Tsang, S.H., Lee W, et al. (2014) Choroidal and retinal thickening in severe preeclampsia. *Investig Ophthalmol Vis Sci*, 55, 5723–9.
- Kalaycı M, Şahin Ö. (2020) Preeklampsia hastalarının göz dibi muayenesinde retina bulgularının değerlendirilmesi. *Pernatoloji Dergisi*, 28(2), 62-67.
- Kim MJ, Kim YN, Jung EJ, Jang HR, Byun JM, Jeong DH et al. (2017) Is massive proteinuria associated with maternal and fetal morbidities in preeclampsia? *Obstet Gynecol Sci*, 2017 May, 60(3), 260-265.
- Iida T, Kishi S. (2002) Choroidal vascular abnormalities in preeclampsia. *Arch Ophthalmol*, 120, 1406-1407.
- Mackensen F, Paulus WE, Max R, Ness T. (2014) Ocular changes during pregnancy. *Dtsch Arztebl Int*, 111, 567–76.
- Murphy MSQ, Casselman RC, Smith GN. (2013) Postpartum alterations in circulating endothelial progenitor cells in women with a history of pre-eclampsia. *Pregnancy Hypertens*, 3, 178–85.
- Radha Bai Prabhu T. (2017) Serious visual (ocular) complications in pre-eclampsia and eclampsia. *J Obstet Gynecol India*, 67, 343–8.
- Sánchez Zamora P, Mejía Arnaud RA, Saz Castro R, Gómez Del Pulgar Vázquez B, Correa Barrera JJ. (2022) Bilateral serous retinal detachment in a patient with atypical presentation of preeclampsia due to HELLP syndrome. *JJ. Rev Esp Anesthesiol Reanim (Engl Ed)*, Feb, 69(2), 114-118.
- Weel CI, Romão-Veiga M, Matias ML, Fioratti EG, Peraçoli JC, Borges VT, et al. (2017) Increased expression of NLRP3 inflammasome in placentas from pregnant women with severe preeclampsia. *J Reprod Immunol*, 123, 40–7.



Bölüm 2

Preterm Eylemin Göz Ardı Edilen Nedeni: Akut Vajinit

Bilge Akay Çolak¹

¹ Op. Dr., Görele Op. Dr. Ergun Özdemir Devlet Hastanesi, Orcid: 0009-0002-1633-8789

PRETERM EYLEM

Preterm Eylem Nedir?

37. gebelik haftasını altında (20+0 hafta ve üzeri) canlı veya ölü doğumun gerçekleşmesi preterm doğum olarak adlandırılır ve tüm doğumların yaklaşık %10'u preterm doğumdur. Bu doğumların %85'i 32 haftanın üzerinde olan doğumlardır.(Dagklis et al., 2023)

Preterm Doğum Risk Faktörleri

Preterm doğum eylemine neden olan geri dönüşümlü ve geri dönüşümsüz birçok risk faktörü bulunmaktadır.(Robinson & Norwitz, 2023) Bu risk faktörleri, uterusun kasılmasını sağlayan kaskadı erken uyardığında, kaskadı inhibe eden ve uterusun sessizliğini koruyan baskılayıcı faktörlerin erken geri çekilmesinde veya her ikisinin birden olmasında rol oynayarak preterm doğuma neden olurlar. (Lockwood, Kuczynski, & Kuczynski, 2001) Preterm eyleme neden olabilecek risk faktörleri Tablo 1’de gösterilmiştir.

Tablo 1 : Preterm Doğum Risk Faktörleri

Obstetrik Öykü	Önceki gebelikte erken doğum öyküsü Çoğul gebeliğe sahip olma Mevcut gebelikte obstetrik komplikasyonlar (erken membran rüptürü, plasenta previa veya dekolmanı, oligohidramnios /polihidramnios, preeklampsi) Yardımcı üreme yöntemi ile gebe kalma Önceden geçirilen küretaj öyküsü
Servikal veya Uterin Faktörler	Orta trimesterde kısa serviks Konizasyon veya leep öyküsü Konjenital uterus anomalisi (septat, bikornu, unikornu, uterus didel-fiz) Erken gebelikte vajinal kanama Uterin leiomyom Servikal polip
Demografik Faktörler	İrk (ABD için Alaska ve Amerika Kızılderili yerli halkı) Adölesan veya 40 yaş üstü gebelik Düşük sosyoekonomik düzey İrkçılığa maruz kalma
Kronik Hastalıklar	Kronik Hipertansiyon, Kronik Böbrek Hastalığı, Tip 1 Diabetes Mellitus, Bazı Otoimmün Hastalıklar, Kronik Anemi, Kalp Hastalığı
Enfeksiyonlar	Genitoüriner Enfeksiyon, Asemptomatik Bakteriüri, Cinsel Yolla Bulaşan Enfeksiyon, Periodontal Hastalık, Sıtma,
Fiziksel ve Genetik Faktörler	Kısa boy Bazı genetik varyantlar Annede veya anne soyunda erken doğum öyküsü
Davranışsal Faktörler	Sigara kullanımı Yasadışı madde kullanımı
	Bazı mesleki fiziksel aktivite türleri

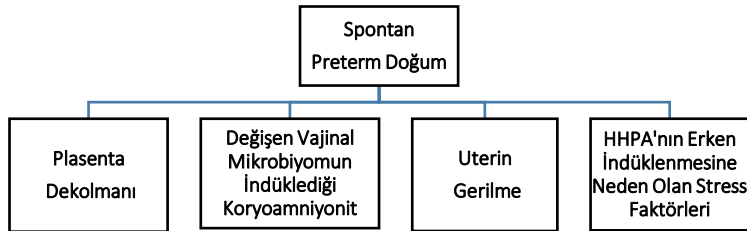
Diyet, Fiziksel aktivite	Gebelik öncesi kilonun ve gebelikte kilo alımının çok düşük veya çok yüksek olması Yetersiz beslenme
Diğer	Aşırı stres, sosyal destek eksikliği Maternal depresyon Doğum öncesi bakım eksikliği Gebelikler arası 6 ay' dan az aralık Sağlıksız ortam (örneğin, havadaki ince partikül maddeler) Erkek fetal cinsiyet Fetal durumlar (örneğin, bazı konjenital anomaliler, büyüme kısıtlılığı, hidrops fetalis)

Robinson, J. N., & Norwitz, E. R. (2023). Spontaneous preterm birth: Overview of risk factors and prognosis.

Gebe ilk prenatal muayeneye geldiği zaman bu risk faktörleri gözden geçirilmelidir. Müdahale edilerek geri dönüşümlü olabilecek durumlar uygun şekilde tedavi edilmeli ve preterm eylem önlenmeye çalışılmalıdır.

Spontan Preterm Doğum Patogenezi

Yapılan araştırmalar sonucunda preterm doğum veya preterm doğum öncesi membran rüptürüne neden olan 4 ana patolojik süreç tanımlanmıştır. (Şekil 1) Bu patolojik süreçler eylem meydana gelmeden çok önce başlayabilirler. Kalıtsal ailesel varyantlar ve servikal yetmezlik diğer patolojik süreçleri oluşturur. Patogeneizde rol oynayan etkenler bir dizi inflamatuvar süreci başlatarak Preterm eyleme neden olurlar. (Lockwood *et al.*, 2001)



Şekil 1: Spontan Preterm Doğuma Neden Olan Dört Ana Patogenez

Lockwood, C. J., Kuczynski, E., & Kuczynski, E. (2001). Risk stratification and pathological mechanisms in preterm delivery. *Paediatric and Perinatal Epidemiology* (Vol. 15)

Gebede anormal yönde değişen vajinal mikrobiyota, asendan kolonizasyon ile fetal membranlarda infiltrasyona, amniyotik kavitenin mikrobiyal invazyonuna ve sonuç olarak preterm eyleme neden olabilir. Nelson ve arkadaşları yaptıkları çalışmada, preterm doğum yapan kadınların vajinal mikrobiyotalarında, term doğum yapan kadınlara oranla daha düşük bakteriyel zenginlik ve çeşitlilik

saptamışlardır. (Nelson DB et al., 2014) Aynı şekilde Haque ve arkadaşları, preterm doğum yapan kadınların, gebeliğinin ilk 15-20 haftalık dönemlerinde vaginal mikrobiyomlarında daha az çeşitlilik görmüşlerdir.(Haque, Merchant, Kumar, Dutta, & Mande, 2017) Gebede vajinal mikrobiyota sağlığının korunması preterm eylemi önlemek için önemli görünmektedir.

AKUT VAJİNİT

Akut Vajinit Nedir?

Vajinit; vajinal mikrobiyotayı oluşturan flora elemanlarının oranlarındaki dengenin bozulması sonucunda meydana gelen enfeksiyon veya iltihaplanma durumu için kullanılan genel bir terimdir. Bu enfeksiyonlar yeni başladıysa akut vajinit olarak adlandırılır. Uzun süreli olan veya tedavi sonrasında tekrarlayan enfeksiyonlar kronik vajinit olarak değerlendirilir.

Vajinal enfeksiyonlar kadın doğum polikliniklerine başvurunun en yaygın nedenlerinden biridir. Yapılan bölgesel bir çalışmaya göre Türkiye’de 15-49 yaş arası kadınlarda vajinal enfeksiyon prevalansı %78 olarak bildirilmiştir.(Yurttaş Akar BÇ, 2020)

Vajinitin Klinik Belirtileri

Vajinal akıntı, ovulasyon zamanına yakın dönemde, hamilelik sırasında veya östrojen içeren kontraseptiflerin kullanımı gibi zamanlarda daha belirgin hale gelebilir. Fizyolojik lökore dediğimiz bu durumlarda vajinal akıntının karakteri her zaman olduğu gibidir. Vajinal akıntının renginde, kokusunda değişiklik olması, kaşıntı ve yanmanın eşlik etmesi, tahrişe bağlı eritem bulgularının olması, lekelenme, disparoni ve dizüri şikayetlerinden en az birinin olması vajinit tanısını destekler. (Paavonen JA & Brunham RC, 2020)

Vajinit; bakteri, mantar, protozoa gibi organizmaların aşırı çoğalmasına bağlı ve bulaşıcı etkenlerden dolayı olabileceği gibi tampon veya prezervatif gibi yabancı cisme, genital bakım ürünleri kullanımına, sistemik tıbbi bozukluklara bağlı da oluşabilir. (Workowski KA et al., 2021)

Yapılan birçok çalışma genitoüriner enfeksiyonların preterm doğum riskini arttırdığını göstermiştir. Tablo 2’de yapılan bir çalışma sonucunda enfeksiyon tipi ve etkenine göre preterm doğum riskleri verilmiştir.(Klein & Gibbs, 2004)

Tablo 2: Seçilmiş Enfeksiyonlarda Preterm Doğum Riski

Enfeksiyon	Odds Ratio (%95 CI)
16 haftadan önce bakteriyel vajinozis	7.55 (1.8-31.7)
<i>Neisseria gonorrhoeae</i>	5.31 (1.57-17.9)
Aseptomatik bakteriüri	2.08 (1.45-3.03)
<i>Chlamydia trachomatis</i>	
• 24 haftada	2.2 (1.03-4.78)
• 28 haftada	0.95 (0.36-2.47)
<i>Trichomonas vaginalis</i>	1.3 (1.1-1.4)
<i>Ureaplasma urealyticum</i>	1.0 (0.8-1.2)

Klein, L. L., & Gibbs, R. S. (2004). Use of microbial cultures and antibiotics in the prevention of infection-associated preterm birth. *American Journal of Obstetrics and Gynecology*, 190(6), 1493–1502. Retrieved 2 September 2024 from <https://doi.org/10.1016/J.AJOG.2004.03.014>

Gebede Bakteriyel Vajinozis

Normalde vajinal florada belli seviyelerde bulunan *Gardnerella*, Mikoplazma, anaeroblar gibi bakterilerin *Laktobasillus* bakterilerinden daha baskın hale gelmesiyle oluşturduğu tablo bakteriyel vajinozis olarak adlandırılır. Bakteriyel vajinozis tanısı gebe olmayan kadınlarda olduğu gibi genellikle Amsel kriterlerinden 3 tanesinin olmasıyla koyulur. Bu kriterler: vajinal pH>4.5 olması, mikroskopide clue hücrelerinin görülmesi, vajen duvarını kaplayan ince, homojen, beyaz-grimsi akıntı ve örnek üzerine %10'luk potasyum hidroksit (KOH) damlatıldığında balık kokusunun oluşmasıyla tanımlanan pozitif 'amin' testidir.(*Workowski KA et al., 2021*)Tanıda altın standart vajinal akıntının gramla boyanarak Nugent kriterleri (Nugent, , Krohn, & Hillier3, 1991)veya Hay/Ison (Ison CA & Hay PE, 2002)kriterlerine göre değerlendirilmesidir.

Bazı yapılan çalışmalar sonucunda Amerika Kadın Hastalıkları ve Doğum Uzmanları Derneği (ACOG), ABD Önleyici Hizmetler Görev Gücü (USPSTF), Hastalık Korunma ve Kontrol Merkezleri (CDC) ve Kanada Kadın Doğum Uzmanları ve Jinekologlar Derneği preterm eylemi ve sonuçlarını önlemek için asemptomatik bakteriyel vajinozisli tüm hamile bireylerin rutin olarak taranmasını ve tedavi edilmesini önermemektedir. (American College of Obstetricians and Gynecologists, 2012; Nygren P et al., 2008; US Preventive Services Task Force, 2020; Workowski KA & Bolan GA, 2015) Daha önce erken doğum öyküsü olan hastaların bakteriyel vajinozis

açısından taranması ve pozitifse tedavi edilmesi gerekip gerekmediği tartışmalıdır, çünkü tekrarlayan erken doğumda bir azalma kanıtlanmamıştır. 2023 yılında yapılan randomize kontrolü çalışmada asemptomatik bakteriyel vajinozisli gebelerde rutin taramanın preterm eylem riskini azaltmadığını göstermiştir.(Bretelle et al., 2023)

Her ne kadar rutin taramanın maliyet etkin olmadığı ve tedavinin preterm eylem oranını azaltmadığına yönelik çalışmalar olsa da tam tersi çalışmalar da mevcuttur.(Lamont RF, Dunchan SLB, Mandal D, & Basset P, 2003; McDonald HM et al., 1997; Morales, Schorr, & Albritton, 1994; Ohn et al., 1995; Ugwumadu A, Manyonda I, Ried F, & Hay P, 2003) Tablo 3'te bakteriyel vajinozisli gebelerde preterm doğumda azalma olduğunu gösteren çalışmalarda kullanılan tedavi rejimleri gösterilmiştir.

Tablo 3: Bakteriyel Vajinozisli Gebelerde Preterm Doğumda Azalma Olduğunu Gösteren Çalışmalarda Kullanılan Tedavi Rejimleri

Tedavi Rejimleri
Metronidazol 400 mg oral günde 2 kez 2 gün. 4 hafta sonraki kontrolde pozitifse tekrarlar ^[1]
Metronidazol 250 mg oral günde 3 kez 7 gün+ Eritromisin 333 mg günde 3 kez 14 gün. 28. Gebelik hafta kontrolünde pozitifse tekrarlar ^[2]
Metronidazol 250 mg günde 3 kez 7 gün. Tedavi tekrarı yok. ^[3]
Klindamisin 300 mg oral günde 2 kez 5 gün. Tedavi tekrarı yok. ^[4]
Klindamisin 5 gram 2% vajinal krem 3 gün gece. 3 hafta sonra test tekrarı yap pozitifse aynı tedaviyi 7 gün ver. ^[5]

1. McDonald HM, O'Loughlin JA, Vigneswaran R, Jolley PT, Harvey JA, Bof A, & McDonald PJ. (1997). Impact of metronidazole therapy on preterm birth in women with bacterial vaginosis flora (*Gardnerella vaginalis*): a randomised, placebo controlled trial. *Br J Obstet Gynaecol*, 104(1391).
2. Ohn, J., Auth, C. H., Obert, R., Oldenberg, L. G., Ndrews, I. W. A., Ard, A. B. D. U. B., ... Oppen, L. C. (1995). Reduced Incidence Of Preterm Delivery With Metronidazole And Erythromycin In Women With Bacterial Vaginosis.
3. Morales, W. J., Schorr, S., & Albritton, J. (1994). Effect of metronidazole in patients with preterm birth in preceding pregnancy and bacterial vaginosis: A placebo-controlled, double-blind study. *American Journal of Obstetrics and Gynecology*, 171(2), 345–349. Retrieved 5 September 2024 from [https://doi.org/10.1016/S0002-9378\(94\)70033-8](https://doi.org/10.1016/S0002-9378(94)70033-8)
4. Ugwumadu A, Manyonda I, Ried F, & Hay P. (2003). Effect of early oral clindamycin on late miscarriage and preterm delivery in asymptomatic women with abnormal vaginal flora and bacterial vaginosis: a randomised controlled trial. *In Lancet* (Vol. 361, pp. 983–988).

5. Lamont RF, Dunchan SLB, Mandal D, & Basset P. (2003). Intravaginal clinda mycin to reduce preterm birth in women with abnormal genital tract flora. *Obs tet Gynecol*, 101, 516–522.

Dünya Sağlık Örgütü (WHO) ve CDC, semptomatik gebe bireylerin tedavisi için oral veya topikal tedaviyi önermektedir. (Workowski KA et al., 2021; World Health Organization, 2021) Kullanılan tedavi rejimleri gebe olmayan kadınlarla aynıdır ve Tablo 4’te gösterilmiştir.

Tablo 4 : Bakteriyel vajinozis tedavisinde gebede kullanılabilen ajanlar Oral Tedavi

Metronidazol	500 mg günde 2 kez oral 7 gün
Metronidazol	250 mg günde 3 kez oral 7 gün
Klindamisin	300 mg günde 2 kez oral 7 gün
Topikal Tedavi	
Metronidazol	%0,75 jel 1 tam aplikatör 5 gece, intravajinal
Klindamisin	% 2 krem, 1 tam aplikatör 7 gece, intravajinal

Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I, ... Bolan GA. (2021). *Sexually Transmitted Infections Treatment Guidelines*. *MMWR Recomm Rep*, 70(4), 1–187.

World Health Organization. (2021). *Guidelines for the management of symptomatic sexually transmitted infections*.

- **Metranidazol**, plasentayı geçtiği için ilk trimesterde kullanımından kaçınan klinisyenler bulunmaktadır. Gebelerde yapılan meta-analiz sonuçlarında ilk trimesterde metronidazol maruziyeti ile konjenital anomaliler arasında herhangi bir ilişki bulunamamıştır. (Sheehy O, Santos F, Ferreira E, & Bérard A, 2015)Metronidazol, farelerde mutajeniktir ve kansere neden olmaktadır. İnsanlarda bu tür zararları olduğuna dair bir etki olmamasına rağmen, CDC ilk trimesterde metronidazol kullanımını önermemektedir. (Workowski KA et al., 2021) Aynı şekilde WHO’da ilk trimester kullanımında dikkatli olunmasını tavsiye etmeye devam etmektedir. (World Health Organization, 2021)
- Hayvanlarda yapılan çalışmalarda **Tinidazolün** konjenital anomalilerle ilişkili olduğunu öne sürüldüğü için, bu ilacın gebelerde kullanılması tavsiye edilmez (Briggs GG, Freeman RK, & Yaffe SJ, 2011; Workowski KA et al., 2021)

- **Seknidazol** ile ilgili veriler yetersiz olduğu için gebelerde kullanımında kaçınılır. (Workowski KA et al., 2021)

Gebede Vulvovajinal Candida

Gebe kadınlar gebe olmayanlara göre vulvovajinal candida enfeksiyonuna yakalanmada 2 kat yüksek prevelansa sahiptir. (Sobel JD, 2007) Gebelikte yükselen östrojen seviyesi, vajinal flora üyesi candida türlerinin maya şeklinden hife dönüşümüne neden olur. Hife dönüşen candidalar vajina epitelinde glikojen yapımını uyararak kolayca kullanabilecekleri karbon kaynağını oluştururlar. Böylece bir yandan çoğalamaya devam ederek candida vajinitine (CV) neden olurlar. (Aguin & Sobel, 2015)

Candida enfeksiyonu belirtilerinde yanma, kaşıntı, kötü kokulu akıntı vardır. Akıntının vasfı süt keşiği gibi peynirimsi akıntı olmasıdır.

Gebelik sırasında CV'nin, erken membran rüptürü ve kötü gebelik sonucu gibi gebelik komplikasyon riskini artırdığına ilişkin kanıtlar vardır. (Aguin & Sobel, 2015; Maki Y, Fujisaki M, Sato Y, & Sameshima H, 2017) Daha önceden yapılan başka bir çalışmaya göre ise düşük doğum ağırlığı veya erken doğum ile CV arasında ilişki bulunamamıştır. (Cotch et al., 1998)

CV'nin neden olduğu semptomlar gebenin yaşam kalitesini olumsuz etkileyebilir. Bu nedenle bu semptomları gidermek için tedavi edilebilir. Ancak 2021 yılında bir Avrupa kılavuzu, yenidoğanlarda oral pamukçuk ve bebek bezi dermatiti oranlarını azaltmak için üçüncü trimesterde kolonize olmuş tüm gebe kişilerin tedavi edilmesini önermektedir. (Farr et al., 2021)

Gebede CV tedavisinde oral form yerine topikal formda imidazol türevi ilaçlar tercih edilir.(Workowski KA et al., 2021; Young & Jewell, 2001) Tedavi süresi olarak genellikle 7 gün yeterli olmakla birlikte semptomları devam eden gebede tedavi süresi 10-14 güne kadar uzatılabilir. CV tedavisi Tablo 5'te gösterilmiştir.

Tablo 5 : Gebede candida vajinit tedavisi

Topikal Tedavi

Klotrimazol % 1 krem günde bir aplikatör, 7 gün intravinal

Mikonazol % 2 krem günde bir aplikatör 7 gün intravinal

Nistatin fitil 100.000 birim her gece 1 fitil. 14 gün intravajinal

Young, G., & Jewell, D. (2001). Topical treatment for vaginal candidiasis (thrush) in pregnancy. *Cochrane Database of Systematic Reviews*. Retrieved from <https://doi.org/10.1002/14651858.CD000225>

Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I, ... Bolan GA. (2021). Sexually Transmitted Infections Treatment Guidelines . *MMWR Recomm Rep*, 70(4), 1–187.

- Oral **flukonazol**, özellikle 1. Trimesterde gebe hastalarda kullanımında kaçınılır. 3315 gebeyi içeren bir kohort çalışmasında flukonazol kullanımıyla gebelik kaybı ve abortus riskinin arttığını bildirmiştir. (Mølgaard-Nielsen D, Svanström H, Melbye M, Hviid A, & Pasternak B, 2016) Daha sonra yapılan daha büyük popülasyon içeren başka bir kohort çalışmasında da gebeliğin erken dönemlerinde flukonazol maruziyetinin doza bağlı olarak gebelik kaybı riskini arttırdığını bildirmiştir. (Bérard et al., 2019) Flukonazolün günde 400-800 mg'lık bir dozda sürekli olarak kullanıldığında bir teratojen görevi gördüğü vaka raporlarıyla da bildirilmektedir. Flukonazol embriyopatisi olarak da tanımlanan kafatası, yüz, kemik ve kalp anomalileri 1.trimesterde flukonazole maruziyet sonucunda kafatası, yüz, kemik ve kalp anomalilerinin görülmesi flukonazol embriyopatisi olarak tanımlanmıştır.(Lopez-Rangel & Van Allen, 2005) 1,9 milyondan fazla gebeyi içeren Amerika Birleşik Devletleri Medicaid Analytic eXtract veritabanı kullanarak yapılan bir çalışmaya göre; İlk trimesterde oral flukonazol kullanımı, dudak-damak yarıkları veya konotrunkal malformasyonlarla ilişkilendirilmemiştir, ancak kas-iskelet sistemi malformasyonları ile ilişki bulunmuştur. Toplamda 10.000 maruz kalan gebelikte yaklaşık 12 vaka gibi küçük bir risk farkına karşılık gelmektedir. (Zhu et al., 2020) Gebe olduklarını fark etmeden önce düşük doz (150 mg) flukonazol kullanımı herhangi bir malformasyon veya abortusla ilişkilendirilmemiş ve güvenli görünmektedir. (Mølgaard-Nielsen, Pasternak, & Hviid, 2013)
- **Otesekonazol**, gebelerde, gebe kalma ihtimali olan hastalarda ve emzirenlerde kullanılmaz. Hayvan deney çalışmaları fetüste ve bebekte (süt yoluyla geçerek) zararlı olduğunu göstermiştir.(VIVJOA-

oteseconazole capsule Mycovia Pharmaceuticals, Inc. HIGHLIGHTS OF PRESCRIBING INFORMATION, n.d.)

- **Ibrexafungerp**, hayvan deney çalışmaları sonucunda gebelikte fetal etkiler nedeniyle kullanılması kontraendikedir. (*BREXAFEMME-ibrexafungerp tablet, film coated SCYNEXIS, INC. HIGHLIGHTS OF PRESCRIBING INFORMATION, n.d.)*
- **Terkonazol**, topikal kullanılan bir triazoldür. Gebelik kategorisi ‘C’ olmakla birlikte tavşanlarda ve sıçanlarda oluşan embriotoksisite nedeniyle özellikle gebeliğin ilk 3 ayında kullanımı önerilmez. Potansiyel faydası zararlardan daha ağır basarsa 2. Ve 3. Trimesterde kullanılabilir. (*Fougera, n.d.)*
- **Vajinal borik asit**, gebelikte borik asit kullanımı zarar riski bilinmediği için kullanılmaz. Oral kullanımı ölüme neden olabilir.

Gebede Trichomonas Vajiniti

Trichomoniasis, bir protozoan olan ‘Trichomonas vaginalis’ in neden olduğu ve Dünya’da en sık görülen non-viral cinsel yolla bulaşan enfeksiyondur (CYBE). Bakteriyel vajinozis ve candida vulvovajinit ile birlikte üreme çağındaki kadınlarda vajinitin en yaygın 3 nedenini oluşturur.

Trichomonas enfeksiyonu olan kişilerin yaklaşık yüzde 70’i asemptomatik olabilir. Asemptomatik olan kişilerde pelvik inflamatuvar hastalık riskinin yanı sıra HIV ve diğer CYBE’lerin bulaşma riskini artırabilir. (Peterman TA et al., 2006)

HIV enfeksiyonu olmayan ve risk faktörleri olmayan asemptomatik kişiler için rutin tarama önerilmemektedir. CDC, HIV ile enfekte olmuş tüm kadınlarda ilk ziyaretlerinde ve yıllık olarak trichomonas taraması yapılmasını önermektedir. (Workowski KA et al., 2021) Eğer klinik semptom ve belirtiler trichomonas enfeksiyonu düşündürüyorsa tarama için endikedir.

Klasik olarak tarif edilen yeşil-sarı, köpüklü, kötü kokulu vajinal akıntı, semptomatik kadınların yüzde 10 ila 30’unda görülür. (Schwebke & Burgess, 2004) Hastaların küçük bir yüzdesinde vajinal mukoza ve/veya servikste (yani çilek serviksi veya kolpitis macularis) görülebilir. (Fouts & Kraus, 1980)

Semptomatik olsun veya olmasın gebelerde trichomonas vajiniti, erken membran rüptürü, preterm doğum ve düşük doğum ağırlıklı bebeğin doğumu gibi

olumsuz gebelik sonuçlarıyla ilişkili olduğu için tedavi edilmelidir. (Kim et al., 2020; Workowski KA et al., 2021) 2021 yılında yayınlanan 19 çalışmanın meta-analizini içeren makalede gebelikte trichomonas vajinitinin, erken doğum riskinde %27 artış (olasılık oranı [OR] 1.27, %95 CI 1.08-1.50), erken membran rüptürü riskinde %87 artış (OR 1.87, %95 CI 1.53-2.29) ve düşük doğum ağırlığı riskinde %112 artışa (OR 2.12, %95 CI 1.15-3.91) neden olduğu bulunmuştur. (Van Gerwen et al., 2021) Gebelikte Trichomonas vajinit tedavisi Tablo 6’da verilmiştir.(LIKMEZ-metronidazole oral suspension Kesin Pharma Corporation HIGHLIGHTS OF PRESCRIBING INFORMATION, n.d.; Workowski KA et al., 2021; World Health Organization, 2021)

Tablo 6 : Gebede Trichomonas Vajinit Tedavisi

Tedavi Rejimleri

Metronidazol 500 mg günde 2 kez, oral, 7 gün ^[1,2]

Metronidazol 2gr/20ml oral süspansiyon tek doz veya 2*1gr ^[3]

Metronidazol 200-250 mg günde 3 kez, oral, 7 gün ^[1,2]

1. World Health Organization. (2021). Guidelines for the management of symptomatic sexually transmitted infections.
2. Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I, ... Bolan GA. (2021). Sexually Transmitted Infections Treatment Guidelines . MMWR Recomm Rep, 70(4), 1–187
3. LIKMEZ-metronidazole oral suspension Kesin Pharma Corporation HIGHLIGHTS OF PRESCRIBING INFORMATION. (n.d.). Retrieved from <http://www.fda.gov/medwatch>

- Trichomonas enfeksiyonu tespit edilen gebelerin eşleri enfeksiyonun yeniden yayılmasını önlemek amacıyla eş zamanlı olarak tedavi edilir. Tedavide genellikle metronidazol 2 gr oral süspansiyon tek doz, Tinidazol 2 gr oral tek doz (Kawamura, 1978)veya Sekdinazol 2gr oral tek dozdan (Muzny et al., 2021)herhangi biri tercih edilir. Metronidazol 500 mg oral günde 2 kez, 7 gün boyunca kullanacak şekilde de tedavi edilebilir.(Workowski KA et al., 2021; World Health Organization, 2021)
- **Metranidazol vajinal jel**, trichomonas enfeksiyonunu tam olarak tedavi etmediği için çok fazla önerilmez. (Workowski KA et al., 2021) Gebelerde **Tinidazol** ve **Seknidazol** kullanımından da kaçınılmaktadır. (Bakınız Gebede Bakteriyel Vajinozis) (Briggs GG et al., 2011; Workowski KA et al., 2021)
- Gebe olsun veya olmasın Trichomonas vajiniti nedeniyle tedavi edilen tüm hastalar 3 hafta ile 3 ay arasında nükleik asit amplifikasyon

testleri ile tekrar test edilmelidirler. Test tekrarı bakılması için eş tedavisi olup olmaması şartı aranmamalıdır. Gebelerde yapılan bir çalışmada test tekrarında pozitiflik oranı %29 olarak bulunmuştur.(Kim et al., 2020)

Gebede Grup B Streptokok Vajiniti

Grup B streptokok (GBS) olarak bilinen *Streptococcus agalactiae*, genellikle insanların genital ve gastrointestinal sistemlerini, daha az sıklıkla çocukların ve yetişkinlerin üst solunum yollarını tutan fakültatif gram pozitif bir organizmadır. Gebe kadınlarda vajinal veya rektal kolonizasyon prevalansı %10 ile %30 arasındadır. (Campbell JR et al., 2000)

GBS, yenidoğanlarda, küçük bebeklerde, gebelerde ve immünsüpresif yetişkinlerde önemli bir hastalık nedenidir. (Frieden et al., 2009)

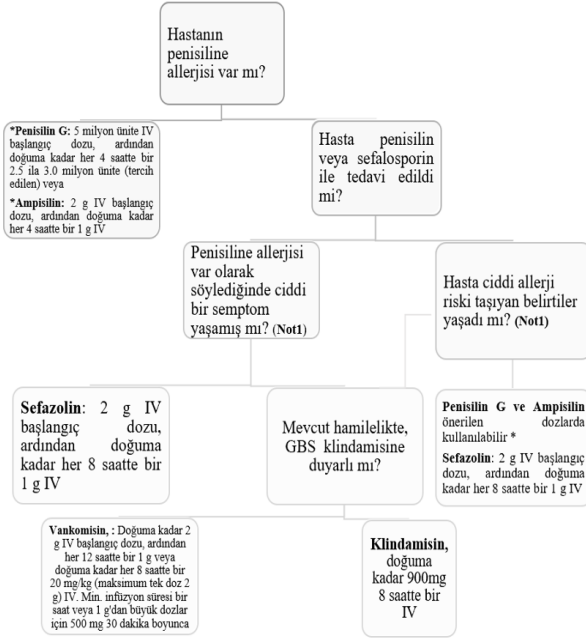
Gebelerde ve postpartum kadınlarda GBS enfeksiyonu, asemptomatik bakteriüri, sistit, piyelonefrit, sezaryen sonrası yara yeri enfeksiyonu, postpartum endometrit, pnömoni, puerperal sepsis ve bakteriyemiye neden olabilir.(Collin et al., 2019; Krohn, Hillier, & Baker, 1999; Regan et al., 1996)

GBS ile invaziv maternal enfeksiyon; abortuslar, preterm doğum ve ölü doğum ile ilişkilidir. (Seale et al., 2017; Zaleznik et al., n.d.)

GBS ile kolonize olan annelerin %50'si enfeksiyonu yenidoğana bulaştırır. Bu bulaş genellikle doğum sırasında veya membran rüptüründen sonra olur. Bulaş olan yenidoğanların yaklaşık %1-2'sinde erken başlangıçlı neonatal hastalıklar gelişecektir. GBS için profilaktik antibiyotik uygulaması yaygınlaşmadan önce annede GBS kolonizasyon varlığı koryoamniyonit ve postpartum erken enfeksiyon riskinde artışa neden olmuştur. Gebelikte GBS kolonizasyonu ile preterm eylem arasında güçlü bir ilişki vardır (Bianchi-Jassir et al., 2017). Ayrıca bazı çalışmalarda fetal GBS enfeksiyonunun üçüncü trimesterde ölü doğumlara neden olduğu gösterilmiştir.(Lamagni et al., 2022; Seale et al., 2017)

GBS'nin neden olduğu erken başlangıçlı neonatal hastalıkların önlenmesi için vajinal-rektal kültür ile evrensel prenatal tarama ve gerekli durumda intrapartum antibiyotik profilaksisinin uygun şekilde uygulanması gerekmektedir. ACOG, 36 0/7 ile 37 6/7 gebelik haftaları arasında evrensel GBS taraması yapılmasını önermektedir. Hastada negatif GBS var fakat testin üzerinden 5 hafta geçtiyse GBS rektovajinal kültür taraması tekrarlanmalıdır. (ACOG COMMITTEE OPINION, 2020)

Gebeliğin 36 0/7–37 6/7 haftasında vajinal-rektal kültürleri GBS için pozitif olan tüm kadınlar uygun intrapartum antibiyotik profilaksisi almalıdır. Membran bütünlüğü olan sezaryen ile doğum yapacak gebelere profilaksi başlanmayabilir. GBS'ler, penisilin G, ampisilin, geniş spektrumlu penisilinler, sefalosporinler ve vankomisine duyarlıdır, ancak penisilin G, in vitro olarak en aktif ve dar spektrumlu ajandır.(Kobayashi et al., 2021) İntrapartum antibiyotik profilaksisi, doğumdan en az dört saat önce uygulanırsa en etkilidir. Ancak doğum ile antibiyotik uygulama süresi arasında 4 saati sağlamak için acil obstetrik girişimler geciktirilmemelidir. (Turrentine, Greisinger, Brown, Wehmanen, & Mouzoon, 2013)



NOT1: İlaç maruziyetinden sonraki bir ila altı saat içinde ortaya çıkan aşağıdaki belirtilerden biri veya daha fazlası, ciddi bir anı (IgE aracılı) alerji riski taşıdığını gösterir: Anafilaksi, Hipotansiyon, Anjiyoödem, Solunum sıkıntısı, Ürtiker, Larinks ödemi, Pruritus veya kızarma (ürtiker veya yukarıdaki diğer belirtilerle birlikte)

NOT2: İlaç maruziyetinden sonra ortaya çıkan aşağıdaki belirtiler düşük alerji riski ve hafif reaksiyonları içerir: İzole mide bulantısı, Kusma, Baş ağrısı, Hafif pruritus, Sistemik belirtiler olmadan nonürtikelyal rash

Şekil 1: GBS'ye karşı İntrapartum Profilaktik Antibiyotik Seçimi (ACOG COMMITTEE OPINION, 2020)

Sonuç

Gebelerde vajinal enfeksiyonların çoğunun asemptomatik seyretmesi, kadınların vajinal muayeneden çekinmesi veya gebelikte artan vajinal akıntının fizyolojik sayılması nedeniyle atlanan vajinitler, bazı gebelerde preterm eyleme neden olabilirler. Kiss ve arkadaşları yaptıkları çalışma sonucunda ikinci trimesterin erken dönemlerinde tarama ve tedavi programının rutin doğum öncesi bakıma dahil edilmesiyle spontan preterm doğum oranını % 50 oranında azalttığını öne sürmüşlerdir.(Kiss, Petricevic, & Husslein, 2004) Yine yapılan birçok çalışma gebelerde vajinal enfeksiyonların taranarak tedavi edilmesiyle preterm doğumların azaldığını göstermiştir.(Lamont RF et al., 2003; McDonald HM et al., 1997; McGregor et al., 1995; Morales et al., 1994; Ugwumadu A et al., 2003)

Preterm doğum ile vajinal enfeksiyonlar arasındaki ilişkiyi değerlendirebilmek için daha fazla çalışma yapılması gerekmektedir. Literatürde vajinitin preterm eyleme neden olmadığını ve rutin tarama yapılmasına gerek olmadığı yönünde düşünceler de vardır. Ancak bizler preterm eylem nedeniyle hastanemizde yatan gebelerin birçoğunda asemptomatik vajinitin mevcut olduğunu gördük ve vajinal mikrobiyomun hem gebenin hem de bebeğin sağlığı için önemli olduğunu düşünüyoruz. Gebeliğin 1. veya 2.trimesterinde vajinal mikrobiyomun değerlendirilmesi ve gerekiyorsa vajinal enfeksiyonların tedavi edilmesi gerekmektedir. Kadınlara, bağlı oldukları Aile Sağlığı Merkezleri tarafından gebelik öncesi bakım programı kapsamında vajinal mikrobiyomu koruyan beslenme önerileri, hijyen uygulamaları gibi konularda eğitim verilmelidir. Gebelikte vajinal mikrobiyota sağlığının korunması preterm eylemin önlenmesinde önemli bir rol oynayabilir. Preterm eylemin azalması bebekte prematüritenin getirdiği maliyetleri de önemli ölçüde azaltacaktır.

KAYNAKÇA

- ACOG COMMITTEE OPINION. (2020). Prevention of Group B Streptococcal Early-Onset Disease in Newborns. *Obstetrics & Gynecology*, 135(2), e51–e72. Retrieved from <https://doi.org/10.1097/AOG.0000000000003668>
- Aguin, T. J., & Sobel, J. D. (2015). Vulvovaginal Candidiasis in Pregnancy. *Current Infectious Disease Reports*, 17(6), 30. Retrieved from <https://doi.org/10.1007/s11908-015-0462-0>
- American College of Obstetricians and Gynecologists. (2012). Practice bulletin no. 130: prediction and prevention of preterm birth. *Obstet Gynecol*, 120(4), 964–973.
- Bérard, A., Sheehy, O., Zhao, J.-P., Gorgui, J., Bernatsky, S., de Moura, C. S., & Abrahamowicz, M. (2019). Associations between low- and high-dose oral fluconazole and pregnancy outcomes: 3 nested case–control studies. *Canadian Medical Association Journal*, 191(7), E179–E187. Retrieved from <https://doi.org/10.1503/cmaj.180963>
- Bianchi-Jassir, F., Seale, A. C., Kohli-Lynch, M., Lawn, J. E., Baker, C. J., Bartlett, L., ... Rubens, C. E. (2017). Preterm Birth Associated with Group B Streptococcus Maternal Colonization Worldwide: Systematic Review and Meta-analyses. *Clinical Infectious Diseases*. Oxford University Press. Retrieved from <https://doi.org/10.1093/cid/cix661>
- Bretelle, F., Loubière, S., Desbriere, R., Loundou, A., Blanc, J., Heckenroth, H., ... Fenollar, F. (2023). Effectiveness and Costs of Molecular Screening and Treatment for Bacterial Vaginosis to Prevent Preterm Birth: The Au-Top Randomized Clinical Trial. *JAMA Pediatrics*, 177(9), 894–902. Retrieved from <https://doi.org/10.1001/jamapediatrics.2023.2250>
- BREXAFEMME-ibrexafungerp tablet, film coated SCYNEXIS, INC. HIGHLIGHTS OF PRESCRIBING INFORMATION. (n.d.). Retrieved from www.fda.gov/medwatch.
- Briggs GG, Freeman RK, & Yaffe SJ. (2011). *Drugs in pregnancy and lactation: a reference guide to fetal and neonatal risk*. . Lippincott Williams & Wilkins.
- Campbell JR, Hillier SL, Krohn MA, Ferrieri P, Zaleznik DF, & Baker CJ. (2000). Group B streptococcal colonization and serotype-specific immunity in pregnant women at delivery. *Obstet Gynecol*, 96, 498–503.
- Collin, S. M., Shetty, N., Guy, R., Nyaga, V. N., Bull, A., Richards, M. J., ... Lamagni, T. (2019). Group B Streptococcus in surgical site and non-invasive bacterial infections worldwide: A systematic review and meta-analysis. *International Journal of Infectious Diseases*, 83, 116–129. Retrieved from <https://doi.org/10.1016/j.ijid.2019.04.017>

- Cotch, M. F., Hillier, S. L., Gibbs, R. S., Eschenbach, D. A., Yaffe, S. J., Catz, C. S., ... Poole, W. K. (1998). Epidemiology and outcomes associated with moderate to heavy *Candida* colonization during pregnancy. *American Journal of Obstetrics and Gynecology*, 178(2), 374–380. Retrieved 8 September 2024 from [https://doi.org/10.1016/S0002-9378\(98\)80028-8](https://doi.org/10.1016/S0002-9378(98)80028-8)
- Dagklis, T., Akolekar, R., Villalain, C., Tsakiridis, I., Kesrouani, A., Tekay, A., ... Sen, C. (2023). Management of preterm labor: Clinical practice guideline and recommendation by the WAPM-World Association of Perinatal Medicine and the PMF-Perinatal Medicine Foundation. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 291, 196–205. Retrieved 2 September 2024 from <https://doi.org/10.1016/J.EJOGRB.2023.10.013>
- Farr, A., Effendy, I., Tirri, B. F., Hof, H., Mayser, P., Petricevic, L., ... Mendling, W. (2021). Vulvovaginal Candidosis (Excluding Mucocutaneous Candidosis): Guideline of the German (DGGG), Austrian (OEGGG) and Swiss (SGGG) Society of Gynecology and Obstetrics (S2k-Level, AWMF Registry Number 015/072, September 2020). *Geburtshilfe Und Frauenheilkunde*, 81(4), 398–421. Retrieved from <https://doi.org/10.1055/a-1345-8793>
- Fougera, E. (n.d.). *TERCONAZOLE-terconazole cream*.
- Fouts, A. C., & Kraus, S. J. (1980). *Trichomonas vaginalis*: Reevaluation of Its Clinical Presentation and Laboratory Diagnosis. *Journal of Infectious Diseases*, 141(2), 137–143. Retrieved from <https://doi.org/10.1093/infdis/141.2.137>
- Frieden, T. R., Director Harold Jaffe, M. W., Stephens, J. W., Thacker, S. B., Spriggs Terraye M Starr, S. R., Doan, Q. M., ... John Ward, G. W. (2009). *Morbidity and Mortality Weekly Report Prevention of Perinatal Group B Streptococcal Disease*. Retrieved from www.cdc.gov/mmwr/cme/conted.html
- Haque, M. M., Merchant, M., Kumar, P. N., Dutta, A., & Mande, S. S. (2017). First-trimester vaginal microbiome diversity: A potential indicator of preterm delivery risk. *Scientific Reports*, 7(1). Retrieved from <https://doi.org/10.1038/s41598-017-16352-y>
- Ison CA, & Hay PE. (2002). Validation of a simplified grading of Gram stained vaginal smears for use in genitourinary medicine clinics. *Sex Transm Infect*, 78(6), 413.
- Kawamura, N. (1978). Metronidazole and tinidazole in a single large dose for treating urogenital infections with *Trichomonas vaginalis* in men. *Sexually Transmitted Infections*, 54(2), 81–83. Retrieved from <https://doi.org/10.1136/sti.54.2.81>

- Kim, T. G., Young, M. R., Goggins, E. R., Williams, R. E., HogenEsch, E., Workowski, K. A., ... Haddad, L. B. (2020). *Trichomonas vaginalis* in Pregnancy. *Obstetrics & Gynecology*, 135(5), 1136–1144. Retrieved from <https://doi.org/10.1097/AOG.0000000000003776>
- Kiss, H., Petricevic, L., & Husslein, P. (2004). Papers Prospective randomised controlled trial of an infection screening programme to reduce the rate of preterm delivery. Retrieved from <https://doi.org/10.1136/bmj.3869.519653.EB>
- Klein, L. L., & Gibbs, R. S. (2004). Use of microbial cultures and antibiotics in the prevention of infection-associated preterm birth. *American Journal of Obstetrics and Gynecology*, 190(6), 1493–1502. Retrieved 2 September 2024 from <https://doi.org/10.1016/J.AJOG.2004.03.014>
- Kobayashi, M., McGee, L., Chochua, S., Apostol, M., Alden, N. B., Farley, M. M., ... Schrag, S. J. (2021). Low but Increasing Prevalence of Reduced Beta-lactam Susceptibility Among Invasive Group B Streptococcal Isolates, US Population-Based Surveillance, 1998–2018. *Open Forum Infectious Diseases*, 8(2). Retrieved from <https://doi.org/10.1093/ofid/ofaa634>
- Krohn, M. A., Hillier, S. L., & Baker, C. J. (1999). Maternal Peripartum Complications Associated with Vaginal Group B Streptococci Colonization. *The Journal of Infectious Diseases*, 179(6), 1410–1415. Retrieved from <https://doi.org/10.1086/314756>
- Lamagni, T., Wloch, C., Broughton, K., Collin, S. M., Chalker, V., Coelho, J., ... Johnson, A. P. (2022). Assessing the added value of group B Streptococcus maternal immunisation in preventing maternal infection and fetal harm: population surveillance study. *BJOG: An International Journal of Obstetrics and Gynaecology*, 129(2), 233–240. Retrieved from <https://doi.org/10.1111/1471-0528.16852>
- Lamont RF, Dunchan SLB, Mandal D, & Basset P. (2003). Intravaginal clindamycin to reduce preterm birth in women with abnormal genital tract flora. *Obstet Gynecol*, 101, 516–522.
- LIKMEZ-metronidazole oral suspension Kesin Pharma Corporation HIGHLIGHTS OF PRESCRIBING INFORMATION.* (n.d.). Retrieved from <http://www.fda.gov/medwatch>.
- Lockwood, C. J., Kuczynski, E., & Kuczynski, E. (2001). *Risk stratification and pathological mechanisms in preterm delivery. Paediatric and Perinatal Epidemiology* (Vol. 15).
- Lopez-Rangel, E., & Van Allen, M. I. (2005). Prenatal exposure to fluconazole: An identifiable dysmorphic phenotype. *Birth Defects Research Part A: Clinical and Molecular Teratology*, 73(11), 919–923. Retrieved from <https://doi.org/10.1002/bdra.20189>

- Maki Y, Fujisaki M, Sato Y, & Sameshima H. (2017). Candida chorioamnionitis leads to preterm birth and adverse fetal-neonatal outcome. *Infectious Diseases in Obstetrics and Gynecology*, 2017, 1–11. Retrieved from <https://doi.org/10.1155/2017/9060138>
- Mattison, D. R., Damus, K., Fiore, E., Petrini, J., & Alter, C. (2001). Preterm delivery: A public health perspective. *Paediatric and Perinatal Epidemiology*, 15(SUPPL. 2), 7–16. Retrieved from <https://doi.org/10.1046/j.1365-3016.2001.00004.x>
- McDonald HM, O’Loughlin JA, Vigneswaran R, Jolley PT, Harvey JA, Bof A, & McDonald PJ. (1997). Impact of metronidazole therapy on preterm birth in women with bacterial vaginosis flora (*Gardnerella vaginalis*): a randomised, placebo controlled trial. *Br J Obstet Gynaecol*, 104(1391).
- McGregor, J. A., French, J. I., Parker, R., Draper, D., Patterson, E., Jones, W., ... McFee, J. (1995). Prevention of premature birth by screening and treatment for common genital tract infections: Results of a prospective controlled evaluation. *American Journal of Obstetrics and Gynecology*, 173(1), 157–167. Retrieved 9 September 2024 from [https://doi.org/10.1016/0002-9378\(95\)90184-1](https://doi.org/10.1016/0002-9378(95)90184-1)
- Mølgaard-Nielsen, D., Pasternak, B., & Hviid, A. (2013). Use of Oral Fluconazole during Pregnancy and the Risk of Birth Defects. *New England Journal of Medicine*, 369(9), 830–839. Retrieved from <https://doi.org/10.1056/nejmoa1301066>
- Mølgaard-Nielsen D, Svanström H, Melbye M, Hviid A, & Pasternak B. (2016). Association between use of oral fluconazole during pregnancy and risk of spontaneous abortion and stillbirth. *Jama*, 315(1), 58–67.
- Morales, W. J., Schorr, S., & Albritton, J. (1994). Effect of metronidazole in patients with preterm birth in preceding pregnancy and bacterial vaginosis: A placebo-controlled, double-blind study. *American Journal of Obstetrics and Gynecology*, 171(2), 345–349. Retrieved 5 September 2024 from [https://doi.org/10.1016/S0002-9378\(94\)70033-8](https://doi.org/10.1016/S0002-9378(94)70033-8)
- Muzny, C. A., Schwebke, J. R., Nyirjesy, P., Kaufman, G., Mena, L. A., Lazenby, G. B., ... Chavoustie, S. E. (2021). Efficacy and Safety of Single Oral Dosing of Secnidazole for Trichomoniasis in Women: Results of a Phase 3, Randomized, Double-Blind, Placebo-Controlled, Delayed-Treatment Study. *Clinical Infectious Diseases*, 73(6), e1282–e1289. Retrieved from <https://doi.org/10.1093/cid/ciab242>
- Nelson DB, Hanlon A, Nachamkin I, Haggerty C, Mastrogianis DS, Liu C, & Fredricks DN. (2014). Early pregnancy changes in bacterial vaginosis-associated bacteria and preterm delivery. *Paediatric and Perinatal Epidemiology*, 28(2), 88–96.

- Nugent, R. P., Krohn, M. A., & Hillier, S. L. (1991). *Reliability of Diagnosing Bacterial Vaginosis Is Improved by a Standardized Method of Gram Stain Interpretation*. *JOURNAL OF CLINICAL MICROBIOLOGY* (Vol. 29). Retrieved from <https://journals.asm.org/journal/jcm>
- Nygren P, Fu R, Freeman M, Bougatsos C, Klebanoff M, & Guise J-M. (2008). Evidence on the Benefits and Harms of Screening and Treating Pregnant Women Who Are Asymptomatic for Bacterial Vaginosis: An Update Review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*, 148(3).
- Ohn, J., Auth, C. H., Obert, R., Oldenberg, L. G., Ndrews, I. W. A., Ard, A. B. D. U. B., ... Oppen, L. C. (1995). *REDUCED INCIDENCE OF PRETERM DELIVERY WITH METRONIDAZOLE AND ERYTHROMYCIN IN WOMEN WITH BACTERIAL VAGINOSIS*.
- Paavonen JA, & Brunham RC. (2020). Vaginitis in Nonpregnant Patients: ACOG Practice Bulletin, Number 215. *Obstet Gynecol*, 135(1).
- Peterman TA, Tian LH, Metcalf CA, Satterwhite CL, Malotte, C., DeAugustine N, ... Douglas JM. (2006). High incidence of new sexually transmitted infections in the year following a sexually transmitted infection: a case for rescreening. *Annals of Internal Medicine*, 145(8), 564–572.
- Regan, J. A., Klebanoff, M. A., Nugent, R. P., Eschenbach, D. A., Blackwelder, W. C., Lou, Y., ... Edelman, R. (1996). Colonization with group B streptococci in pregnancy and adverse outcome. *American Journal of Obstetrics and Gynecology*, 174(4), 1354–1360. Retrieved from [https://doi.org/10.1016/S0002-9378\(96\)70684-1](https://doi.org/10.1016/S0002-9378(96)70684-1)
- Robinson, J. N., & Norwitz, E. R. (2023). Spontaneous preterm birth: Overview of risk factors and prognosis.
- Schwebke, J. R., & Burgess, D. (2004, October). Trichomoniasis. *Clinical Microbiology Reviews*. Retrieved from <https://doi.org/10.1128/CMR.17.4.794-803.2004>
- Seale, A. C., Bianchi-Jassir, F., Russell, N. J., Kohli-Lynch, M., Tann, C. J., Hall, J., ... Lawn, J. E. (2017). Estimates of the Burden of Group B Streptococcal Disease Worldwide for Pregnant Women, Stillbirths, and Children. *Clinical Infectious Diseases*, 65, S200–S219. Retrieved from <https://doi.org/10.1093/cid/cix664>
- Sheehy O, Santos F, Ferreira E, & Bérard A. (2015). The use of metronidazole during pregnancy: a review of evidence. *Current Drug Safety*, 10(2), 170–179.
- Sobel JD. (2007). *Vulvovaginal candidosis* (9577th ed., Vol. 369). Lancet.

- Turrentine, M. A., Greisinger, A. J., Brown, K. S., Wehmanen, O. A., & Mouzoon, M. E. (2013). Duration of Intrapartum Antibiotics for Group B Streptococcus on the Diagnosis of Clinical Neonatal Sepsis. *Infectious Diseases in Obstetrics and Gynecology*, 2013, 1–6. Retrieved from <https://doi.org/10.1155/2013/525878>
- Ugwumadu A, Manyonda I, Ried F, & Hay P. (2003). Effect of early oral clindamycin on late miscarriage and preterm delivery in asymptomatic women with abnormal vaginal flora and bacterial vaginosis: a randomised controlled trial. In *Lancet* (Vol. 361, pp. 983–988).
- US Preventive Services Task Force. (2020). Screening for Bacterial Vaginosis in Pregnant Persons to Prevent Preterm Delivery: US Preventive Services Task Force Recommendation Statement. *Obstetrical & Gynecological Survey*, 75(9), 537–538.
- Van Gerwen, O., Craig-Kuhn, M., Jones, A., Schroeder, J., Deaver, J., Buckens, P., ... Muzny, C. (2021). Trichomoniasis and adverse birth outcomes: a systematic review and meta-analysis. *BJOG: An International Journal of Obstetrics & Gynaecology*, 128(12), 1907–1915. Retrieved from <https://doi.org/10.1111/1471-0528.16774>
- VIVJOA-oteseconazole capsule Mycovia Pharmaceuticals, Inc. HIGHLIGHTS OF PRESCRIBING INFORMATION. (n.d.). Retrieved from www.fda.gov/medwatch.
- Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I, ... Bolan GA. (2021). Sexually Transmitted Infections Treatment Guidelines . *MMWR Recomm Rep*, 70(4), 1–187.
- Workowski KA, & Bolan GA. (2015). Centers for Disease Control and Prevention Sexually Transmitted Disease Treatment Guidelines. *MMWR Recomm Rep*, 64(1).
- World Health Organization. (2021). Guidelines for the management of symptomatic sexually transmitted infections.
- Young, G., & Jewell, D. (2001). Topical treatment for vaginal candidiasis (thrush) in pregnancy. *Cochrane Database of Systematic Reviews*. Retrieved from <https://doi.org/10.1002/14651858.CD000225>
- Yurttaş Akar BÇ. (2020). BİR AİLE SAĞLIĞI MERKEZİ'NE KAYITLI 15-49 YAŞ KADINLAR ARASINDA VAJİNİT PREVALANSI VE ETKİLEYEN FAKTÖRLERİN BELİRLENMESİ PREVALENCE OF VAGINITIS AMONG 15-49 AGE WOMEN REGISTERED IN A FAMILY HEALTH CENTER. *Yurttaş Akar* (Vol. 3).
- Zaleznik, D. F., Rench, M. A., Hillier, S., Krohn, M. A., Platt, R., Lee, M.-L. T., ... Baker, C. J. (n.d.). *Invasive Disease Due to Group B Streptococcus in Pregnant Women and Neonates from Diverse Population Groups*. Retrieved from <https://academic.oup.com/cid/article/30/2/276/378753>

Zhu, Y., Bateman, B. T., Gray, K. J., Hernandez-Diaz, S., Mogun, H., Straub, L., & Huybrechts, K. F. (2020). Oral fluconazole use in the first trimester and risk of congenital malformations: population based cohort study. *BMJ*, m1494. Retrieved from <https://doi.org/10.1136/bmj.m1494>



Bölüm 3

Myoma Uteri ile İlişkili Kanamalarda ve Myomektomide Hemostaz Teknikleri

Yakup Baykuş¹ & .Rulin Deniz²

¹ Doç. Dr. Bandırma Onyedi Üniversitesi Tıp Fakültesi, ORCID: 0000-0001-5730-8477

² Doç. Dr. Bandırma Onyedi Üniversitesi Tıp Fakültesi, ORCID: 0000-0002-7306-8212

1. GİRİŞ

Uterus myomları genetik olarak 7, 12, 14. kromozomlarda bulunan genlerin delesyonu veya translokasyonu sonucu, myometrial hücrelerin monoklonal ekspresyonu ile oluşan benign tümörlerdir (Luciano, 2009). Uterus myomları için leiomyom, fibrom, fibromyom ve fibroid gibi isimlendirmeler de kullanılmaktadır. Kadınlarda en sık görülen pelvik tümörler olup üreme çağındaki kadınların yaklaşık %20-40'ında görülmektedir (Solomon, 2005). Myomların çoğu rutin bir pelvik muayene veya görüntüleme çalışmaları sırasında tesadüfen keşfedilir. Myomların tanısında Transvajinal Ultrasonografi altın standarttır ve sensitivitesi %90-99 civarındadır. Submuköz myomlarda Salin İnfüzyon Sonografi ve Diagnostik Histeroskopi tanıya yardımcı yöntemlerdir. MRI inceleme; tanıda sık kullanılır, myomların sayısı, büyüklüğü, yeri, damarsal yapıları hakkında ayrıntılı bilgi verir. Son yıllarda bu görüntüleme yöntemlerinin daha yaygın kullanılması, kullanılan yöntemlerin duyarlılıklarının ve özgüllüklerinin artışı gibi nedenlerle myom tanısı da önemli ölçüde artmıştır. Myom sıklığı yaşa, kalıtıma ve muhtemelen vücut kitle indeksine göre de değişmektedir.

Myomların çoğunluğu asemptomatiktir. Tedavisiz takip edilebilir. Ancak anemiye sebep olan anormal uterin kanamalar, pelvik ağrı, ureter, mesane, rektuma olan bası semptomları, hızlı büyüme, infertiliteye neden olması durumlarında sıklıkla tedavi gerekir (Vilos, 2015). Tedavide medikal tedavi, cerrahi tedavi, uterin arter embolizasyonu veya miyoliz gibi seçenekler kullanılabilir. Medikal tedavi, günümüzde genellikle preoperatif kanamanın azaltılması ve myom boyutunun küçültülmesi ile sınırlıdır. Cerrahi tedavi, medikal tedaviye yanıtız uterin kanamalar, pelvik ağrı ve bası semptomları, infertilite ve yaşam kalitesini bozan üriner inkontinans gibi şikâyetleri olan hastalarda tercih edilmektedir (Koçak, 2008; Parker, 2006). Myomların özelliklerine, yerleşim yerine, sayı ve büyüklüğüne bağlı olarak laparoskopik, histeroskopik, robotik veya laparotomik cerrahi yaklaşımlar seçilebilir. Submukozal ve intrakaviter myomlar genellikle Histeroskopi kullanılarak opere edilirken, subserozal myomlara genellikle Laparoskopi ile yaklaşılr. Buna karşılık, 4 cm altındaki intramural myomlar cerrahın deneyimine bağlı olarak Histeroskopi veya Laparoskopi ile opere edilebilirler (Carranza-Mamane, 2015).

Çalışmalar, myomektomi ile ilgili komplikasyonların son yıllarda arttığını göstermektedir (Altgassen, 2006). Günümüzde doğum yaşının ileri yaşlara

ötenilmesi, myom varlığına bağlı embriyo implantasyon potansiyelini azaltmakta ve dolayısıyla infertilite sıklığını artırmaktadır. İlerleyen yaşla birlikte myomların sayısında ve boyutlarındaki artış sıklığı aynı yaş grubunda artmaktadır. Fertilitesini korumak veya devam ettirmek isteyen üreme çağındaki kadınlarda Laparoskopik myomektomi tercih edilen cerrahi tedavi seçeneğidir. İnfertilite nedeniyle myomektomi sayısındaki bu artış komplikasyonların artışıyla ilişkili olabilir. Diğer bir sebep ise laparoskopik sütür ve elektromekanik morselasyon konusunda yeterli eğitim alınmadan yapılan myomektomilere bağlanabilir (Tanos, 2016). Laparoskopi konusunda deneyimli bir cerrah tarafından ve titizlikle seçilmiş hastalarla gerçekleştirilen Laparoskopik myomektominin açık cerrahiden daha iyi bir seçim olduğu belirtilmektedir (Jin, 2009). Cerrahi seçenek olarak laparoskopinin laparotomiye oranla daha az hastanede kalma süresi, daha az postoperatif ağrı, daha az intraoperatif kan kaybı, daha hızlı iyileşme, daha az adezyon oluşumu gibi bilinen üstünlükleri vardır (Tanos, 2018).

Laparoskopik myomektomi sırasında ve sonrasındaki en önemli komplikasyonlardan birisi kan kaybıdır. Bu kanamalar, damar yaralanmaları, cerrahın deneyimsizliği, kötü hemostaz, uygunsuz sütürasyon ve myomların kendi özellikleri dahil olmak üzere çok çeşitli nedenlerden kaynaklanabilir. Myomektomiyle ilişkili kanamalar operasyonu önemli ölçüde karmaşıktırabilir. Kan kaybı, transfüzyon oranının artmasına, morbidite ve hatta mortaliteye neden olabilmektedir. Cerrahi sırasında ve sonrasında kanama riskini azaltmada günümüzde birçok yöntem kullanılabilmektedir. Bunlar; uterus hacmini ve myom boyutunu küçültmek için kullanılan preoperatif farmakolojik ajanlar, perioperatif uygulanan farmakolojik ajanlar ve yine uterin arterin ligasyonu veya embolizasyonu gibi kan kaybını azaltmaya yönelik cerrahi yaklaşımlardır (Koçak, 2008). Myomlarla ilişkili kanamalarda tedavide preoperatif, intraoperatif, postoperatif kullanılan medikal ve cerrahi hemostaz teknikleri aşağıda incelenmiştir.

2. MEDİKAL TEDAVİLER

2.1 Hormonal Kontraseptifler

Cerrahi tedaviyi kabul etmeyen fertilite arzusu olmayan anormal uterin kanamalı olgularda seçenektir. Tedavide amaç; kanamayı kontrol altına almak, sonrasındaki kronik uterin kanamaları önlemek, anemiden ve gereksiz cerrahi müdahalelerden korumak ve kadının yaşam kalitesini artırmaktır. Bu tedavi grubu kombine oral kontraseptif ilaçları ve levonorgestrelli rahim içi aracı (LNG-RİA) içerir.

Kombine oral kontraseptifler semptomatik myomlara bağı anormal uterin kanamanın tedavisinde yaygın olarak kullanılmaktadır. Kombine oral kontraseptiflerdeki progestin komponenti, ovulasyon süpresyonu sağlar ve ovaryen streoidogenezisi inhibe ederek endometrial atrofi yaratır. İçeriğindeki östrojen komponenti siklus kontrolü sağlar ve endometriumu destekler. Hastaların % 50-70'inde kanama miktarını azaltır.

Levonorgestrelli RİA, 52 mg 19-norprogesterel levonorgestrel içerir. Günlük 20 µgr levonorgestrel salınır. Ovulatuvar fonksiyonları etkilemez. Endometriyumda etkili yüksek progesteron etkisi nedeniyle menoraji, dismenore, pelvik ağrı gibi semptomların tedavisinde kullanılmaktadır. Aşırı menstrüel kanaması olan kadınlarda kullanıldığında, menstrüel kan akımının 3 ay sonra %83 ve 12. ayda %97 azaldığı gösterilmiştir (Kaunitz, 2009). Beş yıl boyunca hem tedavi edici hem kontrasepsiyon sağlayıcı bir seçenek olarak kullanılabilir. Levonorgestrelli RİA'nın aşırı menstrüel kanaması olan kadınlarda kullanımı FDA tarafından 2009'da onaylanmıştır. Sistemik etkilerinin olmaması ve yan etki profilinin düşük olması nedeniyle günümüzde anormal uterin kanamalı olgularda önerilen hormonal bir tedavi yöntemidir (ACOG, 2008). Kullanımıyla myom çapının küçülmesi arasındaki veriler ise çelişkilidir.

2.2 GnRH Agonist (Leuprolid) ve GNRH Antagonistleri (Cetrotide, Orgolutran)

Bu ajanlar, gonadal hormon üretimini azaltmak için hipofiz bezine etki ederek çalışır. Böylece myomun hormonla uyarılan büyümesini azaltır, myom boyutunu ve kanlanması azaltır. Friedman ve ark. tarafınca yapılan bir çalışmada GnRH agonisti tedavisinin 24. haftasında uterus boyutunda %45 oranında azalma olduğu ve tedavinin kesilmesinden 24 hafta sonra tedavi öncesi boyutuna dönüldüğü gösterilmiştir (Friedman, 1991). GnRH agonisti ile uzun süreli tedavinin osteopeni, osteoporoza neden olabileceği unutulmamalıdır. Bu nedenle Amerikan Kadın Doğum Uzmanları ve Jinekologlar Koleji (ACOG), kullanımının 6 ay veya daha kısa bir süre ile sınırlandırılmasını önermektedir (ACOG, 2008; Surrey, 2002). Bu nedenle anemi dışında rutin kullanımı önerilmemektedir. Ayrıca GnRH agonisti tedavisi sonrasında yapılacak myomektomi cerrahisinde, myom ile myometriyum arasındaki klivajın kaybolabileceği ve bu nedenle diseksiyonun zorlaşabileceği bilinmelidir.

GnRH antagonistleri de tedavide kullanılabilen ve GnRH agonistleri gibi etki eden ama etkisi daha hızlı ortaya çıkan ajanlardır. Fakat günlük enjeksiyon gerektirmeleri ve pahalı olmaları nedeniyle preoperatif rutin kullanımları önerilmemektedir. Bu ajanlarla tedavi sonrası küçülen myomların Laparoskopi

sırasında vizüalize edilememesi nedeniyle çıkarılamaması rekürrens oranı artışına neden olması gibi dezavantajları mevcuttur (Gonzalez-Barcena, 1997; Lewis, 2018).

2.3 Selektif Progesteron Reseptör Modülatörleri (SPRM) (Ulipristal Acetate)

Seçici progesteron reseptör modülatörü olan Ulipristal Asetat, estradiol düzeylerini postmenapozal düzeylere indirmeden, progesteron aktivitesini modüle eder. Myom hücreleri üzerine direk etkiyle proapoptotik ve antiproliferatif etkiler göstererek myom boyutunun küçülmesini sağlarlar. Endometrial dokuda benign ve reversible değişikliklere neden olarak endometriuma direk etkiyle kanamayı azaltır. Hipofize direk etkiyle ovulasyonu inhibe ederler (Donnez, 2016; Yousuf, 2023).

Kısa süreli (3 ay) kullanımıyla ilgili randomize klinik çalışmalar Ulipristal Asetat'ın myomları küçülttüğünü ve kanamayı kontrol altına aldığını göstermektedir. Tedavinin kesilmesinin ardından menstrüasyon genellikle 4-5 haftada geri döner ancak myom hacminin küçülmesi 6 ay devam edebilir. Tedaviyle hastaların yarısından fazlasında myomların hacmini yarı yarıya azaltmıştır. Aynı zamanda hastalarda myom ilişkili ağrı ve güvenlik endişesi duyulmadan yaşam kalitesinde belirgin iyileşme sağladığı bildirilmektedir. Günlük tek doz Ulipristal Asetat (5 mg) Kanada'da ve Avrupa'da preoperatif myom tedavisinde kabul görmüştür. Aralıklı olarak 12 haftalık Ulipristal Asetat tedavisi myomların uzun dönem medikal tedavisinde potansiyel bir seçenektir (Donnez, 2016; Yousuf, 2023).

2.4 Perioperatif Farmakolojik Ajanlar

Myomektomi esnasındaki kan kaybının azaltılmasıyla ilgili olarak son yıllarda çeşitli perioperatif farmakolojik ajanların etkinliğini araştıran çalışmalar yapılmaktadır. Uterotoniklerin, antifibrinolitik ajanların ve vazokonstrüktif ajanların myomektomi operasyonu sırasında kullanılmasıyla intraoperatif kan kaybını ve kan transfüzyonu ihtiyacını önemli ölçüde azalttığını bildiren çalışmalar vardır. Ancak günümüzde elde edilen mevcut verilerle en iyi perioperatif farmakolojik seçeneğin hangisi olduğu konusunda kesin bir sonuca varılamamaktadır. Myomektomi esnasında kanamanın azaltılması amacıyla yapılan işlemlerin etkinliğinin bilinmesi, kanıta dayalı klinik kararların alınabilmesinin sağlaması açısından önemlidir. Konuyla ilgili Vazopressin, Ornipressin, Epinefrin, Oksitosin, Misoprostol, Traneksamik asit (TXA) ve Askorbik asit gibi farmakolojik ajanlar aşağıda incelenmiştir.

2.4.1 Vazokonstrüktörler

Vazopressin (Antidiüretik hormon) hipotalamus tarafından üretilen peptid yapıda bir hormondur. Arteriyollerin ve venüllerin duvarlarındaki düz kasları kasarak etki eder. Myomektomi esnasında; 20 IU/100 ml SF içinde intramyometrial uygulanır. Kullanımıyla bradikardi, kardiyovasküler kollaps ve ölüm vakaları görülebilir. Bu nedenle myometriyum infiltrasyonu sırasında intravasküler enjeksiyondan kaçınmak gerekir. Vasopressinin maksimum güvenli dozu tam olarak bilinmemektedir. Prosedür başına kümülatif Vazopressin dozunun üst sınırı 4 ila 6 ünite olarak önerilmektedir. Myomektomi sırasında Vazopressinin tek başına kullanımıyla Vazopressin+Misoprostol ile kullanılmasını değerlendiren bir çalışmada Vazopressinin, tek başına veya Misoprostol ile birlikte kullanıldığında kan kaybını ve kan transfüzyonu ihtiyacını azaltmada etkili olduğu bulunmuştur (Frederick, 2013).

Üç randomize kontrollü çalışma (RCT), 128 myomektomi olgusunun analizinde intramyometrik Vasopressin uygulamasıyla intraopertaif kan kaybında ve kan transfüzyonu ihtiyacında önemli azalmalar olduğu belirtilmiştir (Kongnyuy, 2014). Vazopressinin myomektomi sırasında kanamayı azaltmasıyla ilgili kanıtlar orta kalitededir. Histeroskopik myomektomi esnasında transservikal intralezyonel vazopressin enjeksiyonu plasebo grubuyla karşılaştırılan bir çalışmada da Vazopressinin sıvı intravazasyonunu, operasyon sırasındaki kan kaybını azalttığı ve görme netliğini iyileştirdiği belirtilmiştir (Wong, 2014).

Isah ve arkadaşlarının bir hemostatik ve vazopressör ajan olan Ornipressin ile yaptıkları bir çalışmada, Laparoskopik myomektomi sırasında kan kaybını azaltmada Ornipressinin rolünü değerlendirmişlerdir. Bu çalışmada Ornipressin uygulamasıyla kan transfüzyonu ihtiyacında önemli bir azalma olduğu bildirilmiştir (Isah, 2020).

Epinefrin, myomektomi sırasında kan kaybını azaltmada etkili olan başka bir vazokonstrüktördür. 1 mg/mL intramyometrial enjeksiyon şeklinde uygulanır. Epinefrinin intravasküler enjeksiyonu, vazopressine benzer şekilde akut kardiyovasküler yan etkilere neden olabilir. 1 RCT, 60 myomektomi olgusunun analizinde, intramyometrik epinefrin+bupivakain uygulamasıyla intraoperatif kan kaybında önemli azalmalar olduğu belirtilmiştir (Kongnyuy, 2014).

Vazopressin, Ornipressin, Epinefrin gibi ajanlar myomektomi sırasındaki kan kaybını azaltmak için tek başına veya diğer ilaçlarla birlikte araştırılmaya devam edilen güçlü periferik vazokonstrüktörlerdir. Aşırı vazokonstrüksiyonun

önlemesi amacıyla bazı otörler vazokonstrüktör ajanlara bupivakain eklenmesini önermektedir.

2.4.2 Uterotonikler

Oksitosin, başlıca işlevi doğum eylemi ve doğum sonrası dönemde uterus kasılmasını sağlamak olan bir hormondur. Doğum sonrası uterus atonisinin ve kanamanın önlenmesinde tercih edilen ajandır. Gebe olmayan uterusda da Oksitosin reseptörleri bulunur. Ancak bu reseptörlerin konsantrasyonu gebeliktekine göre çok daha düşük miktardadır. Bundan dolayı Oksitosinin klinik kullanımı gebelik dışında sınırlıdır. Uterotonik özelliği nedeniyle kanama riskinin çok olduğu myomektomilerde kanamanın azaltılması ve kan transfüzyonunun azaltılmasıyla ilgili bir çok çalışmaya dahil edilmiştir.

423 hastayı ve 8 çalışmayı kapsayan bir metaanalizde Laparoskopik myomektomideki kan kaybına ilişkin kanıtlar, Oksitosinin kan kaybını azalttığı (düşük kanıt) yönündedir. Bu metaanalizin Laparoskopik myomektomi alt grup analizinde Oksitosinin kan kaybını azaltmada ilk sırada yer aldığı gösterilmiştir. 1.117 hastayı ve 16 çalışmayı kapsayan bir metaanalizde açık myomektomi sırasında kan kaybına ilişkin kanıtlar, Oksitosinin kan kaybını azalttığı (düşük kanıt) yönündedir. 393 hastayı kapsayan 7 çalışmayı derleyen bir analizde Laparoskopik myomektomi sırasında Oksitosinin kan transfüzyonu ihtiyacını önemli ölçüde azalttığını göstermiştir. Tedavileri sıralama açısından, Oksitosin kan transfüzyonu ihtiyacını azaltmada ilk sırada yer almıştır (Samy, 2020).

2.4.3 Misoprostol

Prostaglandin E1 analogudur. Uterotonik ve vazokonstriktör olarak etki eder. Doğum sonrası kanamanın yönetiminde sıklıkla kullanılır. Ucuz ve uzun bir raf ömrüne sahiptir. Dünya Sağlık Örgütü tarafından temel bir ilaç olarak sınıflandırılmıştır. Gebelik dışında kullanımıyla uterusda kasılmaya neden olduğu kanıtlarıyla belirlenmiştir. Bundan dolayı myomektomi operasyonlarında kan kaybını ve kan transfüzyonu ihtiyacını azaltma potansiyeline sahiptir.

Toplam 385 hasta 8 çalışmanın dahil edildiği bir metaanalizde, açık myomektomi öncesi Misoprostol kullanımıyla, daha az kan kaybı, kan transfüzyonu ihtiyacının azalmasıyla önemli ölçüde ilişkili (orta kalitede kanıt) bulunmuştur. Bu metaanaliz, açık myomektomide Misoprostol kullanılmasının kan kaybını ve kan transfüzyonu ihtiyacını en aza indirdiğini ortaya koymuştur. Düşük maliyetli ve kolayca bulunabilmesi nedeniyle klinik sonuçların iyileştirilmesi için açık myomektomilerden önce rutin olarak uygulanması gerektiği ifade edilmiştir (Wali, 2021). Operasyon öncesi vajinal Misoprostol

kullanımıyla 89 kadının dahil edildiği başka bir metaanalizde intraoperatif kan kaybında önemli azalmalar olduğu (2 RCT, orta kalitede kanıt) belirtilmiştir (Kongnyuy, 2014).

423 hastayı kapsayan 8 çalışmayı derleyen bir metaanalizde, Laparoskopik myomektomideki kan kaybına ilişkin kanıtlar, Misoprostolün kan kaybını azalttığı (düşük kanıt) yönündedir. Laparoskopik myomektomi alt grup analizine göre Misoprostolün kan kaybını azaltmada ikinci sırada yer aldığı gösterilmiştir. 1.117 hastayı kapsayan 16 çalışmayı derleyen bir metaanalizde, açık myomektomi sırasında kan kaybına ilişkin kanıtlar, Misoprostolün kan kaybını azalttığı (düşük kanıt) yönündedir. Açık myomektominin alt grup analizine dahil edilen tedavilerin sıralama skorunda, Misoprostolün Vazopressinle kullanılması kan kaybını azaltmada ilk sırada yer almaktadır (Samy, 2020).

Prostaglandin E2 analogu olan Dinoprostunun operasyon öncesi vajinal kullanımıyla 108 kadının dahil edildiği başka bir metaanalizde intraoperatif kan kaybında azalmalar (1 RCT, düşük kalitede kanıt) olduğu belirtilmiştir (Kongnyuy, 2014).

2.4.4 Traneksamik Asit (TXA)

Lizin amino asidinin sentetik bir analogu olan TXA, plazminojen üzerine geri dönüşümlü olarak bağlanarak antifibrinolitik olarak görev yapar. Fibrinolizisi inhibe eder. Ciddi kanama riski olan ameliyatlarda ve aşırı menstruel kanama gibi çeşitli durumlarda kan kaybının önlenmesi ve tedavinde kullanılır. Ancak tromboza eğilimi olan hastalarda traneksamik asitin kullanımı kontrendikedir. Cerrahi insizyondan 20 dakika önce 10 mg/kg dozda 10 dakikada intravenöz infüze edilerek kullanılması önerilmektedir. Son zamanlardaki literatür bilgileri, myomektomi sırasında, özellikle açık cerrahide ve minimal invaziv prosedürlerde TXA'nın hemostatik ajan olarak kullanılmasını desteklemektedir.

Myomektomi sırasında intravenöz traneksamik asit kullanılan 100 kadının dahil edildiği bir çalışmada plaseboya göre intraoperatif kan kaybında azalmalar (1 RCT, düşük kaliteli kanıt) olduğu belirtilmiştir. Ancak kan transfüzyonu ihtiyacı üzerinde anlamlı bir etkisi olmadığı gösterilmiştir (Kongnyuy, 2014). Başka bir metaanalizde, açık myomektomi sırasında kan kaybına ilişkin kanıtlar, TXA'nın kan kaybını azalttığı (düşük kanıt) yönündedir (Samy, 2020).

Myomektomi öncesinde intravenöz TXA'nın kullanımını plaseboyla karşılaştıran, çift 4 kör randomize kontrollü çalışmanın metaanalizinde (310 hasta) bulgular, TXA kullanımının plaseboya kıyasla toplam tahmini kan kaybı, intraoperatif ve postoperatif kan kaybı üzerinde olumlu bir etkisi olduğunu ortaya

koymuştur. Ancak postoperatif kan transfüzyonu üzerinde olumlu bir etkisi olmadığı belirtilmiştir (Kathopoulos, 2022).

2.4.5 Askorbik asit

Myomektomi operasyonlarında Askorbik asit uygulanmasının kan kaybını azaltmasıyla ilgili sonuçlar çelişkilidir. Bir RKÇ’de hiçbir tedavi uygulanmamasına kıyasla, myomektomi sırasında askorbik asit uygulanması kan kaybını azalttığı (düşük kaliteli kanıt) ancak tedavi uygulanmayan gruba kıyasla kan transfüzyonu ihtiyacı üzerinde bir etkisi olmadığı belirtilmektedir (Kongnyuy, 2014). Anesteziden 30 dakika önce başlanarak, 2 saat boyunca intraoperatif olarak 2gr Askorbik asit uygulanarak yapılan başka bir RKÇ’de ise Laparoskopik myomektomi olgularında intravenöz Askorbik asit infüzyonunun ameliyat sırasındaki kan kaybını azaltmadığı belirtilmektedir (Lee, 2016).

Myomektomi operasyonlarında Oksitosin, Misoprostol ve TXA kullanımının kanamayı azaltabileceğine dair mevcut RCT'den elde edilen kanıtlar sınırlıdır. Myomektomi operasyonlarında kan kaybının azaltılmasında farklı hemostaz tekniklerinin etkinlikleri, güvenlikleri ve maliyetlerine ışık tutulmasını sağlamak için iyi planlanmış ve yeterli güce sahip RCT'lere ihtiyaç vardır.

3. CERRAHİ YÖNTEMLER

Myomektomi operasyonlarında kanamanın azaltılması amacıyla birçok cerrahi müdahale uygulanabilir. Bu yöntemler; mekanik turnike uygulaması, uterin arter ligasyonu, uterin arterin geçici kliplenmesi ve uterin arter embolizasyonu olarak sıralanabilir.

3.1 Mekanik Turnike Uygulaması

Myomektomi sırasında turnike uygulama prosedürleri çeşitli yöntemlerle yapılabilir. Bir teknik overlerin ve fallop tüplerinin altındaki alt uterin segmentin etrafına bir kateter (örn. Robinson kateteri, Penrose dren) yerleştirmek iken, diğer bir yöntem ise internal os seviyesinde iki taraflı küçük kesiler oluşturarak daha sonra turnike uçları öne doğru çıkacak şekilde bu kesilerden geçilerek turnike uygulanması şeklindedir. Turnikenin uyguladığı basınç uterin artere ve dallarına zarar verebilir ayrıca yetersiz hemostazı maskeleyebilir. Bu nedenle iskemiden kaçınılabilmesi için turnikenin her 20 dakikada bir serbest bırakılması öneriler arasındadır.

Daha fazla sayıda myom varlığı, daha fazla uterus kesisine ve daha fazla kan kaybına yol açar. 84 açık myomektomi uygulanan bir çalışmada turnike kullanılan ve >3 myom çıkarılan hastalarda postoperatif dönemde kan transfüzyonunun anlamlı düştüğü belirtilmiştir. Ayrıca çalışmada geçici uterin

turnike uygulamasının, özellikle vasküler yapılara yakın konumda bulunan çok sayıda, büyük boyutlu myomu olan hastalarda perioperatif kanama miktarını azaltmada etkili görüldüğü belirtilmektedir (Akbaba, 2022). 531 katılımcı ile yapılan 10 RKÇ sonuçları analiz edildiğinde, myomektomilerde turnike uygulamasıyla intraoperatif dönemde kan kaybında önemli azalma olduğunu gösterilmiştir (Kongnyuy, 2014).

Uterusun asıl kan kaynağı uterin arterdir. Uterin arter kan akımının turnikeyle kesilmesinin, uterusu kan akışını azaltarak kan kaybını azaltması beklenir. Yapılan birçok çalışmanın sonuçları beklendiği gibi bu uygulamayla intraoperatif kan kaybının azalmasıyla ilgilidir. Ancak mevcut literatür bilgilerine göre turnike uygulamasının ameliyat süresi üzerinde bir etkisi olduğuna, postoperatif morbidite üzerinde bir etkisi olduğuna ve kan kaybını azalttığına dair yeterli kanıt bulunmamaktadır. Ayrıca fertilité ve over fonksiyonu üzerindeki etkisini belirlemek için randomize prospektif çalışmalara ihtiyaç vardır.

3.2 Uterin Arterlerin Ligasyonu

Laparoskopik myomektomi esnasında hem kanamanın azaltılması hem de histerektomiye geçişin önlenmesi amacıyla uterusu besleyen damarların geçici veya kalıcı ligasyonları kullanılabilir. Bu damarların Laparoskopik yolla ligasyonu, uterin arter embolisine bir alternatif olarak tanımlanmaktadır. Laparoskopik uterin arter ligasyonu bipolar koagülasyon veya sütür ligasyonu ile kalıcı olarak veya titanyum cerrahi klipsler yerleştirilerek geçici olarak gerçekleştirilebilir. Bu yöntemlerle uterin damarların yeniden kanüle olacağından, yeni anastomozlarla uterus ve ilgili organların beslenmesinin sağlanacağından yola çıkılarak reproduktif sonuçların teorik olarak korunacağı düşünülmektedir. Ancak bu işlemler esnasında üreterlere veya çevredeki majör kan damarlarına zarar vermeden uterin arterlerin izole edilmesi iyi derecede Laparoskopik tecrübe gerektirmektedir.

Birçok çalışmada Laparoskopik myomektomide bilateral uterin arter ligasyonu uygulamasıyla, uterus kan hacminin azaldığı, intraoperatif kan kaybının azaldığı bildirilmektedir (Alborzi, 2009; Holub, 2003; Liu, 2000, Moratalla-Bartolomé, 2024). Aksine yine birçok çalışmada ve bazı metaanalizlerde intraoperatif kan kaybını azaltmadığı, postoperatif hemoglobin üzerinde ve postoperatif morbidite üzerinde bir etkisi olmadığıyla ilgilidir (Bae, 2011; Kongnyuy, 2014). Uterin arter ligasyonunun intraoperatif kan kaybını azalttığı ile ilgili kanıtlar yeterli değildir.

Myomektomi operasyonlarında kanamalar intraoperatif veya postoperatif dönemde olabilir. Büyük myomların diseksiyonuyla ilişkili fazla kan kaybı,

myomektomiye histerektomiden daha teknik olarak zor bir prosedür haline getirebilir. Bazen kanama şiddetli ve kontrol edilemez hale geldiğinde veya çok sayıda myom çıkarılmasıyla kalan uterustaki defekt nedeniyle uterusun yeniden yapılandırılması imkansız olduğunda histerektomiye geçilebilir. Günümüz literatür bilgileri bu tekniklerin, diğer hemostaz önlemleri başarısız olduğunda veya histerektomiye geçişin önlenmesi için ek hemostaz gerektiren durumlarda uygulanması yönündedir. Ayrıca reproduktif sonuçlar ve over rezervi üzerindeki etkisi konusunda iyi planlanmış uzun dönem çalışmaların yapılması gerekmektedir. Ayrıca bu prosedürlerle operasyon süresinin önemli ölçüde arttığı da bildirilmektedir. Ancak operasyon öncesinde kanama azaltıcı medikal tedavilerin uygulanması, cerrahi teknik ve deneyimin artması ve ileri Laparoskopik cerrahi aletlerin kullanıma girmesiyle bu süre kısaltılabilir ve Laparoskopiyle ilişkili perioperatif komplikasyonlar da en aza indirilebilir.

3.3 Myom Diseksiyon Teknikleri, Kesi Tipi ve Sütürasyon

Myom diseksiyon teknikleri, kimyasal diseksiyon için karbondioksit lazer ve Mesna (sodium-2-mercaptoethane sulfonate) kullanımını içerir (McLaughlin, 1985). Bu işlemler myom çıkarıldıktan sonraki uterustaki defektleri azaltma potansiyeline sahiptir. Bu tekniklerin uygulanması uterus defektleri tamirini kolaylaştırır, ancak zaman alıcı olabilirler. Myomektomi operasyonlarında Mesna kullanılmasıyla kanamanın azaltılabileceğiyle ilgili birkaç RCT'den elde edilen kanıtlar sınırlıdır. Bir RKÇ'de Mesna ile kimyasal diseksiyonda ameliyat süresinde azalma ile ilişkilendirilmiştir. Ayrıca ameliyat sonrası hemoglobin ve hematokritin mesna ile plaseboya kıyasla anlamlı derecede daha yüksek olduğu bildirilmiştir (Benassi, 2000).

Operasyon esnasındaki uterin insizyonların tipi kanama miktarı üzerinde etkili olabilir. Uterin kesiler doğrudan myomun üzerinden yapılmalıdır ve avasküler düzlem fark edilene kadar derinleştirilmelidir. Transvers insizyonlarda kesi arkuat arterlere paralel olacağından arkuat arterlerin yaralanmasının ve kanama miktarının daha az olacağı düşünülmektedir. Transvers myometrial kesiler ayrıca, uterin defektin daha ergonomik Laparoskopik sütürasyonuna olanak tanır. Midline vertikal uterin insizyonlarda ise multiple arkuat arterler kesileceğinden kanama miktarı artabilir. Ancak posterior yerleşen myomlarda myometriyum onarımı transvers kesilerde daha zordur.

Myomun eksizyonu tamamlandıktan sonra, kan kaybını azaltmak için yeterli ve hızlı cerrahi sütür tekniğinin kullanımı önemlidir. Laparoskopik myomektomide cerrahi sütürasyonda cerrahın tecrübesi de ön plana çıkmaktadır. Geleneksel olarak poliglikolik asit içeren multiflaman sütürler tercih

edilmektedir. Günümüzde ise özellikle minimal invaziv cerrahide daha hızlı s t rasyon saėlaması, d ė m atmaya gerek olmaması gibi nedenlerle daha hızlı teknik saėlayan ve dolayısıyla operasyon s resini ve kanamayı azaltan, kompresif etkisi y ksek, absorbabl, barbed s t r kullanımı yaygınlařmaktadır.

3.4 Diėer Hemostaz Teknikleri

Bazı Laparoskopik myomektomi operasyonlarında, yalnızca basın  uygulanması, elektrocerrahi veya s t rasyon hemostazı saėlamak i in yeterli veya g venli olabilir. Ancak, yaygın k   k damar kanaması veya daha b y k damarlar veya  reterler gibi hayati yapıların yakınında kanama olan durumlarda, bazı teknikler uygun olmayabilir. Bu t r durumlarda, kan kaybını azaltmak, durdurmak, termal hasarı, devask larizasyonu ve doku nekrozunu azaltmak amacıyla alternatif bir se enek olarak topikal hemostatik ajanlar kullanılabilmektedir. Pıhtılařmanın aktive edilmesinden fibrin pıhtısının stabilizasyonuna kadar pıhtılařma kaskatının bir veya daha fazla ařamasına m dahale eden bu teknikler, kanamayı durdurmak veya engellemek ve stabil bir pıhtının oluřması amacıyla kullanılmaktadır.

Bu ama la trombin ve fibrinojenle kaplanmış cerrahi kollajen yamalar kullanılabılır. İnsan pıhtılařma fakt rleri olan fibrinojen ve trombin i eren cerrahi s ngerler olan fibrin yapıřtırıcı cerrahi yamaların, myomektomi sırasında kullanımıyla ilgili bir RK 'de hi bir tedavi uygulanmamasına kıyasla, myomektomi sırasında kan kaybını azalttıėı (d ř k kalite kanıt) bildirilmiřtir. Ancak postoperatif kan transf zyonu  zerinde etkisi bulunmamıřtır (Kongnyuy, 2014). 8  alıřmanın dahil edildiėi bir analizde ise fibrin yapıřtırıcı kullanımının hemostaz s resini, postoperatif hemoglobin d ř ř n  ve kan kaybını azalttıėı ve Laparoskopik myomektomide genel operasyon s resini azalttıėı bildirilmiřtir (Ito, 2018).

Topikal hemostaz amacıyla kullanılan bir teknik olan jelatin-trombin hemostatik yapıřtırıcı kullanılarak yapılan bir RK 'de, bu matrisin uterus kesi b lgesine uygulanmasıyla, ameliyat sırasında kan kaybını ve postop kan transf zyonu ihtiya ını  nemli  l  de azalttıėı (d ř k kalite kanıt) bildirilmiřtir (Kongnyuy, 2014). Bařka bir  alıřmada ise jelatin-trombin matrisi kullanılan grup bipolar enerji grubuyla karřılařtırıldıėında, hemostaz s resinin ve ortalama kan kaybının daha az olduėu ancak bu sonu ların istatistiksel olarak anlamlı olmadıėı bildirilmiřtir (Ito, 2018).

4. SONUÇ

Semptomatik myomlu fertilite arzusu olan kadınlarda histerektomi yerine uygulanan myomektomi operasyonlarında intraoperatif ve postoperatif dönemdeki en önemli komplikasyonlardan biri kanamalardır. Preoperatif ve intraoperatif dönemde aşırı kan kaybının azaltılmasıyla ilgili tanımlanmış birçok hemostaz tekniğine rağmen kanamalar cerrahlar açısından aşılması gereken zorluk olmaya devam etmektedir. Tanımlanmış hemostaz teknikleriyle ilgili daha önce yapılan çalışmaların çoğu randomize olmayan çalışmalardır. Ayrıca bu çalışmaların çoğunda kullanılan yöntemlerle ilgili yan etkilere değinilmemiştir. Bu cerrahın en az yan etkiye sahip en etkili tekniği belirlemede zorluklara sebep olmaktadır. Günümüz literatür bilgilerine göre; Misoprostol, Dinoprostol, Vazopressin, Epinefrin, Traneksamik asit, Mesna, Askorbik asit, mekanik turnike uygulamaları, uterin arterlerin ligasyonu, topikal hemostatik yapıştırıcı yamalar gibi farmakolojik, mekanik veya cerrahi hemostaz yöntemleriyle myomektomi sırasında kanamaların azaltılabileceği yüksek kaliteli kanıtlar olmasa da gösterilmiştir. Ancak bu müdahalelerin hiçbirinin postoperatif kan transfüzyonu oranını azalttığı kanıtlanamamıştır. Myomektomilerde kan kaybının azaltılması ve kan transfüzyon oranlarıyla ilgili; farklı müdahalelerin etkinliği, güvenliği ve maliyetleri hakkında iyi kanıtlar elde edilebilmesi için iyi planlanmış ve yeterli güce sahip randomize kontrollü çalışmalara ihtiyaç bulunmaktadır.

KAYNAKLAR

- Akbaba, E., Sezgin, B., & Sivaslıoğlu, A. A. (2022). Can the application of a temporary uterine tourniquet during an abdominal myomectomy reduce bleeding?. *Journal of the Turkish German Gynecological Association*, 23(2), 111.
- Alborzi, S., Ghannadan, E., Alborzi, S., & Alborzi, M. (2009). A comparison of combined laparoscopic uterine artery ligation and myomectomy versus laparoscopic myomectomy in treatment of symptomatic myoma. *Fertility and sterility*, 92(2), 742-747.
- Altgassen, C., Kuss, S., Berger, U., Löning, M., Diedrich, K., & Schneider, A. (2006). Complications in laparoscopic myomectomy. *Surgical Endoscopy and Other Interventional Techniques*, 20, 614-618.
- American College of Obstetricians and Gynecologists. (2008). ACOG practice bulletin no. 96: alternatives to hysterectomy in the management of leiomyomas. *Obstetrics & Gynecology*, 112(2), 387-400.
- Bae, J. H., Chong, G. O., Seong, W. J., Hong, D. G., & Lee, Y. S. (2011). Benefit of uterine artery ligation in laparoscopic myomectomy. *Fertility and sterility*, 95(2), 775-778.
- Benassi, L., Lopopolo, G., Pazzoni, F., Ricci, L., Kaihura, C., Piazza, F., ... & Zini, C. (2000). Chemically assisted dissection of tissues: an interesting support in abdominal myomectomy. *Journal of the American College of Surgeons*, 191(1), 65-69.
- Carranza-Mamane, B., Havelock, J., Hemmings, R., Cheung, A., Sierra, S., Case, A., ... & Burnett, M. (2015). The management of uterine fibroids in women with otherwise unexplained infertility. *Journal of Obstetrics and Gynaecology Canada*, 37(3), 277-285.
- Donnez, J., Donnez, O., Matule, D., Ahrendt, H. J., Hudecek, R., Zatik, J., ... & Loumaye, E. (2016). Long-term medical management of uterine fibroids with ulipristal acetate. *Fertility and sterility*, 105(1), 165-173.
- Frederick, S., Frederick, J., Fletcher, H., Reid, M., Hardie, M., & Gardner, W. (2013). A trial comparing the use of rectal misoprostol plus perivascular vasopressin with perivascular vasopressin alone to decrease myometrial bleeding at the time of abdominal myomectomy. *Fertility and sterility*, 100(4), 1044-1049.
- Friedman, A. J., Hoffman, D. I., Comite, F., Browneller, R. W., & Miller, J. D. (1991). Treatment of Leiomyomata Uteri with Leuprolide Acetate Depot: A double-blind, Placebo-controlled, multicenter study. *Obstetrics & Gynecology*, 77(5), 720-725.
- Gonzalez-Barcena, D., Alvarez, R. B., Ochoa, E. P., Cornejo, I. C., Comaru-Schally, A. M., Schally, A. V., ... & Riethmüller-Winzen, H. (1997). Treatment of uterine leiomyomas with luteinizing hormone-releasing hormone antagonist Cetrorelix. *Human reproduction (Oxford, England)*, 12(9), 2028-2035.

- Holub, Z., Lukáč, J., Kliment, L., & Urbánek, Š. (2003). Short-term results from laparoscopic dissection of uterine vessels in women with symptomatic fibroids. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 110(1), 94-98.
- Isah, A. D., Agida, E. T., & Isah, A. Y. (2020). Intramyometrial vasopressin for reducing blood loss at myomectomy. *Annals of Medical and Health Sciences Research| Volume*, 10(2).
- Ito, T. E., Martin, A. L., Henderson, E. F., Gaskins, J. T., Vaughn, V. M., Biscette, S. M., & Pasic, R. P. (2018). Systematic review of topical hemostatic agent use in minimally invasive gynecologic surgery. *JSLs: Journal of the Society of Laparoendoscopic Surgeons*, 22(4).
- Jin, C., Hu, Y., Chen, X. C., Zheng, F. Y., Lin, F., Zhou, K., & Gu, H. Z. (2009). Laparoscopic versus open myomectomy—a meta-analysis of randomized controlled trials. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 145(1), 14-21.
- Kathopoulis, N., Prodromidou, A., Zacharakis, D., Chatzipapas, I., Diakosavvas, M., Kypriotis, K., ... & Protopapas, A. (2022). The effect of intravenous tranexamic acid on myomectomy: a systematic review and meta-analysis of randomized controlled trials. *Journal of Personalized Medicine*, 12(9), 1492.
- Kaunitz, A. M., Meredith, S., Inki, P., Kubba, A., & Sanchez-Ramos, L. (2009). Levonorgestrel-releasing intrauterine system and endometrial ablation in heavy menstrual bleeding: a systematic review and meta-analysis. *Obstetrics & Gynecology*, 113(5), 1104-1116.
- Koçak, İ., Üstün, C., Çakıroğlu H., & Güven, D. (2008). Laparoskopik Myomektomi ve Myoliz. *Türkiye Klinikleri Gynecology Obstetrics-Special Topics*, 1(6), 31-35.
- Kongnyuy, E. J., & Wiysonge, C. S. (2014). Interventions to reduce haemorrhage during myomectomy for fibroids. *Cochrane database of systematic reviews*, (8).
- Luciano, A. A. (2009). Myomectomy. *Clinical obstetrics and gynecology*, 52(3), 362-371.
- Lee, B., Kim, K., Cho, H. Y., Yang, E. J., Suh, D. H., No, J. H., ... & Kim, Y. B. (2016). Effect of intravenous ascorbic acid infusion on blood loss during laparoscopic myomectomy: a randomized, double-blind, placebo-controlled trial. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 199, 187-191.
- Lewis, T. D., Malik, M., Britten, J., San Pablo, A. M., & Catherino, W. H. (2018). A comprehensive review of the pharmacologic management of uterine leiomyoma. *BioMed research international*, 2018(1), 2414609.
- Liu, W. M. (2000). Laparoscopic bipolar coagulation of uterine vessels to treat symptomatic leiomyomas. *The Journal of the American Association of Gynecologic Laparoscopists*, 7(1), 125-129.

- McLaughlin, D. S. (1985). Metroplasty and myomectomy with the CO2 laser for maximizing the preservation of normal tissue and minimizing blood loss. *The Journal of Reproductive Medicine*, 30(1), 1-9.
- Moratalla-Bartolomé, E., Lázaro-de-la-Fuente, J., López-Carrasco, I., Cabezas-López, E., Carugno, J., Sancho-Sauco, J., & Pelayo-Delgado, I. (2024). Surgical impact of bilateral transient occlusion of uterine and utero-ovarian arteries during laparoscopic myomectomy. *Scientific Reports*, 14(1), 7044.
- Parker, W. H. (2006). Laparoscopic myomectomy and abdominal myomectomy. *Clinical obstetrics and gynecology*, 49(4), 789-797.
- Samy, A., Raslan, A. N., Talaat, B., El Lithy, A., El Sharkawy, M., Sharaf, M. F., ... & Metwally, A. A. (2020). Perioperative nonhormonal pharmacological interventions for bleeding reduction during open and minimally invasive myomectomy: a systematic review and network meta-analysis. *Fertility and sterility*, 113(1), 224-233.
- Solomon, L. A., Schimp, V. L., Ali-Fehmi, R., Diamond, M. P., & Munkarah, A. R. (2005). Clinical update of smooth muscle tumors of the uterus. *Journal of Minimally Invasive Gynecology*, 12(5), 401-408.
- Surrey, E. S., Hornstein, M. D., & Add-Back Study Group. (2002). Prolonged GnRH agonist and add-back therapy for symptomatic endometriosis: long-term follow-up. *Obstetrics & Gynecology*, 99(5), 709-719.
- Tanos, V., Socolov, R., Demetriou, P., Kyprianou, M., Watrelot, A., Van Belle, Y., & Campo, R. (2016). Implementation of minimal invasive gynaecological surgery certification will challenge gynaecologists with new legal and ethical issues. *Facts, Views & Vision in Obgyn*, 8(2), 111.
- Tanos, V., Berry, K. E., Frist, M., Campo, R., & DeWilde, R. L. (2018). Prevention and management of complications in laparoscopic myomectomy. *BioMed research international*, 2018(1), 8250952.
- Vilos, G. A., Allaire, C., Laberge, P. Y., Leyland, N., Vilos, A. G., Murji, A., & Chen, I. (2015). The management of uterine leiomyomas. *Journal of Obstetrics and Gynaecology Canada*, 37(2), 157-178.
- Wali, S., Balfoussia, D., Touqmatchi, D., & Quinn, S. (2021). Misoprostol for open myomectomy: a systematic review and meta-analysis of randomised control trials. *BJOG: An International Journal of Obstetrics & Gynaecology*, 128(3), 476-483.
- Wong, A. S. W., Cheung, C. W., Yeung, S. W., Fan, H. L., Leung, T. Y., & Sahota, D. S. (2014). Transcervical intralesional vasopressin injection compared with placebo in hysteroscopic myomectomy: a randomized controlled trial. *Obstetrics & Gynecology*, 124(5), 897-903.
- Yousuf, S., Mahmood, S., Rahman, R., Khatun, R., Tanzin, F., Arzoo, S., & Ferdous, N. E. (2023). Efficacy and Safety of Repeated Use of Ulipristal Acetate in Uterine Fibroids. *Mymensingh Medical Journal: MMJ*, 32(1), 168-176.



Bölüm 4

Fetal Development and Maternal Physiological Changes in Pregnancy

Nihan Erdoğan Atalay¹

¹ Opr.Dr., Bolu İzzet Baysal Devlet Hastanesi, BOLU/TÜRKİYE, ORCID: 0000-0002-4905-7425

1. FETAL DEVELOPMENT

The first eight weeks of the zygote cell settling in the uterus after fertilization is the “Embryonic Stage” and the period between the ninth week and birth is the “Fetal Stage” (1).

1.1. Embryonic Stage

The embryonic stage is characterized by embryo development after fertilization and implantation (2). Implantation of the blastocyst into the uterus occurs approximately ten days after ovulation as a result of invasion of trophoblast cells into the decidua layer and placenta formation begins (3). All embryonic structures and organs are differentiated but not activated. As of day 21, only the heart and circulatory system are functioning (2,4).

1.2. Fetal Stage

The embryo takes the name “fetus” with this stage. In this stage, which starts from the third month and continues until birth, rapid growth and organ formation are observed (3). Fetal growth is evaluated with various ultrasonographic parameters including head-hip length (CRL), biparietal diameter (BPD), femur length (FL), head (HC) and abdominal (AC) circumference (5).

The umbilical cord forms between the fetus and placenta in the 4th month of pregnancy. This cord consists of two umbilical arteries carrying oxygen-poor fetal blood and a single umbilical vein carrying clean maternal blood and is called “fetal placental circulation” (6). Oxygen-rich blood coming from the mother through uterine arteries is contaminated with fetal waste and collected in the endometrial veins and passes into the maternal circulation. This is called “maternal placental circulation” (7).

- 12th week: Fetus has a head-butt length of 6-7 cm. Primary ossification centers appear in the extremities (1). Hematopoiesis, which first starts in the vitellus sac in the 3rd week, passes to the liver and thymus (8).

- 16th week: Fetal head-butt distance is 12 cm and weight is 110 grams. By the 14th week, sex can be determined (1).

- 20th week: The fetus weighs around 300 grams (1). Movement starts in the extremities and elongation is observed in the lower extremities. Skeletal ossification and hair appears on the scalp (4).

- 24th week: The fetus weighs approximately 630 grams. Bronchial branches, bronchioles and alveolar sacs are formed, but terminal sacs are not formed (1).

Since the respiratory and central nervous system is not fully developed, there is no chance of survival at birth.

- 28th week: Fetal head-to-butt length is measured approximately 25 cm. Fetal weight is 1100 grams. The chance of survival at birth is approximately 90% (1).

- 36th week: The fetus weighs approximately 2500 grams. Subcutaneous fat tissue is increased (1).

- 40th week: The fetus averages 3400 grams and is considered to be term with this week (3).

2. MATERNAL PHYSIOLOGIC CHANGES IN PREGNANCY

Pregnancy is a 40-week process consisting of 3-month periods. The first 12-week period is called the first trimester. The period between 12 weeks and 27 weeks is considered the second trimester. Between 28 weeks and 40 weeks is the third and last trimester (3).

Anatomic and physiologic changes are observed in body systems to meet the metabolic needs of the developing fetus throughout pregnancy (9). Changes occur in the cardiovascular system, endocrine system, respiratory system, reproductive system, gastro-intestinal system, urinary system and musculoskeletal system. Changes in pelvic floor muscles and joints are observed with weight gain and fetal weight gain (3).

2.1. Reproductive System

Uterus in Pregnancy:

Before conception, the uterus is pear-shaped with a weight of about 70 g and an internal volume of about 10 ml, but with pregnancy it becomes spherical with a weight of about 1100 g and an internal volume of about 20 liters. The enlargement is mainly due to hypertrophy of the muscle cells, accompanied by hyperplasia of the cells. Uterine enlargement is most pronounced in the fundus. Hypertrophy occurs under the influence of steroid hormones until the 12th week, after which it is due to the pressure exerted by fetal growth. The position of the placenta affects uterine growth. The myometrium around the placenta grows faster than other areas. The uterus exceeds the pelvis at 12 weeks, reaches the level of the umbilicus at 20 weeks and is at the level of the xiphoid at 36 weeks. The growing uterus is dextrorotical (1). Nutrients and substances necessary for fetal and placental development pass by blood diffusion. Adequate perfusion of the placental intervillous space is important for the necessary exchange. With fetal growth, uteroplacental blood flow increases throughout pregnancy. The

uteroplacental blood flow, which is approximately 45ml/min in the follicular phase in non-pregnant women, can increase up to 750ml/min in term pregnancy (10). The arteries supplying the uterine corpus expand and lengthen and maintain their contractility functions (11). The spiral arteries supplying the placenta vasodilate, but lose their contractile function during pregnancy. This dilatation of the spiral arteries is responsible for the increase in uteroplacental blood flow. Nitric oxide (NO), a potent vasodilator, increases uterine blood flow during pregnancy by reducing resistance in the vascular bed. Estrogen, progesterone, activin, placental growth factor (PIGF) and vascular endothelial growth factor (VEGF) help vasodilation by increasing endothelial nitric oxide synthase (eNOS) and nitric oxide (NO) production (12). Induced or spontaneous contractions decrease uterine blood flow in proportion to contraction intensity (13).

Cervix in Pregnancy:

The cervix is responsible for holding and protecting the products of conception in place. The cervix is covered with mucus and has sufficient length to prevent the ascent of microbiota from the lower genital tract (14). The cervix undergoes a reversible change during pregnancy. The cervix, which is hard and closed, becomes stretchable and soft to allow the passage of the fetus. Cervical mucus during pregnancy is abundant and acidic due to the effect of progesterone (15). One month after conception, the cervix softens and becomes cyanotic. This is called Goodell's sign (16). The expansion of the endocervical columnar glands towards the ectocervix during pregnancy is called eversion. The everted part of the cervix is red and sensitive for bleeding (14).

Vagina and Perineum:

Bluish or purplish coloration of the vulva, vagina and cervix due to increased vascularity and hyperemia in pregnancy is called Chadwick's sign (1). During pregnancy, vaginal connective tissue relaxes in preparation for delivery, hypertrophy is observed in smooth muscle cells and vaginal mucosa thickness increases (17). Increased estradiol in pregnancy increases glycogen in vaginal epithelial cells and glycogen is metabolized to lactic acid by lactobacilli. Therefore, acidic vaginal pH (3.5-6) is observed (18).

2.2. Cardiovascular Changes

Heart sounds:

The heart sounds increase markedly during pregnancy and the first heart sound shows doubling. In the second heart sound, there is no clear change in the aortic

and pulmonary valve sounds. In addition to the two heart sounds, there is an easily audible third heart sound. Systolic ejection murmurs are considered physiologic up to grade 3 (19).

The Heart Axis:

During pregnancy, the diaphragm rises as the uterus grows. As the diaphragm rises, the heart shifts up and to the left. As a result, the apical beat (point of maximum intensity) shifts laterally (20).

Electrocardiogram (EKG):

Characteristic electrocardiographic changes are observed in a normally progressing pregnancy. Mild left axis deviation due to changing heart position is the most common finding. Q waves in leads II, III and avF and flat or inverted T waves in leads III, V1-V3 may occur (21).

Cardiac Change:

In pregnant women, heart size increases approximately 12% with an increase in myocardial mass and intracardiac volume (approximately 80 mL).

Heart rate starts to increase at 5 weeks and is 15-20 beats higher than in a non-pregnant woman at 32 weeks. The heart rate increases by about 17% during pregnancy. The stroke volume starts to increase at 8 weeks and reaches a maximum level at 20 weeks, increasing by 20% to 30% compared to pre-pregnancy. Cardiac output (CO) increases during pregnancy. Cardiac output (CO) is obtained by multiplying the pulse volume (SV) and heart rate (HR) measurements ($CO = SV \times HR$). Cardiac output increases at week 5 and increases approximately 40% throughout pregnancy (22).

At 24 weeks, due to fetal development, the uterus compresses the vena cava inferior (IVC) in the supine position, decreasing venous return and decreasing cardiac output and arterial pressure. By placing the pregnant woman in the left lateral position, caval compression is relieved, increasing blood return to the heart (22).

Blood pressure (BP) is calculated from cardiac output (CO) and systemic vascular resistance (SVR) ($BP = CO \times SVR$). ($BP = CO \times SVR$) Blood pressure decreases from the beginning of pregnancy until 24-28 weeks of gestation and then increases until term and is at pre-pregnancy value in term pregnant women. The low blood pressure in the first two trimesters of pregnancy is due to the

systemic vascular resistance which decreases significantly in pregnancy despite the increase in cardiac output (20).

2.3. Respiratory System

Oxygen requirement of the fetus, placenta and maternal organs increases with the growth of the baby. As a result, oxygen consumption increases by 20%-40% in pregnancy (23). In pregnancy, hyperventilation and physiologic dyspnea may be observed by increasing the sensitivity of CO₂-sensitive chemoreceptors with the central effect of progesterone (13).

During pregnancy, total lung capacity decreases as the diaphragm rises approximately 4 cm. Although the transverse diameter of the thorax expands by 2 cm and the thorax circumference by 6 cm to increase the total lung capacity, it is not sufficient. In pregnancy, some changes occur in respiratory functions and capacities due to the rising diaphragm (1).

2.4. Endocrine System

Pituitary Gland:

In pregnancy, the pituitary enlarges due to a 40% increase in prolactin-producing lactotropic cells in the anterior lobe in response to maternal estrogen. By the end of pregnancy, prolactin (PRL) level may increase up to 200 ng/ml (24). While the number of gonadotropes and somatotropes decreases, the amount of corticotropes and thyrotroph cells does not change significantly (25). Follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels are suppressed during pregnancy due to negative feedback. Oxytocin secreted from the posterior pituitary increases during pregnancy (26).

Thyroid Gland:

Due to the thyroid stimulating hormone (TSH)-like activity of human chorionic gonadotropin (HCG), there is a decrease in TSH levels in the first trimester. TSH levels return to pre-pregnancy levels in the second and third trimesters. During pregnancy, thyroxine-binding globulin (TBG), the binding protein of thyroid hormones, increases due to the high estrogen effect. TBG levels start to rise at the beginning of the first trimester, reach a peak at 20 weeks and then plateau until sweat. Total serum thyroxine (T4) and triiodothyronine (T3) concentrations increase with high TBG levels, but do not affect physiologically important free T4 and free T3 levels (1).

Adrenal Gland:

Due to the decrease in vascular resistance and blood pressure, aldosterone levels increase up to 10-fold. In pregnancy, angiotensin II increases 2-4 times and renin 3-4 times (27). Plasma levels of deoxycorticosterone (DOC) increase more than 15-fold to 1500 pg/mL. Plasma DOC levels in the third trimester of pregnancy do not respond to ACTH stimulation, dexamethasone suppression or salt intake, unlike before pregnancy (28).

Corticosteroid binding globulin (CBG), adrenocorticotrophic hormone (ACTH), total cortisol and free cortisol serum levels increase in the later weeks of pregnancy. In pregnancy, androgenic activity increases and maternal plasma levels of androstenedione and testosterone increase. Both androgens are converted to estradiol in placental trophoblasts. Therefore, it does not enter the fetal circulation and does not cause fetal side effects (1).

Hormones Affecting Calcium Metabolism:

Parathyroid hormone (PTH) increases from the end of the first trimester until sweat. Active vitamin D (1,25-dihydroxyvitamin D) also increases during pregnancy (1). Calcitonin levels in pregnancy are usually increased by up to 20% to help protect the maternal skeleton from excessive bone loss (29).

2.5. Gastrointestinal System

Nausea and vomiting (emesis gravidarum) is a very common symptom in pregnancy and persists up to 16 weeks. In most pregnant women, minor dietary modification and monitoring of electrolyte balance is sufficient. Dehydration, electrolyte imbalance, ketonuria, weight loss and vitamin-mineral deficiencies may be observed in 0.5-3% of pregnant women caused by severe nausea and excessive vomiting (hyperemesis gravidarum) (30). Hypertrophy and hyperemia may occur in the gums caused by the increase in estrogen during pregnancy and bleeding may occur (20).

Due to the effect of progesterone, there is a decrease in intestinal motility, a decrease in the tone of the lower esophageal sphincter and a decrease in esophageal peristalsis. Compression of the stomach occurs with the enlargement of the uterus. As a result of these, reflux esophagitis (pyrosis) occurs (31). Progesterone decreases the contractility of the gallbladder and slows its emptying. This increases the risk of gallstone formation. Since bile fluid is high in cholesterol in pregnancy, the most common gallstones in pregnancy are cholesterol stones (1). Serum albumin and total protein levels decrease in pregnancy due to hemodilution. Serum alkaline phosphatase (ALP) activity in the

third trimester increases 2-4 times. Most of this increase is due to placental production of heat-stable alkaline phosphatase isoenzymes (20).

2.6. Urinary System

There is an increase in renal blood flow during pregnancy. There is a 1-1.5 cm increase in kidney size, reaching a maximum in mid-pregnancy. The volume of the renal pelvis increases up to 6-fold during pregnancy compared to the pre-pregnancy value of about 10 mL in non-pregnant women. Glomerular filtration rate (GFR) increases by approximately 50%. Renal plasma flow (RPF) increases up to 80% during pregnancy (32). Expansion of the ureters, renal pelvis and calyces occurs due to uterine compression of the ureters with fetal development. Physiologic hydronephrosis is observed in more than 80% of pregnant women. Hydronephrosis is more common on the right side due to uterine dextrorotation. There is a slowdown in urinary blood flow in the expanding ureter, which increases the susceptibility to infection (33).

Daily urine volume increases by 25% due to increased renal perfusion and hyperfiltration, nocturia and frequent urination may be observed. Renal clearance of creatinine increases due to increased GFR in pregnancy. Creatinine levels decrease between 0.7 and 0.5 mg/dL on average, and urea and uric acid levels also decrease (32). Due to decreased tubular reabsorption and increased GFR in pregnant women, glycosuria may be normal up to 150 mg/dL without a diabetic condition. It also increases urinary protein and albumin excretion. Proteinuria up to an upper limit of 300 mg proteinuria or 30 mg albuminuria in a 24-hour period is considered physiologic (34). From the second trimester onwards, bladder pressure increases and bladder capacity decreases (35).

2.7. Musculoskeletal System

A bone structure that is more resistant to the bending forces and biomechanical stresses required to support the developing fetus is needed. There is a change in the micro-architectural structure of the bones without a change in their mass. A characteristic progressive lordosis develops during pregnancy (1).

Exaggerated lordosis of the waist, forward flexion of the neck and downward movement of the shoulders occur and cause traction on the median and ulnar nerves. It may cause symptoms confused with carpal tunnel syndrome (22).

Changes in relaxin, estrogen and progesterone hormone levels lead to increased elasticity of connective tissue (36). Significant enlargement of the pubic symphysis occurs between 28 and 32 weeks and its width may increase from 3 to 4 mm to 7.7 to 7.9 mm (26).

Effects of Pregnancy on the Pelvic Floor:

Many changes occur in pelvic formations during pregnancy. With the effect of increasing progesterone, enlargement is observed in the joints, especially in the symphysis pubis. With this enlargement, mobility increases to help delivery and pelvic joint disability occurs (37).

In the second trimester, the load on the pelvic muscles increases with the growing fetus (38). Laxity is most common in this period. Pelvic floor muscles weaken. Bladder neck mobility increases with weakening of the muscles and causes incontinence (39).

Weight Gain During Pregnancy:

The average weight gain during pregnancy is 12.5 kg. Weight gain during pregnancy is due to fetus, placenta, uterus, amniotic fluid, increase in maternal blood volume, breast growth, increase in maternal adipose tissue and increase in extravascular fluid. In a pregnant woman with an average weight gain, products of conception (placenta, fetus, amniotic fluid) account for approximately 35% of the total weight gained (40).

The recommendations of the Institute of Medicine (IOM) for total recommended weight gain during pregnancy are shown in Table 1 (41).

Pain in Pregnancy:

Pain sensation is defined by the International Association for the Study of Pain as “an emotional and unpleasant experience that may or may not be associated with actual or potential tissue damage and is also related to the individual's experiences” (42). With the progression of pregnancy, the load on the joints increases with the growth of the fetus and the change in the center of gravity, and injuries related to the musculoskeletal system become more frequent. Pre-existing musculoskeletal disorders such as rheumatoid arthritis and scoliosis may also increase during pregnancy (43).

Musculoskeletal findings are most prominent in the third trimester (44). In the study conducted by Kesikburun et al. low back pain was the most common complaint. In the third trimester, an increase in hand-wrist, neck, back, waist, hip, knee and ankle-foot pain was observed most frequently in pregnant women (45). Low back pain affects an average of 50-70% of pregnant women (46-48). Pregnant women who experience pain during pregnancy are more likely to experience pain in their next pregnancy. Low back pain may radiate to the hip, leg and foot (46,49,50). Low back and pelvic pain may be severe enough to cause loss of labor, disrupt sleep quality and even limit daily activities (51-54).

Changing posture, increased lordosis, inadequate neuromuscular function and vascular changes during pregnancy lead to impaired metabolic nutrition in the lumbar region and low back and pelvic pain (50,55). Although low back and pelvic pain in pregnancy is most common between the 4th and 7th months, it can occur at any time(56).

In pregnancy, joint pain is very common with hormonal changes and anatomical changes (87). The pain is usually unilateral, but pain may occur on both sides. Cutaneous branches of the nerves may be stretched due to abdominal tension during pregnancy (58). The iliohypogastric, genitofemoral and lateral femoral cutaneous nerves may also be compressed with increased tension. It may cause pain in the buttocks, labia and thighs (59). Fluid retention and peripheral edema increase in pregnancy. Carpal tunnel syndrome and tarsal tunnel syndrome are commonly observed (60). 20-80% of pregnant women complain of pain arising from dysfunction of the sacroiliac joint that may radiate to the lower back, hip, groin and all lower extremities (61,62).

Thoracic kyphosis increases in pregnant women. As the thoracic cage expands anteriorly and laterally, the load on the costovertebral and costatransverse joints increases. Increased weight in the breasts also increases the thoracic load (63,64). Pain occurs in the costovertebral joints with mechanical effect as a result of expansion of the thorax secondary to changes in the respiratory system (65). Another source of pain in pregnancy is the hips. Vullo et al. reported that 34% of pregnant women experienced hip pain with mechanical load on the hips (66,67). Sciatic pain, caused by compression of the sciatic nerve, may accompany low back pain and sacroiliac dysfunction, or may occur alone. Pregnancy-related pelvic girdle pain is one of the symptoms seen during pregnancy. It affects the pregnant woman physically, psychologically and socioeco (68).

REFERENCES

1. Cunningham, F.G., Leveno, K.J., Bloom SL, Dashe, J.S., Ho\$man, B.L., Casey, B.M. S, C.Y. williams obstetrics. New York McGraw-Hilll. 2018;
2. Dudek RW. Embryology. İrez T, Erkan M, editör. BRS Embriyoloji. 6. Baskı. İstanbul: İstanbul Tıp Kitabevi; 2015. p. 18-60.
3. Rhoades RA, Bell DR. Döllenme, gebelik ve fetal gelişim. Ağar E, Ayyıldız M, Yıldırım M, editör. Tıbbi Fizyoloji: Klinik Tıbbın Temelleri. 4. Baskı. İstanbul: İstanbul Medikal Sağlık ve Yayıncılık Hiz. Tic.Ltd.Şti. İTK Basım; 2017. p. 712-23.
4. Moore KL, Persaud TVN, Torchia MG. Placenta and fetal membrane. Before we are born: essentials of embryology and birth defects. 9. ed. Philadelphia: Elsevier Health Sciences; 2016. p. 71-5.
5. Whitworth M, Bricker L, Mullan C. Ultrasound for fetal assessment in early pregnancy. The Cochrane database of systematic reviews 2015(7):70-8.
6. Rhoades RA, Bell DR. Döllenme, gebelik ve fetal gelişim. Ağar E, Ayyıldız M, Yıldırım M, editör. Tıbbi Fizyoloji: Klinik Tıbbın Temelleri. 4. Baskı. İstanbul: İstanbul Medikal Sağlık ve Yayıncılık Hiz. Tic.Ltd.Şti. İTK Basım; 2017. p. 712-23.
7. Şeftalioğlu A. Fötal Membranlar ve plasenta. genel-özel insan embriyolojisi. 3. Baskı Ankara Tıp & Teknik Yayıncılık Ltd; 1998. Pages.
8. Moore KL, Persaud TVN, Torchia MG. Placenta and Fetal Membrane. The Developing human clinically oriented embryology. 10. ed. Philadelphia: Elsevier Health Sciences; 2016. p. 107-18.
9. Pacheco LD, Costantine MM, Hankins GD V. Physiologic Changes During Pregnancy. Mattison DR, editor. Clinical Pharmacology During Pregnancy: Academic Press. 2013. 5–16 p.
10. Sophian J. Placental Blood-Flow. Lancet. 1953;262(6781):344–5.
11. Mandala M, Osol G. Physiological remodelling of the maternal uterine circulation during pregnancy. Basic Clin Pharmacol Toxicol. 2012;110(1):12–8.
12. Bird MG and JS and RM and I. Vascular endothelial growth factor acts through novel, pregnancy-enhanced receptor signalling pathways to stimulate endothelial nitric oxide synthase activity in uterine artery endothelial cells }. Biochem J. 2009;417 2:501–11.
13. ASSALI NS, DOUGLASS RA Jr, BAIRD WW, NICHOLSON DB SR. Measurement of uterine blood flow and uterine metabolism. IV. Results in normal pregnancy. Am J Obs Gynecol. 1953;
14. Nott JP, Bonney EA, Pickering JD, Simpson NAB. The structure and function of the cervix during pregnancy. Transl Res Anat. 2016;2:1–7.

15. Gordon MC. Maternal physiology. In Gabbe. obstetrics: normal and problem pregnancies. 6th ed. Saunders, editor. Philadelphia; 2012. 42–62 p.
16. Soma-Pillay P, Nelson-Piercy C, Tolppanen H et al. Physiological changes in pregnancy. *Cardiovasc J Afr.* 2016;27:89-94.
17. Farage MA, Maibach HI. Morphology and physiological changes of genital skin and mucosa. *Curr Probl Dermatol.* 2011;40:9-19.
18. Boskey ER, Cone RA, Whaley KJ et al. Origins of vaginal acidity: high D/L lactate ratio is consistent with bacteria being the primary source. *Hum Reprod.* 2001;16:1809-1813.
19. Cutforth R, MacDonald CB. Heart sounds and murmurs in pregnancy. *Am Heart J.* 1966 Jun 1;71(6):741–7.
20. Amy A. Flick, MD; Daniel A. Kahn, MD P. Maternal Physiology during Pregnancy & Fetal & Early Neonatal Physiology. chapter 8.
21. SUNITHA. M.1, CHANDRASEKHARAPPA. S2 S. B. Electrocardiographic QRS Axis, Q Wave and T-wave Changes in 2nd and 3rd Trimester of Normal Pregnancy. :DOI: 10.7860/JCDR/2014/10037.4911. Available from: www.jcdr.net
22. Antony K.M., Racusin, D. A., Aagard, K. D, A. G. Obstetrics: Normal and Problems pregnancies. 2017. 7WK ed., pp. 36–60.
23. CRAPO, ROBERT Normal Cardiopulmonary Physiology During Pregnancy, Clinical Obstetrics and Gynecology: March 1996 - Volume 39 - Issue 1 - p 3-16.
24. Rigg LA, Lein A, Yen SS. Pattern of increase in circulating prolactin levels during human gestation. *Am J Obstet Gynecol.* 1977;129:454-456.
25. Laway BA, Mir SA. Pregnancy and pituitary disorders: Challenges in diagnosis and management. *Indian Journal of Endocrinology and Metabolism.* 2013;17:996-1004.
26. Prager D, Braunstein GD. Pituitary disorders during pregnancy. *Endocrinol Metab Clin North Am.* 1995;24:1-14.
27. Soma-Pillay P, Nelson-Piercy C, Tolppanen H et al. Physiological changes in pregnancy. *Cardiovasc J Afr.* 2016;27:89-94.
28. Noltén WE, Lindheimer MD, Oparil S et al. Desoxycorticosteron in normal pregnancy. I. Sequential studies of the secretory patterns of de- 34 Ȳ Güncel Obstetrik Yaklaşımlar soxycorticosterone, aldosterone, and cortisol. *Am J Obstet Gynecol.* 1978;132:414-.
29. Kovacs CS, Kronenberg HM. Maternal-fetal calcium and bone metabolism during pregnancy, puerperium, and lactation. *Endocr Rev.* 1997;18:832-872.

30. American College of Obstetrics and Gynecology. ACOG (American College of Obstetrics and Gynecology) Practice Bulletin: nausea and vomiting of pregnancy. *Obstet Gynecol.* 2004; 103:803-814.
31. Pessel, C., Tsai, M.C. (2019). "e Normal Puerperium. In A.H. DeCherney, L. Nathan, L, N. Laufer et al. (Eds.), &XUUHQW'DJQRV\ V 7UHDWPHQW_2EVWHWU\FV *QHFRORJ(12th ed., pp.190-213). New York: McGraw-Hill.
32. Cheung KL, Lafayette RA. Renal physiology of pregnancy. *Adv Chronic Kidney Dis.* 2013;20:209- 214.
33. Rasmussen PE, Nielsen FR. Hydronephrosis during pregnancy: a literature survey. *Eur J Obstet Gynecol Reprod Biol.* 1988;27:249-259No Title.
34. Odutayo A, Hladunewich M. Obstetric nephrology: renal hemodynamic and metabolic physiology in normal pregnancy. *Clin J Am Soc Nephrol.* 2012;7:2073-2080.
35. Müderris İİ, Kardaş HY. GEBELİK Ve Dogum SonrasiEgzersizler. *Erciyes Tıp Derg.* 1995;17(3):304–10.
36. Akarcalı I, Akbayrak T, Kara F, İnce Dİ, Çıtak İ. Gebelikte Esneklik. *Türkiye Klin J Gynecol Obs.* 2001;11(5):309–13.
37. Peschers U, Schaer G, Anthuber C, Delancey JOL, Schuessler B. Changes in vesical neck mobility following vaginal delivery. *Obstet Gynecol.* 1996;88(6):1001–6.
38. Wijma J, Weis PAE, de Wolf BT, Tinga DJ, Aarnoudse JG. Anatomical and functional changes in the lower urinary tract during pregnancy. *BJOG.* 2001;108(7):726–32.
39. De Caroci AS, Riesco MLG, Rocha BMC, De Jesus Ventura L, Oliveira SG. Evaluation of perineal muscle strength in the first trimester of pregnancy1. *Rev Lat Am Enfermagem.* 2014;22(6):893–901.
40. World Health Organization: Human energy requirements. Food and nutrition technical report series 1. Rome, Food and Agriculture Organization of the United Nations, 2004, p 53.
41. Institute of Medicine and National Research Council: Weight Gain During Pregnancy: Reexamining the Guidelines. Washington, "e National Academic Press, 2009.
42. Merskey H. Pain terms: alist with definitions and notes on usage. Recommended by the IASPSubcommitte on Taxonomy. *Pain.* 1979;6:247–52.
43. Heckman JD, Sassard R. Musculoskeletal considerations in pregnancy Musculoskeletal Concepts Considerations Review in Pregnancy *. *J BONE Jt Surg.* 1994;76:1720–30.

44. Franklin M, Conner-Kerr T. An analysis of posture and back pain in the first and third trimesters of pregnancy. *J Orthop Sports Phys Ther.* 1998;28(3):133–8.
45. Kesikburun S, Güzelküçük Ü, Fidan U, Demir Y, Ergün A, Tan AK. Musculoskeletal pain and symptoms in pregnancy: a descriptive study. *Ther Adv Musculoskelet Dis.* 2018;10(12):229–34.
46. Malmqvist S, Kjaermann I, Andersen K, Ekland I, Bronnick K, Larsen JP. Prevalence of low back and pelvic pain during pregnancy in a norwegian population. *J Manipulative Physiol Ther* [Internet]. 2012;35(4):272–8. Available from: <http://dx.doi.org/10.1016/j.jmpt.2012.04.004>
47. Bergström C, Persson M, Mogren I. Pregnancy-related low back pain and pelvic girdle pain approximately 14 months after pregnancy - pain status, self-rated health and family situation. *BMC Pregnancy Childbirth.* 2014;14:48.
48. Fast A, Shapiro D, Ducommun EJ, Friedmann LW, Bouklas T, Floman Y. Low-back pain in pregnancy. *Spine (Phila Pa 1976).* 1987;12(4):368–71.
49. Vermani E, Mittal R, Weeks A. Pelvic girdle pain and low back pain in pregnancy: a review. *Pain Pract.* 2010;10(1):60–71.
50. Vleeming A, Albert HB, Ostgaard HC, Sturesson B, Stuge B. European guidelines for the diagnosis and treatment of pelvic girdle pain. *Eur Spine J.* 2008;17:794–819.
51. Sinclair M, Hughes C, Liddle D. How do women manage pregnancy-related low back pain and/or pelvic pain? Descriptive findings from an online survey. *Evid Based Midwifery.* 2014;12(3):76–
52. Kalus S, Kornman L, Quinlivan JA. Managing back pain in pregnancy using support garment: a randomised trial. *BJOG.* 2008;115(1):68–75.
53. Mogren I, Pohjanen A. Low back pain and pelvic pain during pregnancy: prevalence and risk factors. *Spine (Phila Pa 1976).* 2005;30(8):983–91.
54. Skaggs CD, Prather H, Gross G, George JW, Thompson PA, Nelson DM. Back and pelvic pain in an underserved United States pregnant population: a preliminary descriptive survey. *Journal Manip Physiol Ther.* 2007;30(2):130–4.
55. Casagrande D, Gugala Z, Clark SM, Lindsey RW. Low Back Pain and Pelvic Girdle Pain in Pregnancy. *J Am Acad Orthop Surg.* 2015;23(9):539–49.
56. BULLOCK JE, Jull G, Bullock M. The Relationship of Low Back Pain to Postural Changes During Pregnancy. *Aust J Physiother.* 1987;33(1):10–7.
57. Choi HJ, Lee JC, Lee YJ, Lee EB, Shim SS, Park JS, et al. Prevalence and clinical features of arthralgia /arthritis in healthy pregnant women. *Rheumatol Int.* 2008;28(11):1111–5.

58. Peleg R, Gohar J, Koretz M, Peleg A. Abdominal wall pain in pregnant women caused by thoracic lateral cutaneous nerve entrapment. *Eur J Obs Gynecol Reprod Biol.* 1997;74(2):169–71.
59. Deal C, Canoso J. Meralgia paresthetica and large abdomens. *Ann Intern Med.* 1982;96(6):787–8.
60. Padua L, Aprile I, Caliendo P, Carboni T, Meloni A, Massi S, et al. Symptoms and neurophysiological picture of carpal tunnel syndrome in pregnancy. *Clin Neurophysiol.* 2001;112(10):1946–51.
61. Endresen E. Pelvic pain and low back pain in pregnant women-an epidemiological study. *Scand journal Rheumatol.* 1995;24(3):135–41.
62. Zelle BA, Gruen GS, Brown S, George S. Sacroiliac joint dysfunction: evaluation and management. *Clin J Pain.* 2005;21(5):446–55.
63. Polden M, Mantle J. Relieving pregnancy discomfort. In: Butterworth-Heinemann, editor. *Physiotherapy in Obstetric and Gynaecology.* 2nd ed. Oxford; 1990. p. 133–62.
64. Fraser D. Postpartum backache: a preventable condition. *Can Fam Physician.* 1976;22:76.
65. Barton S. Relieving the discomforts of pregnancy. In: Butterworth-Heinemann, editor. *PHYSIOTHERAPY IN OBSTETRICS AND GYNAECOLOGY.* 2nd ed. london; 2004. p. 141–64.
66. Vullo V, Richardson J, Hurvitz E. Hip, knee, and foot pain during pregnancy and the postpartum period. *J Fam Pr.* 1996;43:63–68.
67. Berman AT, Cohen DL, Schwentker EP. The effects of pregnancy on idiopathic scoliosis. A preliminary report on eight cases and a review of the literature. *Spine (Phila Pa 1976).* 1982;7:76–7.
68. Butterworth-Heinemann, editor. Relieving the discomforts of pregnancy. In: *Physiotherapy in Obstetric and Gynaecology.* 2nd ed. London; 2004. p. 141–64.



Bölüm 5

"From Ultrasound to Mri: Advances in Gynecological Imagng"

Samet Kirat¹

¹ MD, 1Kafkas University, Faculty of Medicine, Department of Obstetrics and Gynecology, Kars/Turkey,
ORCID: 0000-0001-7262-4320

1. Introduction

Female patients frequently present to the emergency department with acute or subacute gynecologic symptoms. As clinical symptoms are often non-specific and physical examination findings may be limited in such cases, imaging modalities are critical for accurate and rapid diagnosis. Ultrasonography (USG) is widely used as a noninvasive first-line imaging modality and can rapidly detect many gynecologic and obstetric pathologies. Doppler USG provides real-time information on anatomical structures and blood vessels to guide needle placement, particularly during interstitial brachytherapy (Tonolini et al., 2019).

Magnetic resonance imaging (MRI) plays an important role in determining treatment plans and options, especially for malignant gynecologic pathologies. Its high soft tissue contrast and multiplanar imaging capability facilitate differential diagnosis. Dual-energy computed tomography (CT) is an innovative technology that improves diagnostic accuracy by simultaneously providing data from two different energy spectra (Foti et al., 2019). Furthermore, new techniques, such as molecular imaging and narrow-band imaging, offer advanced diagnostic possibilities in various clinical scenarios (Franco et al., 2023).

Adnexal pathologies, a frequent focus in gynecological emergencies, are generally categorized into three main groups: hemorrhagic conditions, pathologies associated with adnexal tumors, and infectious conditions. Hemorrhagic conditions include hemorrhagic ovarian cysts and ectopic pregnancies, whereas tumor-related pathologies include adnexal torsion and tumor rupture. Among infectious conditions, pelvic inflammatory diseases are particularly notable (Okazaki et al. 2022). Similarly, acute uterine pathologies are classified into two primary categories: acute complications of uterine fibroids and conditions leading to acute uterine bleeding. Acute fibroid complications include red degeneration, subserosal fibroid torsion, and uterine torsion, and acute uterine bleeding is commonly caused by retained products of conception and uterine arteriovenous malformations (Gopireddy et al., 2022).

Prompt and accurate diagnosis is important to prevent infertility and potentially life-threatening complications. USG is usually the first choice; however, in cases where the diagnosis remains unclear, CT and MRI provide additional information to support differential diagnosis. MRI provides a highly accurate differential diagnosis, especially in complex cases such as adnexal masses and leiomyomas (Shetty, 2023).

Artificial intelligence (AI) is increasingly used in gynecologic imaging. AI algorithms facilitate image analysis, quality assurance, and automation processes.

These technologies have the potential to improve diagnostic accuracy in repetitive tasks, such as USG (Lei et al., 2021). Moreover, AI-based applications in CT and MRI data support clinical decision-making processes by enriching image analytics (Paudyal et al., 2023). Radiologists play a vital role in the diagnosis and management of gynecologic emergencies. The effective use of imaging modalities increases diagnostic accuracy and facilitates the implementation of appropriate treatment approaches.

2. Ultrasonography (USG)

USG is widely regarded as the first-line imaging modality for women presenting with pelvic pain, whether acute or chronic, owing to its ability to rapidly and effectively diagnose a wide range of gynecologic and obstetric conditions. However, pelvic pain often presents diagnostic challenges, as it can overlap with symptoms associated with gynecologic, gastrointestinal, and genitourinary pathologies. This overlap can complicate clinical evaluation, necessitating the use of additional imaging modalities, such as MRI or CT, in cases where USG results are inconclusive. This is particularly important in pregnant patients, where accurate and noninvasive diagnostic methods are crucial (Foti et al., 2019).

Gynecologic advancements in imaging have significantly impacted clinical outcomes, particularly in brachial therapy for cervical cancer. The incorporation of MRI into brachytherapy protocols has markedly improved the accuracy of implant placement, enhanced local tumor control, and reduced associated toxicity. Despite these advancements, global disparities in the access to advanced imaging modalities have persisted. Affordable and portable imaging techniques are urgently required to address these inequities. USG, which is already a standard imaging modality in prostate cancer brachytherapy, is a cost-effective and accessible alternative; however, its application in gynecologic brachytherapy remains limited (Mohsen & Auda, 2024).

Concerns regarding the potential thermal and mechanical effects of USG on embryonic and fetal development have been a topic of discussion. Advances in USG technology in recent years have significantly improved imaging quality, making it an indispensable tool for the primary diagnosis of gynecologic cancers, evaluation of tumor extension, and monitoring treatment responses. When performed by experienced sonographers, USG is both safe and reliable, and offers critical insights into disease progression and therapeutic efficacy (Shetty, 2023).

Doppler USG, a specialized application of USG, plays an essential role in guiding needle placement during gynecological brachytherapy by providing real-

time visualization of anatomical structures and vascular systems. While its high sensitivity to macro- and microvascular flow offers substantial advantages in assessing pelvic organs and pregnancy, it is recommended that Doppler USG usage in the first trimester be minimized and limited to the shortest duration necessary to mitigate any potential risks to embryonic or fetal health (Cortellaro et al., 2019).

Both contrast-enhanced and non-contrast-enhanced Doppler USG have proven to be highly valuable in differentiating benign from malignant lesions, underscoring their utility in modern gynecological and obstetric practice. Emerging ultrasonographic techniques are anticipated to further enhance diagnostic accuracy and clinical decision-making in this field (Franco et al., 2023). Among these, transvaginal color Doppler USG is particularly notable for its role in the detection and diagnosis of recurrent pelvic tumors associated with chronic pain. When combined with transvaginal grayscale USG, it provides a comprehensive imaging approach, offering superior sensitivity and specificity for the evaluation of recurrent or complex lesions (Basta Nikolic et al., 2021).

3. Transvaginal Ultrasonography (TVUS)

TVUS plays a pivotal role in the evaluation and management of ovarian abnormalities owing to its high diagnostic accuracy and noninvasive nature. A large-scale study conducted within the University of Kentucky Ovarian Cancer Screening Program assessed the prevalence, incidence, persistence, and resolution of ovarian abnormalities using serial TVUS. This study involved 39,337 women and included 221,576 TVUS examinations, with 81% of the participants having normal results and 17% demonstrating abnormal findings. Notably, ovarian cysts were observed more frequently in premenopausal women, with a prevalence of 35% and an incidence of 15%, compared to a prevalence of 17% and an incidence of 8% in postmenopausal women. Among the abnormal findings, 63% resolved spontaneously in subsequent TVUS evaluations, while 10% of the initially normal cases developed abnormalities during follow-up. Abnormalities were categorized as single-chamber cysts (11.5%), septate cysts (9.8%), cysts containing solid areas (7.1%), and solid masses (1.8%). Surgical intervention was required in 557 participants, of whom 85 were diagnosed with malignant conditions and 472 with benign findings. The study highlighted that a serial approach to TVUS increased the positive predictive value from 8% to 25%, underscoring its role in improving diagnostic precision and reducing false-positive results (Wang et al., 2013).

In a separate investigation evaluating gynecological pathologies in subfertile women, 1,558 women who underwent TVUS were examined. Pathologies were identified in 69.7% of the participants, with the most common findings being uterine fibroids (26.3%), polycystic ovaries (23.3%), endometriosis (11.4%), and benign ovarian cysts (7.8%). Among these, 76.6% of cases presented with a single pathology, whereas 23.4% demonstrated multiple abnormalities. The study emphasized the effectiveness of TVUS as a primary diagnostic tool for identifying gynecological pathologies in the subfertility population, enabling rapid and accurate detection of underlying conditions (Foo et al., 2021).

The diagnostic performance of the Ovarian-Adnexal Report Data System (O-RADS), a classification system for ovarian masses, was examined through a systematic review and meta-analysis. This analysis, encompassing 11 studies and 4,634 masses, demonstrated that the O-RADS achieved a sensitivity of 97% and a specificity of 77%. The system facilitated differentiation between benign and malignant lesions, significantly reducing unnecessary surgical interventions. The findings underscore the ability of TVUS, combined with standardized systems such as O-RADS, to enhance diagnostic accuracy while maintaining a noninvasive approach (Vara et al., 2022).

Another study explored the use of TVUS-guided aspiration as a minimally invasive alternative to surgery for simple ovarian cysts. Among 84 premenopausal and postmenopausal women treated with this technique, cyst recurrence was observed in 20.2%. Despite this, the method effectively reduced the need for surgical intervention. Additionally, TVUS demonstrated 100% diagnostic accuracy in evaluating the malignant potential of ovarian cysts, further establishing its reliability in clinical practice (Kostrzewa et al., 2019).

Collectively, these studies highlight the indispensable role of TVUS in gynecological evaluation. Its application in serial imaging provides high accuracy in identifying ovarian abnormalities and differentiating benign from malignant conditions. This approach not only reduces the need for surgical interventions but also enhances diagnostic performance, particularly in subfertility populations and high-risk groups. As a noninvasive, cost-effective, and reliable modality, TVUS remains integral to the comprehensive management of gynecological pathologies.

4. Magnetic Resonance Imaging (MRI)

MRI plays a pivotal role in the management of gynecological malignancies, encompassing diagnosis, staging, treatment planning, and follow-up. Its importance has grown with advancements in imaging protocols, enabling precise disease evaluation and aiding in the selection of appropriate therapeutic

strategies. The role of MRI in endometrial cancer has been extensively evaluated in a study highlighting the value of multiparametric MRI protocols, including T2-weighted imaging, diffusion-weighted imaging (DWI), and contrast-enhanced imaging. These protocols have been shown to effectively assess critical prognostic factors such as the depth of myometrial invasion, cervical invasion, and lymph node status. Furthermore, MRI has been recognised as a valuable tool for fertility-preservation approaches and as a guidance mechanism in patients who are unable to undergo surgery (Maheshwari et al., 2022).

The utility of MRI in cervical cancer staging is widely acknowledged. According to Otero-García et al., MRI offers high sensitivity and specificity in evaluating prognostic indicators, such as tumor size, parametrial invasion, and pelvic sidewall involvement, consistent with the revised 2018 FIGO staging system. Importantly, its negative predictive value in excluding parametrial invasion is critical for determining whether patients are suitable candidates for surgery or chemotherapy, thereby influencing treatment pathways (Otero-García et al., 2019).

In ovarian cancer, MRI has been proven to be instrumental in assessing the extent and location of peritoneal spread, thereby aiding decisions regarding cytoreductive surgery versus neoadjuvant chemotherapy. This application, as noted in previous research, is particularly effective with advanced techniques, such as diffusion-weighted imaging (DWI) and dynamic contrast-enhanced imaging (DCE-MRI). These modalities provide insights into the biological behavior of ovarian tumors, directly affecting treatment decisions and patient outcomes (Kido, 2020). The role of MRI extends to the evaluation of recurrent gynecological malignancies. Functional MRI techniques, including DWI and DCE-MRI, have demonstrated utility in monitoring treatment responses and identifying local recurrences in endometrial and cervical cancer. These techniques enable precise mapping of pelvic diseases and assessment of treatment eligibility, as emphasized in studies examining recurrent cancer scenarios (De Muzio et al., 2023).

Collectively, these studies underscore the indispensable role of MRI in the comprehensive management of gynecological cancers. By facilitating detailed evaluation of both local and distant disease spread, MRI not only guides therapeutic decisions but also contributes to improved long-term outcomes. Its integration into multidisciplinary oncology teams reinforces its position as a cornerstone in the care of patients with gynecologic malignancies.

5. Computed Tomography (CT)

CT plays a critical role in gynecologic imaging, particularly in cases where USG findings are inconclusive or when the lesion is extensive. In a study evaluating the diagnostic performance of CT in gynecologic emergencies, it was demonstrated that CT effectively identifies acute conditions, such as hemorrhagic ovarian cysts, adnexal torsion, pelvic inflammatory diseases, and cystic adenomyosis. Multidetector CT is frequently utilized in women of reproductive age, providing rapid and accurate diagnostic capabilities that are essential for effective treatment planning in cases of pelvic pain (Foti et al., 2019).

Advanced CT techniques, such as dual-energy CT (DECT), have been shown to significantly enhance diagnostic performance. Research has demonstrated that DECT improves the ability to differentiate between primary tumors and simple cystic lesions, as well as increases the detection rate of metastatic lesions, particularly in the liver and musculoskeletal system. These findings underscore the growing importance of DECT in the management of gynecological malignancies, offering more precise and comprehensive diagnostic results (Benveniste et al., 2020; Lee & Atri, 2019).

A meta-analysis further highlighted the role of CT in diagnosing acute pelvic inflammatory diseases, reporting 79% sensitivity and 99% specificity when using contrast-enhanced CT. This study emphasized that CT is a valuable alternative to invasive diagnostic methods, such as gynecological examination or laparoscopy, especially when standardized diagnostic criteria are applied. This finding reinforces its utility in both emergency and routine clinical settings (Okazaki et al. 2022).

The importance of CT in cervical cancer staging is widely acknowledged. It is particularly effective in identifying pelvic and para-aortic lymph node metastases and provides high accuracy in detecting distant metastases. These capabilities make CT indispensable in treatment planning for advanced cervical cancers. Furthermore, combining CT with transvaginal USG and MRI has been recommended to improve diagnostic accuracy and ensure comprehensive evaluation (Fischerova et al., 2024).

These studies collectively highlight the indispensable role of CT in the diagnosis and management of acute and chronic gynecological conditions. The integration of advanced technologies, such as dual-energy CT, enhances diagnostic precision, reduces the need for invasive procedures, and accelerates clinical decision making. As a rapid, accessible, and effective diagnostic tool, CT

continues to be a cornerstone for the evaluation of gynaecologic emergencies and malignancies.

6. Positron Emission Tomography (PET)

PET plays a vital role in the management of gynecological malignancies, enabling the integration of metabolic and anatomical data for accurate diagnosis, staging, restaging, treatment planning, and follow-up. Fluorodeoxyglucose (FDG)-PET/CT is a standardized imaging method widely used in this context, offering high sensitivity for the detection and assessment of malignancies (Dejanovic et al., 2021).

Despite its high sensitivity, the specificity of FDG-PET/CT can be limited owing to benign inflammatory processes and physiological variations. Hormonal factors, such as those influenced by the menstrual cycle and menopausal status, can alter FDG uptake and potentially lead to false-positive results. These findings underscore the importance of considering the clinical context when interpreting FDG-PET/CT findings to ensure diagnostic accuracy (Dejanovic et al., 2021).

The integration of FDG-PET with MRI has demonstrated enhanced diagnostic accuracy in gynecological cancers. Systematic reviews have indicated that FDG-PET/MRI outperforms PET/CT in evaluating endometrial, cervical, and ovarian cancers (Nguyen et al., 2020). FDG-PET/MRI is particularly effective for lymph node staging and tumor risk stratification. Additionally, its lower radiation exposure makes it a preferred option for younger patients who require repeat imaging (Nguyen et al., 2020).

FDG-PET/CT is superior to conventional imaging modalities for lymph node staging and distant metastasis detection. Studies have reported that this modality leads to changes in treatment plans in approximately 23% of cases, offering more precise guidance for therapeutic interventions. Its high negative predictive value (83.3%) for evaluating suspicious lymph nodes further enhances its utility in clinical decision-making (Al-Ibraheem et al., 2019).

The relationship between glucose metabolism and tumor aggressiveness in gynecological cancers is well established. FDG-PET/CT has demonstrated that poorly differentiated tumors with higher glucose uptake exhibit more aggressive biological behavior. In endometrial cancer, the strong correlation between glucose consumption and tumor grade highlights the prognostic value of FDG-PET/CT in assessing disease aggressiveness and guiding management strategies (Mititelu et al.).

These findings underscore the critical role of molecular imaging modalities, particularly FDG-PET/CT and FDG-PET/MRI, in the diagnosis and management of gynecological malignancies. By integrating metabolic and anatomical data, these advanced imaging techniques can improve diagnostic accuracy, optimize treatment planning, minimize unnecessary interventions, and enhance patient outcomes. The ability of these methods to provide detailed insights into tumor biology and staging makes them indispensable tools in modern oncological practice (Virarkar et al., 2020).

A meta-analysis evaluated the diagnostic performance of FDG-PET/CT and FDG-PET/MRI for gynecologic malignancies. The study demonstrated that PET/MRI had a higher patient-specific sensitivity than PET/CT (73.3% vs. 62.6%), although the difference was not statistically significant. Additionally, PET/MRI showed superior accuracy on a lesion-by-lesion basis and offered better classification of malignancies owing to its enhanced soft tissue contrast (Virarkar et al., 2020).

The staging of primary tumors, lymph node involvement, and recurrence evaluation in gynecologic cancers have significantly improved with FDG-PET/MRI. Studies have highlighted its superior diagnostic accuracy compared to FDG-PET/CT. Furthermore, its lower radiation dose makes it particularly advantageous for younger patients and those requiring long-term follow-up (Nguyen et al., 2020).

PET/MRI has been shown to be highly effective in detecting metastases, mapping recurrences, and assessing treatment responses. This method provides a superior evaluation of local tumor spread and lymph node involvement. Additionally, PET/MRI demonstrates high accuracy in distinguishing between benign and malignant tissues, underscoring its clinical utility in gynecological malignancies (Tarcha et al., 2023).

The roles of FDG-PET/CT and FDG-PET/MRI in the management of endometrial, cervical, and ovarian cancers have been comprehensively reviewed. Both modalities are recognized for their value in staging and prognostication. However, PET/MRI is emphasized as a safer option owing to its lower radiation exposure, which is particularly beneficial for pediatric and young female patients (Allahqoli et al., 2023).

The advantages of PET/MRI in diagnostic accuracy, treatment planning, and patient management are well documented in gynecologic oncology. This modality provides lower radiation exposure, superior soft-tissue resolution, and

higher diagnostic accuracy than PET/CT. These features establish PET/MRI as an indispensable tool in the modern management of gynecological cancers.

7. Narrow Band Imaging (NBI)

NBI is emerging as a valuable tool in gynecological endoscopy, particularly for the diagnosis of conditions such as endometrial lesions and endometriosis. By filtering light into narrow bands, NBI enhances the visualization of mucosal microstructures and capillaries, thereby increasing the detection rate of lesions. A systematic review demonstrated that NBI improves the specificity and sensitivity of hysteroscopy, laparoscopy, and colposcopy for detecting malignant and premalignant lesions. This review highlighted that NBI offers better diagnostic performance than conventional white-light endoscopy for endometrial and cervical lesions. However, the high cost of NBI equipment and the need for experienced personnel are significant barriers to its widespread clinical adoption (Peitsidis et al., 2022).

In the context of endometriosis, a meta-analysis reported that laparoscopic NBI provides higher diagnostic accuracy than conventional white-light imaging. NBI has been shown to identify lesions that are often missed during white-light imaging, thus enabling a more comprehensive evaluation of endometriosis. Despite these promising findings, the long-term impact of NBI on clinical outcomes and patient management remains unclear, emphasizing the need for further research in this area (Maheux-Lacroix et al., 2020).

Training programs specifically designed for NBI-guided hysteroscopy have been shown to improve diagnostic accuracy. A study evaluating both experienced and inexperienced hysteroscopists revealed significant improvements in the detection of malignant endometrial lesions using NBI. Interestingly, a study found that experienced clinicians adapted to this technology with a relatively shorter learning curve, suggesting that expertise plays a crucial role in optimizing the benefits of NBI (Wang et al., 2020).

The use of NBI in endometriosis surgery has also been investigated. Clinical studies have reported that NBI enhances lesion detection rates when compared to three-dimensional (3D) white-light imaging and near-infrared imaging with indocyanine green (NIR-ICG). While NBI alone improves histological accuracy, particularly for pelvic lesions, combining it with 3D white-light imaging yields the best results. This combined approach underscores the complementary role of NBI in enhancing surgical outcomes in endometriosis (Lier et al., 2020).

The potential of NBI to improve the diagnostic accuracy of gynecologic endoscopy is well documented. By offering superior visualization of microstructures, it enables early and accurate detection of lesions, which is crucial for patient outcomes. However, NBI remains in the early stages of clinical application and requires support from larger randomized controlled trials to validate its efficacy. In addition to the need for robust evidence, the high cost of NBI systems and the steep learning curve of clinicians are significant limitations that currently restrict their widespread adoption in routine practice.

These findings highlight both the promise and challenges associated with NBI in gynecologic endoscopy. With ongoing advancements in technology and increasing clinical experience, NBI has the potential to become a cornerstone technique for the diagnosis and management of gynecologic conditions.

8. Conclusions

Imaging modalities are indispensable in the diagnosis, staging, and treatment planning of gynecological cancers, providing critical insights that optimize therapeutic strategies such as surgery, radiotherapy, and chemotherapy. Among these, MRI and FDG-PET/CT have complementary roles in clinical practice. These advanced imaging tools not only assess local and systemic disease spread but also contribute significantly to prognostication. The integration of artificial intelligence (AI) into imaging technologies has revolutionized this field by enabling faster and more precise evaluations.

MRI, renowned for its superior soft-tissue resolution, is considered the gold standard for local tumor staging in gynecologic oncology. In endometrial carcinoma, MRI plays a pivotal role in assessing myometrial invasion depth, cervical stromal involvement, and potential lymph node metastasis, which are key factors in surgical planning and the identification of high-risk patients. Conversely, FDG-PET/CT excels in the noninvasive detection of distant metastases and radiotherapy planning. It is particularly effective in determining tumor size and location in cervical cancer and resolving ambiguous imaging findings in ovarian cancer, especially when associated with elevated CA-125 levels (Nguyen et al., 2020).

USG, the first-line imaging modality for women presenting with acute or chronic pelvic pain, remains the cornerstone of gynecologic imaging. It is highly effective in diagnosing emergencies, such as hemorrhagic ovarian cysts, pelvic inflammatory diseases, and adnexal torsion. Doppler USG further enhances diagnostic capabilities by enabling real-time vascular assessment and guiding needle placement in procedures such as gynecologic interstitial brachytherapy.

Recent advancements in AI-powered ultrasound technologies have facilitated automated image interpretation and quality assurance, streamlining repetitive tasks, and improving efficiency (Maheshwari et al., 2022).

DECT offers a novel approach by simultaneously acquiring datasets of two distinct photon spectra, thereby enhancing the tissue composition analysis. This innovation improves the differentiation between malignant and benign lesions with high sensitivity for detecting primary and metastatic ovarian cancers. Furthermore, DECT provides significant advantages in evaluating liver and musculoskeletal metastases, making it a valuable tool for comprehensive cancer staging (Lee & Atri, 2019).

Molecular imaging has emerged as a transformative field in gynecological oncology, offering advanced diagnostic and therapeutic monitoring capabilities. FDG-PET/CT integrates metabolic and anatomical data to enhance staging accuracy, whereas newer technologies, such as PET/MR, combine low radiation exposure with superior tissue contrast. Molecular imaging also plays a crucial role in assessing treatment responses and evaluating minimally invasive surgical options (Virarkar et al., 2020).

NBI, which uses filtered light to enhance the visualization of mucosal microstructures and capillary networks, has shown promise in improving diagnostic accuracy, particularly in laparoscopy and hysteroscopy, for detecting endometrial lesions and endometriosis. However, its widespread adoption is limited by cost and the need for specialized training (Peitsidis et al., 2022).

In conclusion, advanced imaging modalities, such as MRI, FDG-PET/CT, DECT, USG, and NBI, have become integral to the management of gynecological cancers, reducing reliance on invasive interventions and refining treatment strategies. The incorporation of AI-enhanced imaging into clinical practice has further increased diagnostic precision and facilitated personalized treatment approaches. These technological advancements not only enhance clinical outcomes but also improve the quality of life of patients with gynecologic malignancies, underscoring their critical role in modern oncologic care.

References

- Al-Ibraheem, A., AlSharif, A., Abu-Hijlih, R., Jaradat, I., & Mansour, A. (2019). Clinical impact of 18F-FDG PET/CT on the management of gynecologic cancers: one center experience. *Asia Oceania Journal of Nuclear Medicine and Biology*, 7(1), 7.
- Allahqoli, L., Hakimi, S., Laganà, A. S., Momenimovahed, Z., Mazidimoradi, A., Rahmani, A., Fallahi, A., Salehiniya, H., Ghiasvand, M. M., & Alkatout, I. (2023). 18F-FDG PET/MRI and 18F-FDG PET/CT for the management of gynecological malignancies: a comprehensive review of the literature. *Journal of Imaging*, 9(10), 223.
- Basta Nikolic, M., Spasic, A., Hadnadjev Simonji, D., Stojanović, S., Nikolic, O., & Nikolic, D. (2021). Imaging of acute pelvic pain. *The British Journal of Radiology*, 94(1127), 20210281.
- Cortellaro, F., Perani, C., Guarnieri, L., Ferrari, L., Cazzaniga, M., Maconi, G., Wu, M. A., & Aseni, P. (2019). Point-of-care ultrasound in the diagnosis of acute abdominal pain. *Operative Techniques and Recent Advances in Acute Care and Emergency Surgery*, 383-401.
- De Muzio, F., Fusco, R., Simonetti, I., Grassi, F., Grassi, R., Brunese, M., Ravo, L., Maggialelli, N., D'ANIELLO, R., & Greco, F. (2023). Functional assessment in endometrial and cervical cancer: diffusion and perfusion, two captivating tools for radiologists. *European Review for Medical & Pharmacological Sciences*, 27(16).
- Dejanovic, D., Hansen, N. L., & Loft, A. (2021). PET/CT variants and pitfalls in gynecological cancers. *Seminars in Nuclear Medicine*,
- Fischerova, D., Frühauf, F., Burgetova, A., Haldorsen, I. S., Gatti, E., & Cibula, D. (2024). The role of imaging in cervical cancer staging: ESGO/ESTRO/ESP guidelines (update 2023). *Cancers*, 16(4), 775.
- Foo, X., Lukaszewski, T., Yasmin, E., & Mavrelos, D. (2021). P-727 Prevalence of ultrasound-detected gynaecological pathology in a One-Stop fertility clinic. *Human Reproduction*, 36(Supplement_1), deab130. 726.
- Foti, P. V., Tonolini, M., Costanzo, V., Mammino, L., Palmucci, S., Cianci, A., Ettorre, G. C., & Basile, A. (2019). Cross-sectional imaging of acute gynaecologic disorders: CT and MRI findings with differential diagnosis—part II: uterine emergencies and pelvic inflammatory disease. *Insights into imaging*, 10, 1-19.
- Franco, P. N., García-Baizán, A., Aymerich, M., Maino, C., Frade-Santos, S., Ippolito, D., & Otero-García, M. (2023). Gynaecological causes of acute pelvic pain: common and not-so-common imaging findings. *Life*, 13(10), 2025.
- Gopireddy, D. R., Virarkar, M., Kumar, S., Vulasala, S. S. R., Nwachukwu, C., & Lam-sal, S. (2022). Acute pelvic pain: A pictorial review with magnetic resonance imaging. *Journal of Clinical Imaging Science*, 12.

- Kido, A. (2020). Therapy Response Imaging in Gynecologic Malignancies. *Therapy Response Imaging in Oncology*, 159-176.
- Kostrzewa, M., Zając, A., Wilczyński, J. R., & Stachowiak, G. (2019). Retrospective analysis of transvaginal ultrasound-guided aspiration of simple ovarian cysts. *Advances in Clinical and Experimental Medicine*, 28(11).
- Lee, S. I., & Atri, M. (2019). 2018 FIGO staging system for uterine cervical cancer: enter cross-sectional imaging. *Radiology*, 292(1), 15-24.
- Lei, Y.-M., Yin, M., Yu, M.-H., Yu, J., Zeng, S.-E., Lv, W.-Z., Li, J., Ye, H.-R., Cui, X.-W., & Dietrich, C. F. (2021). Artificial intelligence in medical imaging of the breast. *Frontiers in Oncology*, 11, 600557.
- Lier, M. C., Vlek, S. L., Ankersmit, M., van de Ven, P. M., Dekker, J. J., Bleeker, M. C., Mijatovic, V., & Tuynman, J. B. (2020). Comparison of enhanced laparoscopic imaging techniques in endometriosis surgery: a diagnostic accuracy study. *Surgical endoscopy*, 34(1), 96-104.
- Maheshwari, E., Nougaret, S., Stein, E. B., Rauch, G. M., Hwang, K.-P., Stafford, R. J., Klopp, A. H., Soliman, P. T., Maturen, K. E., & Rockall, A. G. (2022). Update on MRI in evaluation and treatment of endometrial cancer. *Radiographics*, 42(7), 2112-2130.
- Maheux-Lacroix, S., Belanger, M., Pinard, L., Lemyre, M., Laberge, P., & Boutin, A. (2020). Diagnostic accuracy of intraoperative tools for detecting endometriosis: a systematic review and meta-analysis. *Journal of Minimally Invasive Gynecology*, 27(2), 433-440. e431.
- Mititelu, R., Spiridon, P. M., Mazilu, C., Mititelu, T., Sirbu, C. A., Cuzino, D., Calin, C., Mititelu, L., Jinga, M., & Radu, F. I. PET-CT with 18F-FDG in Gynecological Malignancies. Prognostic Significance of the Standardized Uptake Value. *Romanian Journal of*, 127(2), 162.
- Mohsen, M., & Auda, B. (2024). Imaging Modalities in Assessment of Gynecological Causes of Acute Pelvic Pain at Shifa Medical Complex: A Cross-sectional Study. *International Journal of Innovative Research in Medical Science*, 9(08), 469-475. <https://doi.org/10.23958/ijirms/vol09-i08/1942>
- Nguyen, N. C., Beriwal, S., Moon, C.-H., D'Ardenne, N., Mountz, J. M., Furlan, A., Muthukrishnan, A., & Rangaswamy, B. (2020). Diagnostic value of FDG PET/MRI in females with pelvic malignancy—a systematic review of the literature. *Frontiers in oncology*, 10, 519440.
- Okazaki, Y., Tsujimoto, Y., Yamada, K., Arie, T., Taito, S., Banno, M., Kataoka, Y., & Tsukizawa, Y. (2022). Diagnostic accuracy of pelvic imaging for acute pelvic inflammatory disease in an emergency care setting: a systematic review and meta-analysis. *Acute Medicine & Surgery*, 9(1), e806.
- Otero-García, M. M., Mesa-Álvarez, A., Nikolic, O., Blanco-Lobato, P., Basta-Nikolic, M., de Llano-Ortega, R. M., Paredes-Velázquez, L., Nikolic, N., & Szewczyk-

- Bieda, M. (2019). Role of MRI in staging and follow-up of endometrial and cervical cancer: pitfalls and mimickers. *Insights into imaging*, 10, 1-22.
- Paudyal, R., Shah, A. D., Akin, O., Do, R. K., Konar, A. S., Hatzoglou, V., Mahmood, U., Lee, N., Wong, R. J., & Banerjee, S. (2023). Artificial intelligence in CT and MR imaging for oncological applications. *Cancers*, 15(9), 2573.
- Peitsidis, P., Vrachnis, N., Sifakis, S., Katsetos, C., Tsikouras, P., Antonakopoulos, N., Alexopoulos, E., & Kalmantis, K. (2022). Improving tissue characterization, differentiation and diagnosis in gynecology with the narrow-band imaging technique: A systematic review. *Experimental and Therapeutic Medicine*, 23(1), 1-16.
- Shetty, M. (2023). Acute pelvic pain: Role of imaging in the diagnosis and management. *Seminars in Ultrasound, CT and MRI*,
- Tarcha, Z., Konstantinoff, K. S., Ince, S., Fraum, T. J., Sadowski, E. A., Bhosale, P. R., Derenoncourt, P.-R., Zulfiqar, M., Shetty, A. S., & Ponisio, M. R. (2023). Added value of FDG PET/MRI in gynecologic oncology: a pictorial review. *Radiographics*, 43(8), e230006.
- Tonolini, M., Foti, P. V., Costanzo, V., Mammino, L., Palmucci, S., Cianci, A., Ettorre, G. C., & Basile, A. (2019). Cross-sectional imaging of acute gynaecologic disorders: CT and MRI findings with differential diagnosis—part I: corpus luteum and haemorrhagic ovarian cysts, genital causes of haemoperitoneum and adnexal torsion. *Insights into imaging*, 10, 1-25.
- Vara, J., Manzour, N., Chacon, E., Lopez-Picazo, A., Linares, M., Pascual, M. A., Guerrero, S., & Alcazar, J. L. (2022). Ovarian adnexal reporting data system (O-RADS) for classifying adnexal masses: a systematic review and meta-analysis. *Cancers*, 14(13), 3151.
- Virarkar, M., Ganeshan, D., Devine, C., Bassett Jr, R., Kuchana, V., & Bhosale, P. (2020). Diagnostic value of PET/CT versus PET/MRI in gynecological malignancies of the pelvis: A meta-analysis. *Clinical imaging*, 60(1), 53-61.
- Wang, H., Wang, X., Wang, P., Zhang, K., Yang, S., & Liu, Q. (2013). Ultrasound enhances the efficacy of chlorin E6-mediated photodynamic therapy in MDA-MB-231 cells. *Ultrasound in medicine & biology*, 39(9), 1713-1724.
- Wang, W., Chen, F., Kong, L., Guo, Y., Cheng, J., & Zhang, Y. (2020). Prospective evaluation of the accuracy of a training program in image recognition by narrow-band imaging guided hysteroscopy of endometrial neoplasms. *Gynecologic and Obstetric Investigation*, 85(3), 284-289.



Bölüm 6

The Rate of Subclinic Intraamniotic Infection in Preterm Labour and the Role of Amniotic Fluid Analyses in Determining Infection*

Gonul Ozer^{1,2} & Gokhan Bayhan³

* This book chapter is based on the author's medical speciality thesis entitled 'The Rate of Subclinical Intraamniotic Infection and the Role of Amniotic Fluid Analysis in the Detection of Infection in Preterm Labour', defended in 1999. The original thesis is available in the Dicle University Faculty of Medicine archive.

¹ MD., Memorial Sisli Hospital IVF and Reproductive Genetics Centre, Istanbul, Turkey
ORCID:0000-0003-2900-8623

² -Uskudar University, Department of Obstetrics and Gynaecology, Uskudar, Istanbul, Turkey

³ Prof. Dr., Süleyman Demirel University, Department of Obstetrics and Gynecology, Isparta, Turkey.
ORCID:0000-0003-0874-0778

Introduction

Preterm birth, defined as delivery before 37 weeks of gestation, is a leading cause of neonatal morbidity and mortality, accounting for approximately 13.4 million preterm births worldwide in 2020 (Ohuma et al., 2023). Complications of prematurity claimed the lives of approximately 900,000 children in 2019, and many survivors face long-term disabilities, including learning difficulties and sensory impairments (Perin et al., 2022). Globally, preterm birth remains the leading cause of death in children under 5 years of age, although three-quarters of these deaths could be prevented with cost-effective interventions (WHO, May 2023). Among the multifactorial causes of preterm birth, intra-amniotic infection is particularly significant in spontaneous preterm labour. Subclinical intra-amniotic infections, in which microbes invade the amniotic cavity without apparent symptoms, are increasingly seen as a significant cause of preterm birth. These infections can trigger inflammatory pathways, leading to uterine contractions, membrane rupture, and adverse neonatal outcomes. However, diagnosing subclinical intra-amniotic infections remains challenging due to their asymptomatic presentation and the limitations of traditional culture methods. Recent advancements in molecular diagnostics have improved our ability to detect these infections, uncovering greater microbial diversity and prevalence than previously understood. This chapter explores findings from my thesis, which investigated the rate of subclinical intra-amniotic infections in preterm labour and evaluated the role of amniotic fluid analysis in diagnosing these infections, emphasising its potential to enhance diagnostic accuracy and guide clinical management.

2. Pathophysiology of preterm labour and the role of intra-amniotic infection

Preterm birth, which can occur spontaneously or as a result of medical indications such as infections or maternal-fetal complications, remains a major contributor to neonatal morbidity and mortality. Subclinical intra-amniotic infection is a significant etiological factor in spontaneous preterm labour, playing a critical role in the initiation of the labour cascade (Goldenberg, Hauth, & Andrews, 2000). These infections trigger an inflammatory response, leading to the release of prostaglandins, cytokines such as interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF- α), and other mediators that stimulate uterine contractions, cervical ripening, and membrane rupture, ultimately precipitating labour (Romero et al., 2006). Amniotic fluid analysis remains a cornerstone in

diagnosing intra-amniotic infections with traditional methods, including microbial culture, Gram staining, leukocyte count, glucose levels, and lactate dehydrogenase (LDH) activity (Musilova et al., 2015; Romero, Espinoza, Chaiworapongsa, & Kalache, 2002; Tita & Andrews, 2010). Emerging biomarkers, particularly inflammatory proteins, offer promise for enhancing diagnostic sensitivity and specificity. Advances in molecular and proteomic techniques are paving the way for more accurate and timely identification of subclinical infections. A multidisciplinary approach involving obstetricians, microbiologists, and neonatologists is essential for optimising diagnostic strategies and clinical outcomes. As diagnostic and therapeutic technologies evolve, personalised approaches to amniotic fluid analysis may become the standard of care, enabling more targeted management of preterm labour and improving maternal and neonatal outcomes (Hobel, Dolan, Hindoyan, Zhong, & Menon, 2019; Singh et al., 2020).

Diagnostic Approaches for Detecting Subclinical Intra-Amniotic Infection

Bobbitt and Ledger were the first to identify a potential link between infection in the amniotic fluid and preterm labour in 1978 (Bobbitt & LEDGER, 1978). Since then, extensive research has been conducted to explore the role of intra-amniotic infection in preterm labour (Cháfer-Pericás et al., 2015; Conde-Agudelo, Papageorgiou, Kennedy, & Villar, 2011; Jung et al., 2021; Lee et al., 2015; Liu, Liu, Zhang, Zhu, & Feng, 2017). Reported rates of intra-amniotic infection in cases of preterm labour vary widely, ranging from 4% to 27%, as documented in studies conducted between 1981 and 2021 (Jung et al., 2021; Wallace & Herrick, 1981). These variations are primarily attributed to differences in the study populations and microbiological techniques. Detecting intra-amniotic infection remains a clinical challenge due to the late onset of overt symptoms, such as fever, uterine tenderness, foul-smelling vaginal discharge, and leukocytosis, which occur in only 12.5% of cases (Romero et al., 2014). Consequently, amniotic fluid culture is regarded as the gold standard for identifying microbial invasion. Additional diagnostic tests performed on amniotic fluid, such as Gram staining, leukocyte counts, and glucose level measurements, are commonly employed to improve diagnostic accuracy. Notably, most culture-positive cases are subclinical, underscoring the importance of early detection.

Timely diagnosis and treatment of intra-amniotic infections are crucial due to the heightened risks and complications faced by neonates born to mothers with culture-positive amniotic fluid compared to those born to mothers with culture-negative fluid. Culture-positive cases are also associated with increased

resistance to tocolytic treatment and a higher likelihood of early membrane rupture, further emphasising the clinical significance of effectively detecting and managing intra-amniotic infections (Lee et al., 2015; Torricelli et al., 2011).

Amniocentesis and laboratory results in preterm labour

Transabdominal amniocentesis was performed on 40 pregnant women diagnosed with preterm labor between 28 and 37 weeks of gestation. An average of 10 mL of amniotic fluid was collected from each participant. Of this, 2 mL was sent to the microbiology laboratory for Gram staining and culture, 2 mL to the hematology laboratory for leukocyte count, and 5 mL to the biochemistry laboratory for glucose level determination. Amniotic fluid cultures were conducted under both aerobic and anaerobic conditions, with a positive culture result observed in 5% of cases. Group B beta-hemolytic streptococci were identified in one patient, and *Peptostreptococcus* species were isolated in another. Gram staining was positive in both culture-positive cases. Amniotic fluid glucose concentrations were significantly lower in patients with culture-positive amniotic fluid compared to those with culture-negative results ($p < 0.05$). A glucose threshold value of 15 mg/dL was identified. In the culture-positive group, one patient had a glucose concentration of 15 mg/dL, while another had 16 mg/dL. In contrast, within the culture-negative group, only one patient exhibited a glucose level of 15 mg/dL, while 98% of patients had glucose levels exceeding 15 mg/dL. Leukocytes were undetectable in the amniotic fluid of both culture-positive cases. Furthermore, the efficacy of tocolysis was significantly reduced in culture-positive cases, with a duration ranging from 2 to 8 hours, compared to 23 to 1,184 hours in culture-negative cases.

The study revealed that only 5% of women with preterm labour had culture-positive infections. However, the observed biochemical alterations, particularly the reduced glucose concentrations in infected cases, underscore the importance of considering intra-amniotic infection as a potential contributor to preterm labour. These findings emphasize the need for vigilance in diagnosing and managing intra-amniotic infections, even in the absence of overt clinical signs.

Implications for Clinical Practice

The early detection of intra-amniotic infection has been a central focus of research due to its significant role in the aetiology of preterm labour. In the present study, the incidence of subclinical intra-amniotic infection in preterm labour was 5% (2 out of 40 cases). Among the culture-positive cases, one sample grew *beta-haemolytic streptococcus* under aerobic conditions, whereas the other yielded *Pepto streptococcus* under anaerobic conditions. A limitation of our study

was the use of only aerobic and anaerobic culture media, which may have restricted the detection of a broader range of microbial species. Romero et al. (1989) reported a prevalence of 9.1% using culture-based methods (Romero et al., 1989), whereas DiGiulio et al. found a higher prevalence of 15% using combined molecular and culture techniques (DiGiulio et al., 2008). Yoon et al. showed that intra-amniotic inflammation/infection complicates one-third of the patients with preterm labour (32%). Recent studies have highlighted the limitations of traditional culture methods in detecting intraamniotic infections associated with preterm labour. Conventional culture methods often fail to detect uncultivated or difficult-to-cultivate species, leading to underestimating infection rates. Culture-independent molecular techniques, such as PCR and 16S rRNA analysis, have identified additional bacterial species in culture-negative samples, including *Fusobacterium nucleatum* and *Leptotrichia* spp. (Han, Shen, Chung, Buhimschi, & Buhimschi, 2008). Recognising the role of subclinical infection in preterm birth may lead to new approaches for preventing premature birth and its associated complications (Gibbs, 2001). These findings emphasise the importance of combining molecular and culture methods for more accurate detection of intraamniotic infections and inflammation in preterm labour cases.

While amniotic fluid culture is considered the gold standard for confirming intra-amniotic infection, its results can take up to 48 h, prompting efforts to develop faster diagnostic methods. As a result, studies have focused on rapid diagnostic tools, such as Gram staining of amniotic fluid, measuring glucose levels in the fluid, and leukocyte counts.

Amniotic fluid glucose measurement is a simple and rapid diagnostic tool for identifying intra-amniotic infections, particularly in preterm labour. Recent studies have highlighted its potential utility as a biomarker. In our study, mean amniotic fluid glucose levels were reported to be significantly lower in culture-positive cases (15.5 mg/dL, range: 15–16 mg/dL) than in culture-negative cases (52.4 mg/dL, range: 15–102 mg/dL). A threshold value of 15 mg/dL has been suggested as the diagnostic cut-off for detecting intra-amniotic infection. The literature supports the sensitivity of decreased amniotic fluid glucose levels in identifying intrauterine infections. Some studies have emphasised that low glucose levels are more sensitive than Gram staining for detecting microbial invasion of the amniotic cavity (Ford & Genc, 2011; Zahorodnia, Bila, Antoniuk, & Tymoschuk, 2023). Mynti et al. indicated that reduced glucose concentrations are strongly associated with microbial invasion and histological chorioamnionitis (Myntti et al., 2016). In pregnancies complicated by preterm prelabour rupture of membranes (PPROM), amniotic fluid glucose levels have been shown to reliably

differentiate between various inflammatory and infectious conditions (Kacerovský et al., 2020). In another study, a glucose level of 10 mg/dL was found to be the optimal concentration for detecting intra-amniotic inflammation in PPRM pregnancies. Additionally, cases of foetal infection have been shown to have significantly reduced amniotic fluid glucose levels (Abehsera et al., 2014). Collectively, these findings underscore the value of amniotic fluid glucose as a diagnostic marker for intra-amniotic infection and inflammation in preterm labour. By providing rapid and sensitive detection, this measure facilitates early diagnosis and timely management, potentially improving maternal and neonatal outcomes (Cobo et al., 2019; Kacerovsky et al., 2020).

Gram staining has proven to be a practical and rapid diagnostic method for identifying intra-amniotic infection, particularly during preterm labour. In this study, positive amniotic fluid cultures were observed in two out of 40 patients who underwent amniocentesis, with Gram staining also yielding positive results in both culture-positive cases. This concordance highlights the sensitivity of Gram staining in detecting microbial presence, offering clinicians timely diagnostic insights that are essential for early intervention. Unlike culture methods, which require extended processing times, Gram staining delivers prompt results, facilitating immediate clinical decision-making (Romero et al., 2015). The diagnostic performance of Gram staining has been well documented in the literature. Fan et al. reported a sensitivity of approximately 65% and a specificity exceeding 99% for gram staining to detect intra-amniotic infection, demonstrating it as a reliable diagnostic tool, especially in cases of preterm labour with intact membranes (Fan, Liu, Yan, Peng, & Liu, 2020). This diagnostic utility is especially significant for subclinical infections, which often present without overt clinical symptoms.

When combined with additional diagnostic indicators, such as amniotic fluid glucose levels and leukocyte counts, Gram staining significantly enhances the precision of infection detection. Despite its high specificity, the potential for false negatives warrants the use of Gram staining along with other biochemical tests to ensure diagnostic accuracy. This integrative approach strengthens clinical decision making, particularly in pregnancies at risk for preterm delivery, where timely and accurate diagnosis is critical (Fan et al., 2020; Liu et al., 2017).

The presence of leukocytes in amniotic fluid as a marker for detecting subclinical intra-amniotic infection remains a contentious topic in the literature. In our study, leukocytes were not detected in two culture-positive cases. This finding contrasts with some studies reporting an increased presence of leukocytes in amniotic fluid in cases of preterm labour, particularly in preterm premature

rupture of membranes (PPROM) (Galaz et al., 2020; Helmig et al., 2002). Galaz et al. demonstrated that women with PPRM and positive amniotic fluid cultures exhibited higher levels of total leukocytes, neutrophils, monocytes/macrophages, and T cells. Helming et al. showed that neutrophil elastase (NE), a protease released during neutrophil activation, was significantly increased in cases of microbial invasion and preterm labour, while protective factors such as secretory leukocyte protease inhibitor (SLPI) were decreased during these processes. The researchers reported that this imbalance between inflammatory and anti-inflammatory mediators promotes tissue remodelling, cervical maturation, and membrane rupture, which are key events leading to preterm birth. Although intra-amniotic leukocytosis is a valuable marker for infection and inflammation, its diagnostic utility is enhanced when combined with other biomarkers such as amniotic fluid glucose, interleukins, and tumour necrosis factor-alpha (TNF- α) (Vrachnis et al., 2012). These findings underscore the importance of leukocytes and inflammatory mediators in amniotic fluid as potential biomarkers for detecting intra-amniotic infection and understanding the mechanisms underlying preterm labour. However, the absence of leukocytes in some culture-positive cases, as observed in our study, highlights the need for a multifaceted diagnostic approach that includes other markers, such as biochemical and molecular analyses, to improve diagnostic accuracy.

Tocolysis is widely employed to suppress preterm labour by inhibiting uterine contractions; however, its effectiveness is often compromised in the presence of intra-amniotic infections. In this study, all patients received intravenous ritodrine for tocolysis following amniocentesis. The mean duration of tocolysis was significantly shorter in culture-positive cases (5.00 ± 4.243 hours) than in culture-negative cases (263.763 ± 301.902 hours, $p < 0.001$). These findings underscore the influence of intra-amniotic infection on the limited efficacy of tocolytic agents in such cases. This observation aligns with that of previous studies. Torricelli et al. (evaluated the relationship between inflammatory and infectious risk factors, the response to prolonged tocolysis, and the timing of delivery in women presenting with preterm labor. Their findings indicated that higher rates of inflammatory and infectious risk factors were associated with delivery within 48 h of tocolysis, compared to those who delivered at least seven days after tocolysis (Torricelli et al., 2011). Similarly, Yoon et al. analysed 206 cases of preterm labour and found that the average duration of tocolysis was markedly reduced in culture-positive patients (20 h) compared to culture-negative cases (701 h). These results collectively highlight that intra-amniotic infection severely limits the ability of tocolysis to delay delivery (Yoon et al., 2001). Consistent

findings across studies suggest that intra-amniotic infection plays a pivotal role in triggering uterine contractions and promoting labour, thereby diminishing the efficacy of tocolytic interventions. Subclinical infections may exacerbate inflammation and lead to biochemical changes in the uterus and fetal membranes, which undermine the action of tocolytic agents. Thus, timely identification and management of intra-amniotic infections are essential for optimising outcomes in preterm labour. The use of tocolysis in such cases should be complemented with targeted antimicrobial therapy and close monitoring to effectively address the underlying infection and inflammation.

Conclusion

Understanding the role of subclinical intra-amniotic infection in preterm labour has significant clinical implications.

- **Early Diagnosis and Intervention:** Accurate and early detection of infection can guide clinical decision-making, including the use of antibiotics and the timing of interventions such as delivery or tocolysis.
- **Infection Management:** Clinicians should consider the possibility of subclinical infection in cases of preterm labour, even in the absence of clinical symptoms, and monitor amniotic fluid parameters accordingly..

Further research is needed to refine diagnostic methods and optimise treatment strategies. This chapter underscores the need for a comprehensive approach to diagnosing and managing preterm labour, with careful attention to the potential role of intra-amniotic infection.

Tablo I: Maternal characteristics of cases undergoing amniocentesis

	Culture-negative (n=38)	Culture-positive (n=2)	P-value
Maternal age Min-max Mean±SD	17-36 25.5 ± 2.5	22-26 24 ± 3.2	p> 0.05
Gravida Min-max Mean±SD	1-12 2.5 ± 0.8	1-5 3 ± 1.5	p> 0.05
Parity Min-max Mean±SD	0-11 1.3±0.9	0-4 2.0 ± 1	p> 0.05
Gestational week Min-max Mean±SD	29-36 33.6 ± 3.1	33-35 34 ± 3.8	p> 0.05

Table 2. Laboratory characteristics of amniocentesis cases

	Culture-negative (n=38)	Culture-positive (n=2)	P value
Effect of tocolysis(hour) Min-max Mean±SD	23-118 42.36±38	2-8 5±1.4	p<0.001
Amniotic fluid glucos level(mg/dl) Min-max Mean±SD	15-102 52.4±21.75	15-16 15.5±0.25	p<0.001
Glucose level,n(%) <15mg/dl >15mg/dl	1(2) 37(98)	1(50) 1(50)	p<0.001

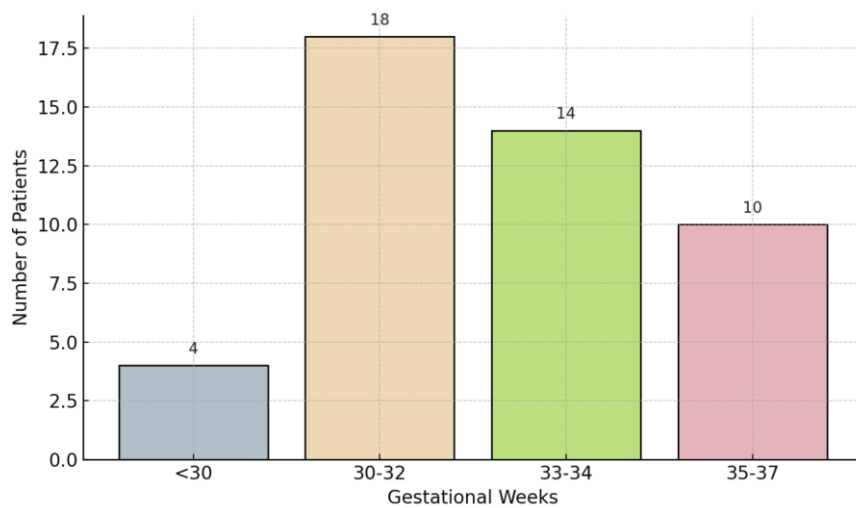


Figure 1. Distribution of patients by gestational weeks

REFERENCES

- Abehsera, D., Rodrigues, Y. V. S., Mingorance, J., Suarez, A., Magdaleno, F., & Bartha, J. L. (2014). Prediction and clinical relevance of pathologic patterns of injury associated with chorioamnionitis. *Placenta*, 35 1, 70-71.
- Bobitt, J., & LEDGER, W. J. (1978). Amniotic fluid analysis Its role in maternal and neonatal infection. *Obstetrics & Gynecology*, 51(1), 56-62.
- Cháfer-Pericás, C., Stefanovic, V., Sánchez-Illana, Á., Escobar, J., Cernada, M., Cubells, E., . . . Kuligowski, J. (2015). Novel biomarkers in amniotic fluid for early assessment of intraamniotic infection. *Free Radical Biology and Medicine*, 89, 734-740.
- Cobo, T., Ana, H., Montse, I., Aldecoa, V., Murillo, C., Amoedo, R., . . . Palacio, M. (2019). Targeting pregnancy management according to information of intra-amniotic infection/inflammation in women with preterm labor: 485. *American journal of obstetrics and gynecology*, 220, S324–S325.
- Conde-Agudelo, A., Papageorgiou, A., Kennedy, S., & Villar, J. (2011). Novel biomarkers for the prediction of the spontaneous preterm birth phenotype: a systematic review and meta-analysis. *BJOG: An International Journal of Obstetrics & Gynaecology*, 118(9), 1042-1054.
- DiGiulio, D. B., Romero, R., Amogan, H. P., Kusanovic, J. P., Bik, E. M., Gotsch, F., . . . Relman, D. A. (2008). Microbial prevalence, diversity and abundance in amniotic fluid during preterm labor: a molecular and culture-based investigation. *PLoS One*, 3(8), e3056. Retrieved from <https://pmc.ncbi.nlm.nih.gov/articles/PMC2516597/pdf/pone.0003056.pdf>
- Fan, S.-R., Liu, P., Yan, S.-M., Peng, J.-Y., & Liu, X.-P. (2020). Diagnosis and management of intraamniotic infection. *Maternal-Fetal Medicine*, 2(04), 223-230.
- Ford, C., & Genc, M. R. (2011). *Optimized amniotic fluid analysis in patients suspected of intrauterine infection/inflammation*. Paper presented at the Journal of Perinatal Medicine.
- Galaz, J., Romero, R., Slutsky, R., Xu, Y., Motomura, K., Para, R., . . . Kacerovsky, M. (2020). Cellular immune responses in amniotic fluid of women with preterm prelabor rupture of membranes. *Journal of Perinatal Medicine*, 48(3), 222-233. Retrieved from <https://pmc.ncbi.nlm.nih.gov/articles/PMC7147947/pdf/nihms-1563244.pdf>
- Gibbs, R. S. (2001). The relationship between infections and adverse pregnancy outcomes: an overview. *Annals of periodontology*, 6 1, 153-163.
- Goldenberg, R. L., Hauth, J. C., & Andrews, W. W. (2000). Intrauterine infection and preterm delivery. *New England Journal of Medicine*, 342(20), 1500-1507. Retrieved from https://www.nejm.org/doi/10.1056/NEJM200005183422007?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

- Han, Y. W., Shen, T., Chung, P., Buhimschi, I. A., & Buhimschi, C. S. (2008). Uncultivated Bacteria as Etiologic Agents of Intra-Amniotic Inflammation Leading to Preterm Birth. *Journal of Clinical Microbiology*, 47, 38 - 47. Retrieved from <https://pmc.ncbi.nlm.nih.gov/articles/PMC2620857/pdf/1206-08.pdf>
- Helmig, B. R., Romero, R., Espinoza, J., Chaiworapongsa, T., Bujold, E., Gomez, R., . . . Uldbjerg, N. (2002). Neutrophil elastase and secretory leukocyte protease inhibitor in prelabor rupture of membranes, parturition and intra-amniotic infection. *J Matern Fetal Neonatal Med*, 12(4), 237-246. doi:10.1080/jmf.12.4.237.246
- Hobel, C. J., Dolan, S. M., Hindoyan, N. A., Zhong, N., & Menon, R. (2019). History of the establishment of the Preterm Birth international collaborative (PREBIC). *Placenta*, 79, 3-20. Retrieved from <https://www.sciencedirect.com/science/article/abs/pii/S0143400419300165?via%3Dihub>
- Jung, E., Romero, R., Yoon, B. H., Theis, K. R., Gudicha, D. W., Tarca, A. L., . . . Yeo, L. (2021). Bacteria in the amniotic fluid without inflammation: early colonization vs. contamination. *Journal of Perinatal Medicine*.
- Kacerovský, M., Holečková, M., Štěpán, M., Gregor, M., Vescicik, P., Leško, D., . . . Musilová, I. (2020). Amniotic fluid glucose level in PPRM pregnancies: a glance at the old friend. *The Journal of Maternal-Fetal & Neonatal Medicine*, 35, 2247 - 2259.
- Kacerovsky, M., Romero, R., Stepan, M., Stranik, J., Maly, J., Pliskova, L., . . . Musilova, I. (2020). Antibiotic administration reduces the rate of intraamniotic inflammation in preterm prelabor rupture of the membranes. *American journal of obstetrics and gynecology*, 223(1), 114.e111-114.e120. doi:<https://doi.org/10.1016/j.ajog.2020.01.043>
- Lee, S., Park, J., Norwitz, E., Oh, S., Kim, E., Kim, S., . . . Jun, J. (2015). Mid-trimester amniotic fluid pro-inflammatory biomarkers predict the risk of spontaneous preterm delivery in twins: a retrospective cohort study. *Journal of Perinatology*, 35(8), 542-546.
- Liu, Y., Liu, Y., Zhang, R., Zhu, L., & Feng, Z. (2017). Early- or mid-trimester amniocentesis biomarkers for predicting preterm delivery: a meta-analysis. *Ann Med*, 49(1), 1-10. doi:10.1080/07853890.2016.1211789
- Musilova, I., Kutová, R., Pliskova, L., Stepan, M., Menon, R., Jacobsson, B., & Kacerovsky, M. (2015). Intraamniotic inflammation in women with preterm prelabor rupture of membranes. *PLoS One*, 10(7), e0133929. Retrieved from <https://pmc.ncbi.nlm.nih.gov/articles/PMC4514652/pdf/pone.0133929.pdf>
- Myntti, T., Rahkonen, L., Tikkanen, M., Pätäri-Sampo, A., Paavonen, J., & Stefanovic, V. (2016). Amniotic fluid rapid biomarkers are associated with intra-amniotic infection in preterm pregnancies regardless of the membrane status. *Journal of Perinatology*, 36, 606-611. Retrieved from <https://www.nature.com/articles/jp201659>

- Ohuma, E. O., Moller, A.-B., Bradley, E., Chakwera, S., Hussain-Alkhateeb, L., Lewin, A., . . . Lavin, T. (2023). National, regional, and global estimates of preterm birth in 2020, with trends from 2010: a systematic analysis. *The Lancet*, 402(10409), 1261-1271. Retrieved from [https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(23\)00878-4.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(23)00878-4.pdf)
- Perin, J., Mulick, A., Yeung, D., Villavicencio, F., Lopez, G., Strong, K. L., . . . Liu, L. (2022). Global, regional, and national causes of under-5 mortality in 2000–19: an updated systematic analysis with implications for the Sustainable Development Goals. *The Lancet Child & Adolescent Health*, 6(2), 106-115.
- Romero, R., Espinoza, J., Chaiworapongsa, T., & Kalache, K. (2002). *Infection and prematurity and the role of preventive strategies*. Paper presented at the Seminars in Neonatology.
- Romero, R., Espinoza, J., Kusanovic, J. P., Gotsch, F., Hassan, S., Erez, O., . . . Mazor, M. (2006). The preterm parturition syndrome. *BJOG: An International Journal of Obstetrics & Gynaecology*, 113, 17-42.
- Romero, R., Miranda, J., Chaiworapongsa, T., Chaemsaitong, P., Gotsch, F., Dong, Z., . . . Kim, C. J. (2014). A novel molecular microbiologic technique for the rapid diagnosis of microbial invasion of the amniotic cavity and intra-amniotic infection in preterm labor with intact membranes. *American Journal of Reproductive Immunology*, 71(4), 330-358.
- Romero, R., Miranda, J., Kusanovic, J. P., Chaiworapongsa, T., Chaemsaitong, P., Martinez, A., . . . Shaman, M. (2015). Clinical chorioamnionitis at term I: microbiology of the amniotic cavity using cultivation and molecular techniques. *Journal of Perinatal Medicine*, 43(1), 19-36. Retrieved from <https://pmc.ncbi.nlm.nih.gov/articles/PMC5881909/pdf/nihms951614.pdf>
- Romero, R., Sirtori, M., Oyarzun, E., Avila, C., Mazor, M., Callahan, R., . . . Hobbins, J. C. (1989). Infection and labor V. Prevalence, microbiology, and clinical significance of intraamniotic infection in women with preterm labor and intact membranes. *American journal of obstetrics and gynecology*, 161(3), 817-824. doi:[https://doi.org/10.1016/0002-9378\(89\)90409-2](https://doi.org/10.1016/0002-9378(89)90409-2)
- Singh, N., Bonney, E., McElrath, T., Lamont, R. F., Shennan, A., Gibbons, D., . . . Rajl, H. (2020). Prevention of preterm birth: Proactive and reactive clinical practice—are we on the right track? *Placenta*, 98, 6-12. Retrieved from <https://www.sciencedirect.com/science/article/abs/pii/S0143400420302113?via%3Dihub>
- Tita, A. T., & Andrews, W. W. (2010). Diagnosis and management of clinical chorioamnionitis. *Clinics in perinatology*, 37(2), 339-354. Retrieved from <https://pmc.ncbi.nlm.nih.gov/articles/PMC3008318/pdf/nihms204875.pdf>
- Torricelli, M., Voltolini, C., Conti, N., De Bonis, M., Biliotti, G., Picciolini, E., & Petraglia, F. (2011). Inflammatory and infectious risk factors are associated with the response to tocolysis in patients with preterm labor. *The Journal of Maternal-Fetal & Neonatal Medicine*, 24, 43 - 46.

- Vrachnis, N., Karavolos, S., Iliodromiti, Z., Sifakis, S., Siristatidis, C., Mastorakos, G., & Creatsas, G. C. (2012). Review: Impact of mediators present in amniotic fluid on preterm labour. *In vivo*, 26 5, 799-812.
- Wallace, R. L., & Herrick, C. N. (1981). Amniocentesis in the evaluation of premature labor. *Obstetrics and gynecology*, 57(4), 483-486.
- Yoon, B. H., Romero, R., Moon, J. B., Shim, S.-S., Kim, M., Kim, G., & Jun, J. K. (2001). Clinical significance of intra-amniotic inflammation in patients with preterm labor and intact membranes. *American journal of obstetrics and gynecology*, 185(5), 1130-1136.
- Zahorodnia, O. S., Bila, V. V., Antoniuk, M. I., & Tymoschuk, K. V. (2023). Glucose level in amniotic fluid as a preclinical marker of chorioamnionitis. *Reproductive health of woman*.



Bölüm 7

From Ultrasound to MRI: Advances in Gynecological Imaging

Samet Kirat¹

¹ Kafkas University, Faculty of Medicine, Department of Obstetrics and Gynecology, Kars/Turkey
ORCID: 0000-0001-7262-4320

1. Introduction

Female patients frequently present to the emergency department with acute or subacute gynecologic symptoms. As clinical symptoms are often non-specific and physical examination findings may be limited in such cases, imaging modalities are critical for accurate and rapid diagnosis. Ultrasonography (USG) is widely used as a noninvasive first-line imaging modality and can rapidly detect many gynecologic and obstetric pathologies. Doppler USG provides real-time information on anatomical structures and blood vessels to guide needle placement, particularly during interstitial brachytherapy (Tonolini et al., 2019).

Magnetic resonance imaging (MRI) plays an important role in determining treatment plans and options, especially for malignant gynecologic pathologies. Its high soft tissue contrast and multiplanar imaging capability facilitate differential diagnosis. Dual-energy computed tomography (CT) is an innovative technology that improves diagnostic accuracy by simultaneously providing data from two different energy spectra (Foti et al., 2019). Furthermore, new techniques, such as molecular imaging and narrow-band imaging, offer advanced diagnostic possibilities in various clinical scenarios (Franco et al., 2023).

Adnexal pathologies, a frequent focus in gynecological emergencies, are generally categorized into three main groups: hemorrhagic conditions, pathologies associated with adnexal tumors, and infectious conditions. Hemorrhagic conditions include hemorrhagic ovarian cysts and ectopic pregnancies, whereas tumor-related pathologies include adnexal torsion and tumor rupture. Among infectious conditions, pelvic inflammatory diseases are particularly notable (Okazaki et al. 2022). Similarly, acute uterine pathologies are classified into two primary categories: acute complications of uterine fibroids and conditions leading to acute uterine bleeding. Acute fibroid complications include red degeneration, subserosal fibroid torsion, and uterine torsion, and acute uterine bleeding is commonly caused by retained products of conception and uterine arteriovenous malformations (Gopireddy et al., 2022).

Prompt and accurate diagnosis is important to prevent infertility and potentially life-threatening complications. USG is usually the first choice; however, in cases where the diagnosis remains unclear, CT and MRI provide additional information to support differential diagnosis. MRI provides a highly accurate differential diagnosis, especially in complex cases such as adnexal masses and leiomyomas (Shetty, 2023).

Artificial intelligence (AI) is increasingly used in gynecologic imaging. AI algorithms facilitate image analysis, quality assurance, and automation processes.

These technologies have the potential to improve diagnostic accuracy in repetitive tasks, such as USG (Lei et al., 2021). Moreover, AI-based applications in CT and MRI data support clinical decision-making processes by enriching image analytics (Paudyal et al., 2023). Radiologists play a vital role in the diagnosis and management of gynecologic emergencies. The effective use of imaging modalities increases diagnostic accuracy and facilitates the implementation of appropriate treatment approaches.

2. Ultrasonography (USG)

USG is widely regarded as the first-line imaging modality for women presenting with pelvic pain, whether acute or chronic, owing to its ability to rapidly and effectively diagnose a wide range of gynecologic and obstetric conditions. However, pelvic pain often presents diagnostic challenges, as it can overlap with symptoms associated with gynecologic, gastrointestinal, and genitourinary pathologies. This overlap can complicate clinical evaluation, necessitating the use of additional imaging modalities, such as MRI or CT, in cases where USG results are inconclusive. This is particularly important in pregnant patients, where accurate and noninvasive diagnostic methods are crucial (Foti et al., 2019).

Gynecologic advancements in imaging have significantly impacted clinical outcomes, particularly in brachial therapy for cervical cancer. The incorporation of MRI into brachytherapy protocols has markedly improved the accuracy of implant placement, enhanced local tumor control, and reduced associated toxicity. Despite these advancements, global disparities in the access to advanced imaging modalities have persisted. Affordable and portable imaging techniques are urgently required to address these inequities. USG, which is already a standard imaging modality in prostate cancer brachytherapy, is a cost-effective and accessible alternative; however, its application in gynecologic brachytherapy remains limited (Mohsen & Auda, 2024).

Concerns regarding the potential thermal and mechanical effects of USG on embryonic and fetal development have been a topic of discussion. Advances in USG technology in recent years have significantly improved imaging quality, making it an indispensable tool for the primary diagnosis of gynecologic cancers, evaluation of tumor extension, and monitoring treatment responses. When performed by experienced sonographers, USG is both safe and reliable, and offers critical insights into disease progression and therapeutic efficacy (Shetty, 2023).

Doppler USG, a specialized application of USG, plays an essential role in guiding needle placement during gynecological brachytherapy by providing real-

time visualization of anatomical structures and vascular systems. While its high sensitivity to macro- and microvascular flow offers substantial advantages in assessing pelvic organs and pregnancy, it is recommended that Doppler USG usage in the first trimester be minimized and limited to the shortest duration necessary to mitigate any potential risks to embryonic or fetal health (Cortellaro et al., 2019).

Both contrast-enhanced and non-contrast-enhanced Doppler USG have proven to be highly valuable in differentiating benign from malignant lesions, underscoring their utility in modern gynecological and obstetric practice. Emerging ultrasonographic techniques are anticipated to further enhance diagnostic accuracy and clinical decision-making in this field (Franco et al., 2023). Among these, transvaginal color Doppler USG is particularly notable for its role in the detection and diagnosis of recurrent pelvic tumors associated with chronic pain. When combined with transvaginal grayscale USG, it provides a comprehensive imaging approach, offering superior sensitivity and specificity for the evaluation of recurrent or complex lesions (Basta Nikolic et al., 2021).

3. Transvaginal Ultrasonography (TVUS)

TVUS plays a pivotal role in the evaluation and management of ovarian abnormalities owing to its high diagnostic accuracy and noninvasive nature. A large-scale study conducted within the University of Kentucky Ovarian Cancer Screening Program assessed the prevalence, incidence, persistence, and resolution of ovarian abnormalities using serial TVUS. This study involved 39,337 women and included 221,576 TVUS examinations, with 81% of the participants having normal results and 17% demonstrating abnormal findings. Notably, ovarian cysts were observed more frequently in premenopausal women, with a prevalence of 35% and an incidence of 15%, compared to a prevalence of 17% and an incidence of 8% in postmenopausal women. Among the abnormal findings, 63% resolved spontaneously in subsequent TVUS evaluations, while 10% of the initially normal cases developed abnormalities during follow-up. Abnormalities were categorized as single-chamber cysts (11.5%), septate cysts (9.8%), cysts containing solid areas (7.1%), and solid masses (1.8%). Surgical intervention was required in 557 participants, of whom 85 were diagnosed with malignant conditions and 472 with benign findings. The study highlighted that a serial approach to TVUS increased the positive predictive value from 8% to 25%, underscoring its role in improving diagnostic precision and reducing false-positive results (Wang et al., 2013).

In a separate investigation evaluating gynecological pathologies in subfertile women, 1,558 women who underwent TVUS were examined. Pathologies were identified in 69.7% of the participants, with the most common findings being uterine fibroids (26.3%), polycystic ovaries (23.3%), endometriosis (11.4%), and benign ovarian cysts (7.8%). Among these, 76.6% of cases presented with a single pathology, whereas 23.4% demonstrated multiple abnormalities. The study emphasized the effectiveness of TVUS as a primary diagnostic tool for identifying gynecological pathologies in the subfertility population, enabling rapid and accurate detection of underlying conditions (Foo et al., 2021).

The diagnostic performance of the Ovarian-Adnexal Report Data System (O-RADS), a classification system for ovarian masses, was examined through a systematic review and meta-analysis. This analysis, encompassing 11 studies and 4,634 masses, demonstrated that the O-RADS achieved a sensitivity of 97% and a specificity of 77%. The system facilitated differentiation between benign and malignant lesions, significantly reducing unnecessary surgical interventions. The findings underscore the ability of TVUS, combined with standardized systems such as O-RADS, to enhance diagnostic accuracy while maintaining a noninvasive approach (Vara et al., 2022).

Another study explored the use of TVUS-guided aspiration as a minimally invasive alternative to surgery for simple ovarian cysts. Among 84 premenopausal and postmenopausal women treated with this technique, cyst recurrence was observed in 20.2%. Despite this, the method effectively reduced the need for surgical intervention. Additionally, TVUS demonstrated 100% diagnostic accuracy in evaluating the malignant potential of ovarian cysts, further establishing its reliability in clinical practice (Kostrzewa et al., 2019).

Collectively, these studies highlight the indispensable role of TVUS in gynecological evaluation. Its application in serial imaging provides high accuracy in identifying ovarian abnormalities and differentiating benign from malignant conditions. This approach not only reduces the need for surgical interventions but also enhances diagnostic performance, particularly in subfertility populations and high-risk groups. As a noninvasive, cost-effective, and reliable modality, TVUS remains integral to the comprehensive management of gynecological pathologies.

4. Magnetic Resonance Imaging (MRI)

MRI plays a pivotal role in the management of gynecological malignancies, encompassing diagnosis, staging, treatment planning, and follow-up. Its importance has grown with advancements in imaging protocols, enabling precise disease evaluation and aiding in the selection of appropriate therapeutic

strategies. The role of MRI in endometrial cancer has been extensively evaluated in a study highlighting the value of multiparametric MRI protocols, including T2-weighted imaging, diffusion-weighted imaging (DWI), and contrast-enhanced imaging. These protocols have been shown to effectively assess critical prognostic factors such as the depth of myometrial invasion, cervical invasion, and lymph node status. Furthermore, MRI has been recognised as a valuable tool for fertility-preservation approaches and as a guidance mechanism in patients who are unable to undergo surgery (Maheshwari et al., 2022).

The utility of MRI in cervical cancer staging is widely acknowledged. According to Otero-García et al., MRI offers high sensitivity and specificity in evaluating prognostic indicators, such as tumor size, parametrial invasion, and pelvic sidewall involvement, consistent with the revised 2018 FIGO staging system. Importantly, its negative predictive value in excluding parametrial invasion is critical for determining whether patients are suitable candidates for surgery or chemotherapy, thereby influencing treatment pathways (Otero-García et al., 2019).

In ovarian cancer, MRI has been proven to be instrumental in assessing the extent and location of peritoneal spread, thereby aiding decisions regarding cytoreductive surgery versus neoadjuvant chemotherapy. This application, as noted in previous research, is particularly effective with advanced techniques, such as diffusion-weighted imaging (DWI) and dynamic contrast-enhanced imaging (DCE-MRI). These modalities provide insights into the biological behavior of ovarian tumors, directly affecting treatment decisions and patient outcomes (Kido, 2020). The role of MRI extends to the evaluation of recurrent gynecological malignancies. Functional MRI techniques, including DWI and DCE-MRI, have demonstrated utility in monitoring treatment responses and identifying local recurrences in endometrial and cervical cancer. These techniques enable precise mapping of pelvic diseases and assessment of treatment eligibility, as emphasized in studies examining recurrent cancer scenarios (De Muzio et al., 2023).

Collectively, these studies underscore the indispensable role of MRI in the comprehensive management of gynecological cancers. By facilitating detailed evaluation of both local and distant disease spread, MRI not only guides therapeutic decisions but also contributes to improved long-term outcomes. Its integration into multidisciplinary oncology teams reinforces its position as a cornerstone in the care of patients with gynecologic malignancies.

5. Computed Tomography (CT)

CT plays a critical role in gynecologic imaging, particularly in cases where USG findings are inconclusive or when the lesion is extensive. In a study evaluating the diagnostic performance of CT in gynecologic emergencies, it was demonstrated that CT effectively identifies acute conditions, such as hemorrhagic ovarian cysts, adnexal torsion, pelvic inflammatory diseases, and cystic adenomyosis. Multidetector CT is frequently utilized in women of reproductive age, providing rapid and accurate diagnostic capabilities that are essential for effective treatment planning in cases of pelvic pain (Foti et al., 2019).

Advanced CT techniques, such as dual-energy CT (DECT), have been shown to significantly enhance diagnostic performance. Research has demonstrated that DECT improves the ability to differentiate between primary tumors and simple cystic lesions, as well as increases the detection rate of metastatic lesions, particularly in the liver and musculoskeletal system. These findings underscore the growing importance of DECT in the management of gynecological malignancies, offering more precise and comprehensive diagnostic results (Benveniste et al., 2020; Lee & Atri, 2019).

A meta-analysis further highlighted the role of CT in diagnosing acute pelvic inflammatory diseases, reporting 79% sensitivity and 99% specificity when using contrast-enhanced CT. This study emphasized that CT is a valuable alternative to invasive diagnostic methods, such as gynecological examination or laparoscopy, especially when standardized diagnostic criteria are applied. This finding reinforces its utility in both emergency and routine clinical settings (Okazaki et al. 2022).

The importance of CT in cervical cancer staging is widely acknowledged. It is particularly effective in identifying pelvic and para-aortic lymph node metastases and provides high accuracy in detecting distant metastases. These capabilities make CT indispensable in treatment planning for advanced cervical cancers. Furthermore, combining CT with transvaginal USG and MRI has been recommended to improve diagnostic accuracy and ensure comprehensive evaluation (Fischerova et al., 2024).

These studies collectively highlight the indispensable role of CT in the diagnosis and management of acute and chronic gynecological conditions. The integration of advanced technologies, such as dual-energy CT, enhances diagnostic precision, reduces the need for invasive procedures, and accelerates clinical decision making. As a rapid, accessible, and effective diagnostic tool, CT

continues to be a cornerstone for the evaluation of gynaecologic emergencies and malignancies.

6. Positron Emission Tomography (PET)

PET plays a vital role in the management of gynecological malignancies, enabling the integration of metabolic and anatomical data for accurate diagnosis, staging, restaging, treatment planning, and follow-up. Fluorodeoxyglucose (FDG)-PET/CT is a standardized imaging method widely used in this context, offering high sensitivity for the detection and assessment of malignancies (Dejanovic et al., 2021).

Despite its high sensitivity, the specificity of FDG-PET/CT can be limited owing to benign inflammatory processes and physiological variations. Hormonal factors, such as those influenced by the menstrual cycle and menopausal status, can alter FDG uptake and potentially lead to false-positive results. These findings underscore the importance of considering the clinical context when interpreting FDG-PET/CT findings to ensure diagnostic accuracy (Dejanovic et al., 2021).

The integration of FDG-PET with MRI has demonstrated enhanced diagnostic accuracy in gynecological cancers. Systematic reviews have indicated that FDG-PET/MRI outperforms PET/CT in evaluating endometrial, cervical, and ovarian cancers (Nguyen et al., 2020). FDG-PET/MRI is particularly effective for lymph node staging and tumor risk stratification. Additionally, its lower radiation exposure makes it a preferred option for younger patients who require repeat imaging (Nguyen et al., 2020).

FDG-PET/CT is superior to conventional imaging modalities for lymph node staging and distant metastasis detection. Studies have reported that this modality leads to changes in treatment plans in approximately 23% of cases, offering more precise guidance for therapeutic interventions. Its high negative predictive value (83.3%) for evaluating suspicious lymph nodes further enhances its utility in clinical decision-making (Al-Ibraheem et al., 2019).

The relationship between glucose metabolism and tumor aggressiveness in gynecological cancers is well established. FDG-PET/CT has demonstrated that poorly differentiated tumors with higher glucose uptake exhibit more aggressive biological behavior. In endometrial cancer, the strong correlation between glucose consumption and tumor grade highlights the prognostic value of FDG-PET/CT in assessing disease aggressiveness and guiding management strategies (Mititelu et al.).

These findings underscore the critical role of molecular imaging modalities, particularly FDG-PET/CT and FDG-PET/MRI, in the diagnosis and management of gynecological malignancies. By integrating metabolic and anatomical data, these advanced imaging techniques can improve diagnostic accuracy, optimize treatment planning, minimize unnecessary interventions, and enhance patient outcomes. The ability of these methods to provide detailed insights into tumor biology and staging makes them indispensable tools in modern oncological practice (Virarkar et al., 2020).

A meta-analysis evaluated the diagnostic performance of FDG-PET/CT and FDG-PET/MRI for gynecologic malignancies. The study demonstrated that PET/MRI had a higher patient-specific sensitivity than PET/CT (73.3% vs. 62.6%), although the difference was not statistically significant. Additionally, PET/MRI showed superior accuracy on a lesion-by-lesion basis and offered better classification of malignancies owing to its enhanced soft tissue contrast (Virarkar et al., 2020).

The staging of primary tumors, lymph node involvement, and recurrence evaluation in gynecologic cancers have significantly improved with FDG-PET/MRI. Studies have highlighted its superior diagnostic accuracy compared to FDG-PET/CT. Furthermore, its lower radiation dose makes it particularly advantageous for younger patients and those requiring long-term follow-up (Nguyen et al., 2020).

PET/MRI has been shown to be highly effective in detecting metastases, mapping recurrences, and assessing treatment responses. This method provides a superior evaluation of local tumor spread and lymph node involvement. Additionally, PET/MRI demonstrates high accuracy in distinguishing between benign and malignant tissues, underscoring its clinical utility in gynecological malignancies (Tarcha et al., 2023).

The roles of FDG-PET/CT and FDG-PET/MRI in the management of endometrial, cervical, and ovarian cancers have been comprehensively reviewed. Both modalities are recognized for their value in staging and prognostication. However, PET/MRI is emphasized as a safer option owing to its lower radiation exposure, which is particularly beneficial for pediatric and young female patients (Allahqoli et al., 2023).

The advantages of PET/MRI in diagnostic accuracy, treatment planning, and patient management are well documented in gynecologic oncology. This modality provides lower radiation exposure, superior soft-tissue resolution, and

higher diagnostic accuracy than PET/CT. These features establish PET/MRI as an indispensable tool in the modern management of gynecological cancers.

7. Narrow Band Imaging (NBI)

NBI is emerging as a valuable tool in gynecological endoscopy, particularly for the diagnosis of conditions such as endometrial lesions and endometriosis. By filtering light into narrow bands, NBI enhances the visualization of mucosal microstructures and capillaries, thereby increasing the detection rate of lesions. A systematic review demonstrated that NBI improves the specificity and sensitivity of hysteroscopy, laparoscopy, and colposcopy for detecting malignant and premalignant lesions. This review highlighted that NBI offers better diagnostic performance than conventional white-light endoscopy for endometrial and cervical lesions. However, the high cost of NBI equipment and the need for experienced personnel are significant barriers to its widespread clinical adoption (Peitsidis et al., 2022).

In the context of endometriosis, a meta-analysis reported that laparoscopic NBI provides higher diagnostic accuracy than conventional white-light imaging. NBI has been shown to identify lesions that are often missed during white-light imaging, thus enabling a more comprehensive evaluation of endometriosis. Despite these promising findings, the long-term impact of NBI on clinical outcomes and patient management remains unclear, emphasizing the need for further research in this area (Maheux-Lacroix et al., 2020).

Training programs specifically designed for NBI-guided hysteroscopy have been shown to improve diagnostic accuracy. A study evaluating both experienced and inexperienced hysteroscopists revealed significant improvements in the detection of malignant endometrial lesions using NBI. Interestingly, a study found that experienced clinicians adapted to this technology with a relatively shorter learning curve, suggesting that expertise plays a crucial role in optimizing the benefits of NBI (Wang et al., 2020).

The use of NBI in endometriosis surgery has also been investigated. Clinical studies have reported that NBI enhances lesion detection rates when compared to three-dimensional (3D) white-light imaging and near-infrared imaging with indocyanine green (NIR-ICG). While NBI alone improves histological accuracy, particularly for pelvic lesions, combining it with 3D white-light imaging yields the best results. This combined approach underscores the complementary role of NBI in enhancing surgical outcomes in endometriosis (Lier et al., 2020).

The potential of NBI to improve the diagnostic accuracy of gynecologic endoscopy is well documented. By offering superior visualization of microstructures, it enables early and accurate detection of lesions, which is crucial for patient outcomes. However, NBI remains in the early stages of clinical application and requires support from larger randomized controlled trials to validate its efficacy. In addition to the need for robust evidence, the high cost of NBI systems and the steep learning curve of clinicians are significant limitations that currently restrict their widespread adoption in routine practice.

These findings highlight both the promise and challenges associated with NBI in gynecologic endoscopy. With ongoing advancements in technology and increasing clinical experience, NBI has the potential to become a cornerstone technique for the diagnosis and management of gynecologic conditions.

8. Conclusions

Imaging modalities are indispensable in the diagnosis, staging, and treatment planning of gynecological cancers, providing critical insights that optimize therapeutic strategies such as surgery, radiotherapy, and chemotherapy. Among these, MRI and FDG-PET/CT have complementary roles in clinical practice. These advanced imaging tools not only assess local and systemic disease spread but also contribute significantly to prognostication. The integration of artificial intelligence (AI) into imaging technologies has revolutionized this field by enabling faster and more precise evaluations.

MRI, renowned for its superior soft-tissue resolution, is considered the gold standard for local tumor staging in gynecologic oncology. In endometrial carcinoma, MRI plays a pivotal role in assessing myometrial invasion depth, cervical stromal involvement, and potential lymph node metastasis, which are key factors in surgical planning and the identification of high-risk patients. Conversely, FDG-PET/CT excels in the noninvasive detection of distant metastases and radiotherapy planning. It is particularly effective in determining tumor size and location in cervical cancer and resolving ambiguous imaging findings in ovarian cancer, especially when associated with elevated CA-125 levels (Nguyen et al., 2020).

USG, the first-line imaging modality for women presenting with acute or chronic pelvic pain, remains the cornerstone of gynecologic imaging. It is highly effective in diagnosing emergencies, such as hemorrhagic ovarian cysts, pelvic inflammatory diseases, and adnexal torsion. Doppler USG further enhances diagnostic capabilities by enabling real-time vascular assessment and guiding needle placement in procedures such as gynecologic interstitial brachytherapy.

Recent advancements in AI-powered ultrasound technologies have facilitated automated image interpretation and quality assurance, streamlining repetitive tasks, and improving efficiency (Maheshwari et al., 2022).

DECT offers a novel approach by simultaneously acquiring datasets of two distinct photon spectra, thereby enhancing the tissue composition analysis. This innovation improves the differentiation between malignant and benign lesions with high sensitivity for detecting primary and metastatic ovarian cancers. Furthermore, DECT provides significant advantages in evaluating liver and musculoskeletal metastases, making it a valuable tool for comprehensive cancer staging (Lee & Atri, 2019).

Molecular imaging has emerged as a transformative field in gynecological oncology, offering advanced diagnostic and therapeutic monitoring capabilities. FDG-PET/CT integrates metabolic and anatomical data to enhance staging accuracy, whereas newer technologies, such as PET/MR, combine low radiation exposure with superior tissue contrast. Molecular imaging also plays a crucial role in assessing treatment responses and evaluating minimally invasive surgical options (Virarkar et al., 2020).

NBI, which uses filtered light to enhance the visualization of mucosal microstructures and capillary networks, has shown promise in improving diagnostic accuracy, particularly in laparoscopy and hysteroscopy, for detecting endometrial lesions and endometriosis. However, its widespread adoption is limited by cost and the need for specialized training (Peitsidis et al., 2022).

In conclusion, advanced imaging modalities, such as MRI, FDG-PET/CT, DECT, USG, and NBI, have become integral to the management of gynecological cancers, reducing reliance on invasive interventions and refining treatment strategies. The incorporation of AI-enhanced imaging into clinical practice has further increased diagnostic precision and facilitated personalized treatment approaches. These technological advancements not only enhance clinical outcomes but also improve the quality of life of patients with gynecologic malignancies, underscoring their critical role in modern oncologic care.

References

- Al-Ibraheem, A., AlSharif, A., Abu-Hijlih, R., Jaradat, I., & Mansour, A. (2019). Clinical impact of 18F-FDG PET/CT on the management of gynecologic cancers: one center experience. *Asia Oceania Journal of Nuclear Medicine and Biology*, 7(1), 7.
- Allahqoli, L., Hakimi, S., Laganà, A. S., Momenimovahed, Z., Mazidimoradi, A., Rahmani, A., Fallahi, A., Salehiniya, H., Ghiasvand, M. M., & Alkatout, I. (2023). 18F-FDG PET/MRI and 18F-FDG PET/CT for the management of gynecological malignancies: a comprehensive review of the literature. *Journal of Imaging*, 9(10), 223.
- Basta Nikolic, M., Spasic, A., Hadnadjev Simonji, D., Stojanović, S., Nikolic, O., & Nikolic, D. (2021). Imaging of acute pelvic pain. *The British Journal of Radiology*, 94(1127), 20210281.
- Cortellaro, F., Perani, C., Guarnieri, L., Ferrari, L., Cazzaniga, M., Maconi, G., Wu, M. A., & Aseni, P. (2019). Point-of-care ultrasound in the diagnosis of acute abdominal pain. *Operative Techniques and Recent Advances in Acute Care and Emergency Surgery*, 383-401.
- De Muzio, F., Fusco, R., Simonetti, I., Grassi, F., Grassi, R., Brunese, M., Ravo, L., Maggialelli, N., D'ANIELLO, R., & Greco, F. (2023). Functional assessment in endometrial and cervical cancer: diffusion and perfusion, two captivating tools for radiologists. *European Review for Medical & Pharmacological Sciences*, 27(16).
- Dejanovic, D., Hansen, N. L., & Loft, A. (2021). PET/CT variants and pitfalls in gynecological cancers. *Seminars in Nuclear Medicine*,
- Fischerova, D., Frühauf, F., Burgetova, A., Haldorsen, I. S., Gatti, E., & Cibula, D. (2024). The role of imaging in cervical cancer staging: ESGO/ESTRO/ESP guidelines (update 2023). *Cancers*, 16(4), 775.
- Foo, X., Lukaszewski, T., Yasmin, E., & Mavrelos, D. (2021). P-727 Prevalence of ultrasound-detected gynaecological pathology in a One-Stop fertility clinic. *Human Reproduction*, 36(Supplement_1), deab130. 726.
- Foti, P. V., Tonolini, M., Costanzo, V., Mammino, L., Palmucci, S., Cianci, A., Ettorre, G. C., & Basile, A. (2019). Cross-sectional imaging of acute gynaecologic disorders: CT and MRI findings with differential diagnosis—part II: uterine emergencies and pelvic inflammatory disease. *Insights into imaging*, 10, 1-19.
- Franco, P. N., García-Baizán, A., Aymerich, M., Maino, C., Frade-Santos, S., Ippolito, D., & Otero-García, M. (2023). Gynaecological causes of acute pelvic pain: common and not-so-common imaging findings. *Life*, 13(10), 2025.
- Gopireddy, D. R., Virarkar, M., Kumar, S., Vulasala, S. S. R., Nwachukwu, C., & Lam-sal, S. (2022). Acute pelvic pain: A pictorial review with magnetic resonance imaging. *Journal of Clinical Imaging Science*, 12.

- Kido, A. (2020). Therapy Response Imaging in Gynecologic Malignancies. *Therapy Response Imaging in Oncology*, 159-176.
- Kostrzewa, M., Zając, A., Wilczyński, J. R., & Stachowiak, G. (2019). Retrospective analysis of transvaginal ultrasound-guided aspiration of simple ovarian cysts. *Advances in Clinical and Experimental Medicine*, 28(11).
- Lee, S. I., & Atri, M. (2019). 2018 FIGO staging system for uterine cervical cancer: enter cross-sectional imaging. *Radiology*, 292(1), 15-24.
- Lei, Y.-M., Yin, M., Yu, M.-H., Yu, J., Zeng, S.-E., Lv, W.-Z., Li, J., Ye, H.-R., Cui, X.-W., & Dietrich, C. F. (2021). Artificial intelligence in medical imaging of the breast. *Frontiers in Oncology*, 11, 600557.
- Lier, M. C., Vlek, S. L., Ankersmit, M., van de Ven, P. M., Dekker, J. J., Bleeker, M. C., Mijatovic, V., & Tuynman, J. B. (2020). Comparison of enhanced laparoscopic imaging techniques in endometriosis surgery: a diagnostic accuracy study. *Surgical endoscopy*, 34(1), 96-104.
- Maheshwari, E., Nougaret, S., Stein, E. B., Rauch, G. M., Hwang, K.-P., Stafford, R. J., Klopp, A. H., Soliman, P. T., Maturen, K. E., & Rockall, A. G. (2022). Update on MRI in evaluation and treatment of endometrial cancer. *Radiographics*, 42(7), 2112-2130.
- Maheux-Lacroix, S., Belanger, M., Pinard, L., Lemyre, M., Laberge, P., & Boutin, A. (2020). Diagnostic accuracy of intraoperative tools for detecting endometriosis: a systematic review and meta-analysis. *Journal of Minimally Invasive Gynecology*, 27(2), 433-440. e431.
- Mititelu, R., Spiridon, P. M., Mazilu, C., Mititelu, T., Sirbu, C. A., Cuzino, D., Calin, C., Mititelu, L., Jinga, M., & Radu, F. I. PET-CT with 18F-FDG in Gynecological Malignancies. Prognostic Significance of the Standardized Uptake Value. *Romanian Journal of*, 127(2), 162.
- Mohsen, M., & Auda, B. (2024). Imaging Modalities in Assessment of Gynecological Causes of Acute Pelvic Pain at Shifa Medical Complex: A Cross-sectional Study. *International Journal of Innovative Research in Medical Science*, 9(08), 469-475. <https://doi.org/10.23958/ijirms/vol09-i08/1942>
- Nguyen, N. C., Beriwal, S., Moon, C.-H., D'Ardenne, N., Mountz, J. M., Furlan, A., Muthukrishnan, A., & Rangaswamy, B. (2020). Diagnostic value of FDG PET/MRI in females with pelvic malignancy—a systematic review of the literature. *Frontiers in oncology*, 10, 519440.
- Okazaki, Y., Tsujimoto, Y., Yamada, K., Ariie, T., Taito, S., Banno, M., Kataoka, Y., & Tsukizawa, Y. (2022). Diagnostic accuracy of pelvic imaging for acute pelvic inflammatory disease in an emergency care setting: a systematic review and meta-analysis. *Acute Medicine & Surgery*, 9(1), e806.
- Otero-García, M. M., Mesa-Álvarez, A., Nikolic, O., Blanco-Lobato, P., Basta-Nikolic, M., de Llano-Ortega, R. M., Paredes-Velázquez, L., Nikolic, N., & Szewczyk-

- Bieda, M. (2019). Role of MRI in staging and follow-up of endometrial and cervical cancer: pitfalls and mimickers. *Insights into imaging*, 10, 1-22.
- Paudyal, R., Shah, A. D., Akin, O., Do, R. K., Konar, A. S., Hatzoglou, V., Mahmood, U., Lee, N., Wong, R. J., & Banerjee, S. (2023). Artificial intelligence in CT and MR imaging for oncological applications. *Cancers*, 15(9), 2573.
- Peitsidis, P., Vrachnis, N., Sifakis, S., Katsetos, C., Tsikouras, P., Antonakopoulos, N., Alexopoulos, E., & Kalmantis, K. (2022). Improving tissue characterization, differentiation and diagnosis in gynecology with the narrow-band imaging technique: A systematic review. *Experimental and Therapeutic Medicine*, 23(1), 1-16.
- Shetty, M. (2023). Acute pelvic pain: Role of imaging in the diagnosis and management. *Seminars in Ultrasound, CT and MRI*,
- Tarcha, Z., Konstantinoff, K. S., Ince, S., Fraum, T. J., Sadowski, E. A., Bhosale, P. R., Derenoncourt, P.-R., Zulfiqar, M., Shetty, A. S., & Ponisio, M. R. (2023). Added value of FDG PET/MRI in gynecologic oncology: a pictorial review. *Radiographics*, 43(8), e230006.
- Tonolini, M., Foti, P. V., Costanzo, V., Mammino, L., Palmucci, S., Cianci, A., Ettorre, G. C., & Basile, A. (2019). Cross-sectional imaging of acute gynaecologic disorders: CT and MRI findings with differential diagnosis—part I: corpus luteum and haemorrhagic ovarian cysts, genital causes of haemoperitoneum and adnexal torsion. *Insights into imaging*, 10, 1-25.
- Vara, J., Manzour, N., Chacon, E., Lopez-Picazo, A., Linares, M., Pascual, M. A., Guerrero, S., & Alcazar, J. L. (2022). Ovarian adnexal reporting data system (O-RADS) for classifying adnexal masses: a systematic review and meta-analysis. *Cancers*, 14(13), 3151.
- Virarkar, M., Ganeshan, D., Devine, C., Bassett Jr, R., Kuchana, V., & Bhosale, P. (2020). Diagnostic value of PET/CT versus PET/MRI in gynecological malignancies of the pelvis: A meta-analysis. *Clinical imaging*, 60(1), 53-61.
- Wang, H., Wang, X., Wang, P., Zhang, K., Yang, S., & Liu, Q. (2013). Ultrasound enhances the efficacy of chlorin E6-mediated photodynamic therapy in MDA-MB-231 cells. *Ultrasound in medicine & biology*, 39(9), 1713-1724.
- Wang, W., Chen, F., Kong, L., Guo, Y., Cheng, J., & Zhang, Y. (2020). Prospective evaluation of the accuracy of a training program in image recognition by narrow-band imaging guided hysteroscopy of endometrial neoplasms. *Gynecologic and Obstetric Investigation*, 85(3), 284-289.



Bölüm 8

Pelvic Girdle Pain in Pregnancy and Pelvic Region Anatomy

Nihan Erdoğan Atalay¹

¹Opr.Dr. Bolu İzzet Baysal Devlet Hastanesi, BOLU/TÜRKİYE
ORCID: 0000-0002-4905-7425

Pelvic girdle pain has been known for centuries. Symphysis pubis dysfunction was mentioned by Hippocrates in his “Dysjunctio Pelvica” theory. In the 20th century, the first estimates of the frequency of pelvic girdle pain in pregnancy were made. In Norway, Skajaa found that 31 out of 185 women (16.8%) had “painful loosening of the symphysis and sacroiliac joints” at the end of pregnancy.

Pelvic girdle pain (PGP) is characterized by pain between the posterior iliac crest and the gluteal fold, especially around the sacroiliac joints (SIJ). The pain may radiate posteriorly to the thigh and may be associated with or separate from the symphysis pubis. The pain is intermittent and intermittent. It has been shown that pain can be triggered by activities of daily living such as standing, walking or sitting. Lumbopelvic pain increases both during the day and as the pregnancy progresses. Pelvic girdle pain typically begins at the end of the first trimester and peaks between 24 and 36 weeks. It usually resolves spontaneously within 6 months postpartum. However, in approximately 10% of women, pain may persist for 2 years after delivery.

There are different names used in the literature for pelvic girdle pain and pregnancy-related low back pain. These include symphysis pubis dysfunction, pelvic girdle pain, lumbopelvic pain, pelvic girdle relaxation, pelvic insufficiency, pelvic arthropathy, back pain during pregnancy, prenatal pelvic pain, symptomatic pelvic girdle relaxation, pregnancy-induced pelvic pain, pelvic joint relaxation during pregnancy, symphysiolysis and pelvic instability.

Low back pain is defined as pain and discomfort felt below the costae and above the lower gluteal folds and may radiate into the leg. Lumbar pain is defined as pain and discomfort felt superficially between the erector spinae from the last thoracic spinous process to the first sacral spinous process.

Lumbopelvic pain is defined as a combination of pelvic girdle pain and low back pain. In the presence of both low back pain and pelvic pain, the term “pregnancy-related lumbopelvic pain” is recommended. The use of the term “pelvic girdle pain” instead of “pelvic pain” indicates that the pain is musculoskeletal rather than gynecologic in origin.

1. Pelvic Girdle Anatomy

The pelvic girdle is a closed osteoarticular ring consisting of the bony structure including the two coccyx bones, sacrum, coccyx and two femurs

and the sacroiliac joints, sacrococcygeal joint, intercoccygeal joint, symphysis pubis and hip joints. The pelvic girdle supports the abdomen and lower pelvic organs and also provides a dynamic connection between the vertebral column and the lower extremities.

Bone Structures:

The pelvis, which forms the connection of the axial skeleton between the lower extremities, continues in the trunk with the lumbar bones. The pelvis consists of two coccyx bones and the sacrum to which the coccyx is attached. Each coccyx consists of three bones: ilium, ischium and pubis. The ilium is a fan-like bone structure that forms the superior part of the coccyx. The spina iliaca anterior superior (SIAS) and spina iliaca posterior superior (SIPS) form the two ends of the crista iliaca. Inferior to the SIPS, the ilium curves irregularly and this is usually the site of the sacroiliac joint. The articular surface where the ilium articulates with the sacrum is L-shaped.

The ischium forms the inferolateral third of the coccyx. The tuberositas ischium is a roughened area inferior to the ischial body and is the attachment site for strong muscles and ligaments. Superior to the tuberosity ischium, the ischial spine extends medially and this projection provides an attachment point for ligaments and ligaments. The pubis forms the inferomedial aspect of the coxa. The pubis articulates with the pubis of the opposite side through the symphysis pubis configuration. Inferiorly, the inferior pubic ramus protrudes posterolaterally to join the ischium on the medial aspect of the obturator foramen. The lateral surface of the pubis is directed towards the lower limb and provides the attachment point for many of the medial muscles of the thigh. The acetabulum is a hemispherical structure formed by the fusion of the three bones that form the coccyx. The lunate surface represents the articular portion of the acetabulum, while the extra-articular portion represents the acetabular fossa.

The sacrum consists of five fused sacral vertebrae. It lies between the two coccyx bones and is a large triangular bone. It is the center of gravity in the transverse plane, the keystone of the pelvis and the foundation of the spine. There are 3 deep fossae in the lateral crests of the S1, S2 and S3 vertebrae. These contain the connections of the interosseous sacroiliac ligament. The surface where the sacrum articulates with the ilium is L-shaped like the ilium.

The coccyx is a bone composed of four fused coccygeal segments, the first of which is separate. It is roughly triangular in shape with the base of the triangle articulating with the S5 vertebra.

The femur, another element of the pelvic girdle, is an appendicular skeletal bone that attaches to the pelvis at the acetabulum. The inclination angle between the anatomical axis of the femoral head and neck and the anatomical axis of the femoral shaft and the anteversion angle between the femoral neck and the frontal plane are clinically highly variable and should be carefully examined. This variability may be reflected in the range of motion in the hip joint.

Joints:

The joints that make up the pelvic girdle are the sacroiliac joint, sacrococcygeal joint, intercoccygeal joint, symphysis pubis and hip joint.

The sacroiliac joint is classified as a diarthrosis or synovial joint. The sacral surface is covered with hyaline cartilage and the iliac surface with fibrocartilage tissue. The depth of the articular cartilage varies between joints. As in synovial joints, it is supported by strong ligaments and fascia. Ligaments providing support to the sacroiliac joint are ventral sacroiliac ligament, interosseous sacroiliac ligament, long dorsal sacroiliac ligament, sacrotuberous ligament, sacrospinous ligament and iliolumbar ligament. Ligaments supporting the sacrococcygeal joint are the ventral sacrococcygeal ligament, dorsal sacrococcygeal ligament and lateral sacrococcygeal ligament.

The first two segments of the intercoccygeal joint are separated by a fibrocartilaginous disc, and while the joint is a symphyseal joint in young people, it ossifies with aging and rarely remains synovial. The symphysis pubis joint contains a fibrocartilaginous disc and does not contain synovial tissue or joint fluid. It is called symphysis joint. The bony surfaces are covered with a thin layer of hyaline cartilage and separated by a fibrocartilaginous disc. Superior pubic ligament, inferior arcuate ligament, posterior pubic ligament and anterior pubic ligament are the ligaments supporting this joint.

The hip joint is a synovial joint. The femoral head forms roughly two-thirds of a sphere. The lunate surface of the acetabulum is covered with hyaline cartilage, while the extra-articular acetabular fossa is covered with areolar tissue and synovium. The joint capsule covers the joint and most of the femoral neck. Ligaments supporting the joint include the iliofemoral ligament, pubofemoral ligament, ischiofemoral ligament and femoral arcuate ligament. Ligamentum teres and transverse acetabular ligament are intra-articular ligaments.

Joint range of motion is small in the sacroiliac joint and symphysis pubis. Movement in one joint can affect other joints in different ways. The increase in estrogen, progesterone and relaxin hormone levels during pregnancy plays a major role in increasing the laxity of pelvic girdle joints.

Muscles:

The muscles that support the pelvic girdle include the transversus abdominis, multifidus, ischiococcygeus, piriformis, levator ani, diaphragm, external oblique, internal oblique, rectus abdominis, pyramidalis and erector spinae muscles. The thoracodorsal fascia, pelvic fascia and leg fascia also support the pelvic girdle. It is thought that the congruence of the sacroiliac joint faces to each other can be ensured by the joint's shape, and its dynamic stability can be provided by muscle strength and the tone of the ligaments. The transversus abdominis, internal oblique, diaphragm and pelvic floor muscles work together to generate and control intra-abdominal pressure and thus increase the stability of the lumbar spine.

2. Pain Location

Classification of pelvic girdle pain according to pain localization;

Pelvic Girdle Syndrome: Pain involving bilateral sacroiliac joints, symphysis pubis, anterior and posterior pelvic girdle.

Symphysiolysis: Involves the symphysis pubis and anterior pelvic girdle. Symphysiolysis does not mean a true lysis, but the nomenclature is used by the Danish Health Authorities as a classification of pregnant women with pelvic pain.

Unilateral Sacroiliac Syndrome: Involves the unilateral sacroiliac joint and posterior pelvic girdle

Bilateral Sacroiliac Syndrome: Involves two sacroiliac joints and the posterior pelvic girdle.

Unspecified-Diverse: There is pain in one or more pelvic joints, but inconsistent objective findings from pelvic joints - for example, a history of pain from the pubic symphysis and objective findings from a sacroiliac joint.

3. Etiology

It has been suggested that pelvic girdle pain is usually associated with pregnancy, trauma or osteoarthritis. It is thought that mechanical, traumatic, hormonal, metabolic and degenerative factors play a role in the development of pelvic girdle pain. Pelvic girdle pain is caused by hormonal and biomechanical factors.

Hormonal Factors:

Relaxin provides relaxation of the pelvic girdle joints and sacroiliac ligaments and enlargement of the symphysis pubis. Differences in the degree of enlargement of the symphysis pubis in both transverse and superoinferior directions have been noted and the mean increase was found to be 5 mm. Accordingly, some studies have suggested that asymmetric enlargement of the sacroiliac joints may cause low back pain and pelvic pain.

Increased relaxin, a structurally insulin-like hormone, has also been associated with type 1 diabetes in pregnancy. Serum relaxin concentrations are higher in women with type 1 diabetes than in non-diabetic women at all stages of pregnancy.

Biomechanical Factors:

The pelvis is a formation that transmits body weight from the trunk to the legs. The pelvis ensures that the body load transferred to the joints is balanced by active, passive and neuromotor control systems. Optimal stabilization of the pelvis is required. Reaction forces acting along the joint are important to provide stability. Joint reaction force varies with gravity, shape of the joint surfaces, normal joint position, proprioceptive muscle reflexes, level of muscle contractions, increased ligament tension.

It is thought that pelvic girdle pain is associated with changes due to insufficiency and excessive motor activation of the lumbopelvic muscles and muscles around the pelvic girdle. In a review, individuals with pelvic girdle pain were found to have increased joint motion in their pelvic joints compared to healthy pregnant women. This increased motion in pelvic joints in pelvic girdle pain has been reported to decrease the efficiency of load transfer and increase the shear forces acting across the joint. It is thought that these increased shear forces may be responsible for the pain.

The contribution of the pelvic floor muscles (PFM) to the development of PGP during pregnancy is not fully understood. There are changes in natural pelvic asymmetry, contraction and relaxation patterns and muscle strength associated with hormonally increased ligament laxity. Muscle length changes and tenderness may occur in the pelvic floor muscles. Women with pelvic girdle pain have been reported to have deep pelvic floor muscle tenderness in both the levator ani and obturator interni muscles. Vaginally palpated pelvic floor muscle tenderness has not been described in pregnancy-related pelvic girdle pain.

4. Risk Factors

Vermani et al. categorized risk factors under four headings: psychosocial factors, pregnancy and childbirth and other factors. Other factors include low age at menarche, oral contraceptive use, smoking and social status. Psychosocial factors include stress level, job satisfaction and heavy working conditions. Risk factors related to pregnancy and delivery include high birth weight, prolonged second stage of labor, traumatic delivery, excessive hip abduction. Other risk factors include history of low back pain, pelvic girdle pain or pregnancy-related low back pain, menstrual low back pain, back trauma. Physical risk factors were age, body weight, height, body mass index, and number of births. Low back pain or pelvic girdle pain in the year before pregnancy, history of back, bone, joint disease or lower abdominal pain are among the causes of pregnancy-related pelvic girdle pain.

Some studies have reported that height, body weight, age and use of birth control pills do not constitute risk factors in pelvic girdle pain (80). Advanced age at menarche was considered a risk factor. Multiparity and high fetal weight increase the risk of pregnancy-related pelvic girdle pain. Smoking is a risk factor due to reduced blood flow to the tissues around the pelvic girdle joints. Working in a physically demanding job, working in uncomfortable positions in the workplace, and working in a cold environment increase the risk of pelvic girdle pain in women.

There is no association between educational level and the severity of pregnancy-related pelvic girdle pain. Although hormonal contraception is not considered a risk factor, the use of progestin intrauterine devices in the year before pregnancy has been associated with an increased risk of pelvic girdle syndrome in multiparous women. Mild pre-eclampsia, diabetes mellitus and gestational diabetes have been associated with symphysiolis. Regular exercise and exercise initiated before pregnancy reduces the risk of pregnancy-related pelvic girdle pain.

Psychological factors; depression, anxiety and stress levels were evaluated. Women with high levels of anxiety, depression and daily stress were more likely to have pelvic girdle syndrome and unilateral sacroiliac syndrome.

5. Prevalence

The diagnosis of pelvic girdle pain is most commonly confused with lumbopelvic pain. Vleeming et al. found the prevalence of pelvic girdle pain to be 20% in their study. In the control study, it was observed that approximately 45% of pregnant women had lumbopelvic pain, but approximately 20% of them were diagnosed with pelvic girdle pain.

6. Diagnosis

In order to make the diagnosis of pelvic girdle pain, other causes should be ruled out, a detailed history and physical examination should be performed. Pelvic girdle pain and low back pain should be differentiated. A personalized treatment plan should be made by determining the level of disability.

Underlying inflammatory diseases, infectious conditions, traumas, neoplastic diseases, degenerative or metabolic diseases should be questioned as they may cause low back pain. Unexplained weight loss, steroid use, history of malignancy, immune system disorders, drug use and fever should be investigated.

Spinal focal inflammatory findings and tenderness may suggest osteomyelitis. On spinal examination, a sticking in the joints suggests spondylolisthesis. The presence of neurologic symptoms such as bowel and bladder dysfunction, sensory, motor or reflex disturbances may suggest cauda equina syndrome, lumbar disc lesion, spinal stenosis or any other compressive lesion around the spinal cord. These diseases should also be ruled out in the examination.

Careful recording of the history of pain is important for accurate diagnosis. Prolonged standing, prolonged sitting, positional changes during sexual activity, factors that increase intra-abdominal pressure (coughing, sneezing, urination, defecation) should be investigated. Pain referral maps can be used for localization of pain. Visual analog scale can be used to determine the severity of pain. Leadbetter et al. described a scoring system for screening pregnant women. There were five basic symptoms in this system: Symphysis pubis pain when walking, standing on one leg, climbing stairs or turning in bed and a history of injury to the pelvis or lumbosacral region. Specific pain provocation tests can be used as a differential diagnosis in pelvic girdle pain. These tests have high specificity but lower sensitivity. A combination of all these tests is suitable for accurate diagnosis.

Women with pelvic girdle pain may have limping while walking, coordination disorders and slowing of gait. The diagnosis is based on symptoms and clinical examination. In addition, imaging techniques have rarely been used to confirm the diagnosis in severe cases.

Differentiation of Pelvic Girdle Pain and Pregnancy Low Back Pain

Differential diagnostic methods include pain site, character, intensity, disability rate and response to pain provocation tests. Pain referral maps can help to differentiate pelvic girdle pain and low back pain of pregnancy. In a typical pelvic girdle pain diagram, pain is concentrated below the spina iliaca posterior superior,

in the gluteal region, posterior thigh and groin. In contrast, the diagrammatic drawing of patients with pregnancy low back pain has been shown to concentrate pain in the lumbar region above the sacrum. However, according to the recommendations of the European Pelvic Girdle Pain research group, radiography, computed tomography scans and scintigraphy are insufficient for diagnosis.

References

1. Lee D. Anatomy. In: The Pelvic Girdle. 3rd ed. EDINBURGH, LONDON, NEW YORK, OXFORD, PHILADELPHIA, ST LOUIS, SYDNEY, TORONTO: Churchill Livingstone; 2004. p. 16–41.
2. Haslam J. Physiotherapy in Obstetrics and Gynecology. 2nd ed. Mantle J, Haslam J, Cardozo L, editors. 2004. 1–25 p.
3. Tortter M. Accessory sacro-iliac articulations. *Am J Phys Anthropol.* 1937;22(2):247–61.
4. Solonen KA. The Sacroiliac Joint in the Light of Anatomical, Roentgenological and Clinical Studies. *Acta Orthop Scand.* 1957;28(27).
5. Kotarinos RK, Chapter Three - Musculoskeletal Pelvic Anatomy. *Biomechanics of the Female Pelvic Floor*, Academic Press, [Internet]. 2006. 53–87 p.
6. Kapandji IA. The physiology of the joints I I: the lower. 2nd ed. Edinburg: Churchill Livingstone; 1970.
7. Bowen V, Cassidy JD. Macroscopic and microscopic anatomy of the sacroiliac joint from embryonic life until the eighth decade. *Spine (Phila Pa 1976).* 1981;6:602.
8. MacDonald GR, Hunt TE. Sacro-iliac joint observations on the gross and histological changes in the various age groups. *Can Med Assoc J.* 1951;66:157.
9. Fryette HH. Principles of osteopathic technique. Colorado: American Academy of Osteopathy; 1954.
10. Gamble JG, Simmons SC, Freedman M. The symphysis pubis. Anatomic and pathologic considerations. *Clin Orthop.* 1986;203:261.
11. Williams P, Bannister L, Berry M, Collins P, Dyson M, Dussek J. Nervous System. In: *Grays Anatomy*. 38th ed. Edinburg: Churchill Livingstone; 1995. p. 1266–74.
12. MacConaill MA, Basmajian J V. Muscles and movements; a basis for human kinesiology. 2nd ed. Krieger, New York; 1977.
13. Norén L, Ostgaard S, Johansson G, Ostgaard HC. Lumbar back and posterior pelvic pain during pregnancy: a 3-year follow-up. *Eur Spine J.* 2002;11(3):267–71.
14. Mens JM, Vleeming A, Snijders CJ, Stam HJ, Ginai AZ. The active straight leg raising test and mobility of the pelvic joints. *Eur Spine J.* 1999;8:468–73.
15. Snijders CJ, Vleeming A, Stoeckart R. Transfer of lumbosacral load to iliac bones and legs. Part 1: Biomechanics of self-bracing of the sacroiliac joints and its significance for treatment and exercise. *Clin Biomech.* 1993;

16. A, Buyruk HM, Stoeckart R, Karamursel S, Snijders CJ. An integrated therapy for peripartum pelvic instability: a study of the biomechanical effects of pelvic belts. *Am J Obs Gynecol*. 1992;166(4):1243–7.
17. Hodges P, Holm AK, Holm S, Ekström L, Cresswell A, Hansson T, et al. Intervertebral stiffness of the spine is increased by evoked contraction of transversus abdominis and the diaphragm: in vivo porcine studies. *Spine (Phila Pa 1976)*. 2003;28(23):2594–601.
18. Hodges P, Richardson C. Inefficient muscular stabilization of the lumbar spine associated with low back pain. A motor control evaluation of transversus abdominis. *Spine (Phila Pa 1976)*. 1996;21(22):2640–50.
19. Sapsford R, Hodges P. Contraction of the pelvic floor muscles during abdominal maneuvers. *Arch Phys Med Rehabil*. 2001;82(8):1081–8.
20. Critchley D. Instructing pelvic floor contraction facilitates transversus abdominis thickness increase during low-abdominal hollowing. *Physiother Res Int*. 2002;7(2):65–75.
21. Abramson D, Summer M, Wilson P. Relaxation of the pelvic joints in pregnancy. *Surg Gynecol Obs*. 1934;58:595–613.
22. Heyman J, Lundqvist A. The symphysis pubis in pregnancy and parturition. *Acta Obs Gynecol Scand*. 1932;191–226.
23. Skajaa K. Om svangerskapopbløtning av bekkenets ledd og smerter som følge herav. *Norsk magasin fo'r lægevidenskab*. 1929;90:713–29.
24. Walde J. Obstetrical and gynecological back and pelvic pains, especially those contracted during pregnancy. *Acta Obs Gynecol Scand Suppl*. 1962;2:11–53.
25. Rost CC, Jacqueline J, Kaiser A, Verhagen AP, Koes BW. Pelvic pain during pregnancy: a descriptive study of signs and symptoms of 870 patients in primary care. *Spine (Phila Pa 1976)*. 2004;29:2567–72.
26. Kristiansson P, Svardsudd K, von Schoultz B. Back pain during pregnancy: a prospective study. *Spine (Phila Pa 1976)*. 1996;21:702–9.
27. Kanakaris N, Roberts C, Giannoudis P. Pregnancy-related pelvic girdle pain: An update. *BMC Med*. 2011;9:15.
28. Van Tulder M, Becker A, Bekkering T, Breen A, Del Real MTG, Hutchinson A, et al. Chapter 3: European guidelines for the management of acute nonspecific low back pain in primary care. *Eur Spine J*. 2006;15(SUPPL. 2):169–91.
29. Merskey H. Classification of chronic pain: Descriptions of chronic pain syndromes and definitions of pain terms. *Pain*. 1986;Suppl 3:226.
30. Wu WH, Meijer OG, Uegaki K, Al E. Pregnancy- related pelvic girdle pain (PGP), I: terminology, clinical presentation, and prevalence. *Eur Spine J*. 2004;13:575–89.

31. Albert H, Godskesen M, Westergaard J. Incidence of four syndromes of pregnancy-related pelvic joint pain. *Spine (Phila Pa 1976)*. 2002;27(24):2831–4.
32. Brooke R. The sacroiliac joint. *J Anat*. 1924;58:299–305.
33. GOLD JC, EMERY FE. Relaxation of the symphysis pubis in monkeys. *West J Surg Obstet Gynecol*. 1953;61(1):24–6.
34. Wist A. Treatment of symphysiolysis with hydrocortisone-procaine injections. *Ann Chir Gynaecol Fenn*. 57(1):98–100.
35. MacLennan AH, Nicolson R, Green RC, Bath M. Serum relaxin and pelvic pain of pregnancy. *Lancet*. 1986;2(8501):243–5.
36. Björklund K, Naessén T, Nordström ML, Bergström S. Pregnancy-related back and pelvic pain and changes in bone density. *Acta Obs Gynecol Scand*. 1999;78(8):681–5.
37. Damen L, Buyruk HM, Guler-Uysal F, Lotgering FK, Snijders CJ, Stam HJ. Pelvic pain during pregnancy is associated with asymmetric laxity of the sacroiliac joints. *Acta Obs Gynecol Scand*. 2001;80:1019–24.
38. Hagen R. Pelvic girdle relaxation from an orthopaedic point of view. *Acta Orthop Scand*. 1974;45:550–63.
39. Buyruk HM, Stam HJ, Snijders CJ, Lameris JS, Holland WP, Stijnen TH. Measurement of sacroiliac joint stiffness in peripartum pelvic pain patients with Doppler imaging of vibrations (DIV). *Eur J Obstet Gynecol Reprod Biol*. 1999;83(2):159–63.
40. Damen L, Buyruk HM, Guler-Uysal F, Lotgering FK, Snijders CJ, Stam HJ. The prognostic value of asymmetric laxity of the sacroiliac joints in pregnancy-related pelvic pain. *Spine (Phila Pa 1976)*. 2002;27(24):2820–4.
41. Eberhard-Gran M, Eskild A. Diabetes mellitus and pelvic girdle syndrome in pregnancy—Is there an association? *Acta Obs Gynecol Scand*. 2008;87(10):1015–9.
42. Steinetz B, Whitaker P, Edwards J. Maternal relaxin concentrations in diabetic pregnancy. *Lancet*. 1992;340(8822):752–5.
43. Snijders CJ, Vleeming A, Stoeckart R. Transfer of lumbosacral load to iliac bones and legs. 2: Loading of the sacroiliac joints when lifting in a stooped posture. *Clin Biomech*. 1993;8:295–301.
44. Panjabi M. The stabilizing system of the spine. Part I:Function, dysfunction, adaptation, and enhancement. *J Spinal Dis*. 1992;5:383–389.
45. Vleeming A, Volkers AC, Snijders CJ, Stoeckart R. Relation between form and function in the sacroiliac joint. Part 2. Biomechanical aspects. *Spine (Phila Pa 1976)*. 1990;15:133–136.

46. O'Sullivan P, Beales D. Diagnosis and classification of pelvic girdle pain disorders --- Part 1: a mechanism based approach within a biopsychosocial framework. *Man Ther.* 2007;12:86–97.
47. Mens JMA, Pool-Goudzwaard, Annelies Stam HJ. Mobility of the pelvic joints in pregnancy-related lumbopelvic pain: a systematic review. *Obs Gynecol Surv.* 2009;64(3):200–8.
48. Fitzgerald CM, Mallinson T. The association between pelvic girdle pain and pelvic floor muscle function in pregnancy. *Int Urogynecol J.* 2012;23(7):893–8.
49. Pool-Goudzwaard AL, Sliker ten Hove MCPH, Vierhout ME, Mulder PH, Pool JJM, Snijders CJ, et al. Relations between pregnancy-related low back pain, pelvic floor activity and pelvic floor dysfunction. *Int Urogynecol J.* 2005;16(6):468–74.
50. Bjelland EK, Eberhard-Gran M, Nielsen CS, Eskild A. Age at menarche and pelvic girdle syndrome in pregnancy: a population study of 74 973 women. *BJOG.* 2011;118(13):1646–52.
51. et al. Wu WH, Meijer OG, Uegaki K, Mens JM, van Dieen JH, Wuisman PI. Pregnancy-related pelvic girdle pain (PPP), I: Terminology, clinical presentation, and prevalence. *Eur Spine J.* 2004;13(7):575–89.
52. Larsen EC, Wilken-Jensen C, Hansen A, Jensen D V, Johansen S, Minck H, et al. Symptom-giving pelvic girdle relaxation in pregnancy. I: Prevalence and risk factors. *Acta Obs Gynecol Scand.* 1999;78:105–10.
53. Albert H, Godskesen M, Korsholm L, Westergaard JG. Risk factors in pregnancy-related pelvic joint pain. *Acta Obs Gynecol Scand.* 2006;85(5):539–44.
54. Kumle M, Weiderpass E, Alsaker E, Lund E. Use of hormonal contraceptives and occurrence of pregnancy-related pelvic pain: a prospective cohort study in Norway. *BMC Pregnancy Childbirth.* 2004;4(1):11.
55. Berg G, Hammar M, Möller-Jensen J, Linden U, Thorblad J. Low back pain during pregnancy. *Obs Gynecol.* 1988;1:71–5.
56. Bjelland EK, Eskild A, Johansen R, Eberhard-Gran M. Pelvic girdle pain in pregnancy: The impact of parity. *Am J Obs Gynecol.* 2010;203(2):146–8.
57. Wergeland E, Strand K. Work pace control and pregnancy health in a population-based sample of employed women in Norway. *Scand J Work Env Heal.* 1998;24(3):206–12.
58. Mens J, Snijders CJ, Stam H. Diagonal trunk muscle exercises in peripartum pelvic pain: a randomized clinical trial. *Phys Ther.* 2000;80:1164–73.
59. Biering K, Aagaard NE, Olsen J, Hjollund N, Nybo AAM, Juhl M. Smoking and pregnancy-related pelvic pain. *BJOGInt J Obs Gy.* 2010;117(8):1019–26.

60. Bjelland EK, Kristiansson P, Nordeng H, Vangen S, Eberhard-Gran M. Hormonal contraception and pelvic girdle pain during pregnancy: a population study of 91,721 pregnancies in the Norwegian mother and child cohort. *Hum Reprod.* 2013;28(11):3134–40.
61. Lebel DE, Levy A, Holcberg G, Sheiner E. Symphysiolysis as an independent risk factor for cesarean delivery. *J Matern Fetal Neonatal Med.* 2010;23(5):417–20.
62. Gjestland K, Bo K, Owe KM, Eberhard-Gran M. Do pregnant women follow exercise guidelines? Prevalence data among 3482 women, and prediction of low-back pain, pelvic girdle pain and depression. *Br J Sport Med.* 2013;47(8):515–20.
63. Albert H, Godsken M, Korsholm L, Westergaard J. Risk factors in developing pregnancy-related pelvic girdle pain. *Acta Obstet Gynecol Scand.* 2006;85(5):539–44.
64. Meucci RD, Perceval AH, Lima DR, Cousin E, Marmitt LP, Pizzato P, et al. Occurrence of combined pain in the lumbar spine, pelvic girdle and pubic symphysis among pregnant women in the extreme south of Brazil. *Rev Bras Epidemiol.* 2020;23:e200037.
65. Hakansson A. Equality in health and health care during pregnancy. A prospective population-based study from southern Sweden. *Acta Obs Gynecol Scand.* 1994;73(9):674–9.
66. Gutke A, Ostgaard HC, Oberg B. Pelvic girdle pain and lumbar pain in pregnancy: a cohort study of the consequences in terms of health and functioning. *Spine (Phila Pa 1976).* 2006;31:149–55.
67. van Tulder M, Becker A, et al. Bekerring T. European guidelines on the management of acute nonspecific low back pain in primary care Available at: [http:// www.backpainurope.org/web/files/WG1_Guidelines.pdf](http://www.backpainurope.org/web/files/WG1_Guidelines.pdf) (accessed April 22, 2009). [European Commission Research Directorate General Web site]. 2004.
68. Stureson B, Uden G, Uden A. Pain pattern in pregnancy and “catching” of the leg in pregnant women with posterior pelvic pain. *Spine (Phila Pa 1976).* 1997;22:1880–3.
69. Leadbetter R, Mawer D, Lindow S. Symphysis pubis dysfunction: a review of the literature. *J Matern neonatal Med.* 2004;16(6):349–54.
70. Van Wingerden J, Vleeming A, Ronchetti I. Differences in standing and forward bending in women with chronic low back or pelvic girdle pain: indications for physical compensation strategies. *Spine (Phila Pa 1976).* 2008;33:334–41.
71. Wu WH, Meijer OG, Bruijn SM, Hu H, Van Dieën JH, Lamothe CJC, et al. Gait in pregnancy-related pelvic girdle pain: Amplitudes, timing, and coordination of horizontal trunk rotations. *Eur Spine J.* 2008;17(9):1160–9.

72. Wu W, Meijer OG, Lamothe CJ, Uegaki K, van Dieen JH, Wuisman PI, et al. Gait coordination in pregnancy: Transverse pelvic and thoracic rotations and their relative phase. *Clin Biomech.* 2004;19(5):480–8.
73. Ostgaard HC, Zetherstrom G, Roos-Hansson E, Svanberg B. Reduction of back and posterior pelvic pain in pregnancy. *Spine (Phila Pa 1976).* 1994;19:894–900.
74. Vleeming A, Albert HB, Ostgaard HC, Sturesson B, Stuge B. European guidelines on the diagnosis and treatment of pelvic girdle pain Available at: <http://www.backpaineurope.org/web/files/WG>. [European Commission Research Directorate General Web site]. 2005.