ISSN 0974-5319

Volume 4 Issue 10

IJCP

International Journal of Community Pharmacy

The Official Publication of ACPI

www.acpisouth.in

International Journal of Community Pharmacy
(ISSN-0974-5319)
The Official Publication of ACPI

EDITORIAL OFFICE
INTERNATIONAL JOURNAL OF COMMUNITY PHARMACY
The Official Publication of Association of Community Pharmacists of India [ACPI]
Secretariat & Communication Address
Sarada Vilas College of Pharmacy
Krishnamurthy Puram, Mysuru – 570004, Karnataka
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Table of Contents

Editorial

Need of Pharmaceutical Care Every Where

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Principal, Sarada Vilas College of Pharmacy, Mysuru, India.

Pharmaceutical care as a concept has moved the pharmacy profession from primarily focusing on the product (the drug itself) to the patient's drug therapy and how it should be optimized for the individual patient. The roles of pharmacists have evolved from product oriented, dispensing of medications to more patient-focused services such as the provision of pharmaceutical care, which includes the identification, prevention, and resolution of drug-related problems (DRPs). The term "pharmaceutical care" was defined by Hepler and Strand [1]. Basically, it is the responsible provision of drug therapy by the collaboration of a clinical pharmacist with the patient as well as other members of the healthcare team in designing, implementing and monitoring a therapeutic plan that will produce specific outcomes. DRPs are defined as "problems in the pharmacotherapy of the individual patient that actually or potentially interfere with desired health outcomes" [2]. Among the most common DRPs are: adverse drug reactions, drug choice problem, dosing problem, drug-use problem and interactions [3]. Other terminology such as pharmaceutical care issues (PCIs) has also been used [4]. Studies have shown that the cost associated with DRPs far exceed the cost of medications. Ernst & Grizzle [5] found that the estimated cost of morbidity and mortality due to DRPs was more than USD177.4 billion yearly. Wermeille and colleagues [6] reported PCIs resolved by community pharmacists in collaboration with medical general practitioners (GPs). Other studies reported a significant reduction in HbA_{1c} in community-based patients with diabetes provided pharmaceutical care by a pharmacist [7–12]. A systematic review conducted by Royal and colleagues [13] showed that pharmacist-initiated medication review was effective in reducing hospital admission by 36%. However, most of the studies on pharmaceutical care were conducted in countries such as Australia, the United Kingdom and the United States [6, 7, 14–20].

It is a practice in which the practitioner takes responsibility for a patient's drug-related needs, and is held accountable for this commitment. In the course of this practice, responsible drug therapy is provided for the purpose of achieving positive patient outcomes. However, it has always been challenging across the globe. Pharmacists are not only actively involved in the drug research, pharmaceutical care but also in pharmacovigilance. Global outbreak of Corona and challenges faced by pharmacists was very significant [21]. It is a practice in which the practitioner takes responsibility for a patient's drug-related needs, and is held accountable for this commitment. However, it has always been challenging across the globe. Pharmacists are not only actively involved in the drug research, pharmaceutical care but also in pharmacovigilance.

The revamping and release of 10th Volume of International Journal of Community Pharmacy, official journal of ACPI, is cherishable as it is being released during the International Conference on Pharmacovigilance, Pharmaceutical Care and Biomedical Research, 24-25 January 2023, Sarada Vilas College of Pharmacy, Mysuru. The editorial board is confident that the contribution from researchers and fellow pharmacists shall continue in future.

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The International Journal of Pharmacy Practice is theme based journal aiming at patient and health consumer safety by publishing quality papers. The first issue was released in the year 2008 . Due to some logistic issues the there is a gap in Publication. New editorial team is formed under the leadership of Dr Hanumanth Joshi ,Principal Sharadha Vilas College of Pharmacy Mysore. to promote pharmacy practice globally. I invite all the liked professionals to join hands with editorial board and contribute research and review articles. There are no page charges or any fee for publication of articles

The practice of medicine is teamwork of allied professions like physicians, pharmacists and nurses. Pharmacist occupies the central place indicating their role as interface between physicians, nurses and patients. There is always a felt need of relevant information regarding diseases, drugs, mode of administration, drug interactions and quality use of medicines due to apathy the infrastructure to alter the need of this vital issue has been ignored in our country. It has resulted in confusion, fear, and lack of transparency, irrational use of drugs in our ACPI. The drugs being double-edged swords need to be handled carefully to impart best of modern medicine to the suffering patients. It is the responsibility of pharmacy profession to establish norms and standards of pharmacy practice, and to provide with appropriate knowledge to the patients so that they become intelligent users of drugs.

It is call to all like-minded pharmacists registered pharmacists of this country from Kashmir to Kanyakumari to educate patients when they actually need education and information. Due to several Socioeconomic causes in developing countries the pharmacy practice and related services have not developed like in other developed world. This leaves lacunae in community pharmacy, which makes unsatisfactory services. This has been realized even by global agencies like WHO, FIP and Governments of developing nations. The FIP has prepared the documents like,

Guidelines for Pharmacy Practice Regulations 2015, Good Pharmacy Practice in Developing Countries.

Recommendations for step-wise implementation with an intention to establish and improve the standard pharmacy practice in developing countries. To fulfil the aspirations of the subjects from developing nations the need for organized efforts to be put for with the Association of community pharmacists comes into existence.

Pharmacy Profession is fragmented into different streams like Academic pharmacy, Industrial Pharmacy, Regulatory Pharmacy and Community Pharmacy. Pharmacists Unlike medical and nursing professions who directly in live contact with patients are recognized in the society. The community pharmacy which is public face of the profession, is hardly professional in any standards. The community pharmacy are nicknamed as retail traders who are engaged in handing over the prescribed medicines to the patients and earns trade margins provided by the manufacturer. Apart from dispensing medicines they cannot offer any information about drugs, and technical information as patients wants to know. Hence Medical stores and person who runs medical stores goes unnoticed by patients and health consumers. Due to this simplicity in medical store running ,other competitors are posing challenge by offering heavy discounts and door delivery through online pharmacy.

PPR 2015 ,A Registered Pharmacist (RPh) shall review the patient record and each prescription presented for supply for the purpose of promoting therapeutics appropriateness by identifying :

Over utilization or under utilization

Therapeutic duplication

Drug Disease interactions

Drug-drug interactions

Incorrect drug dosage or duration of drug treatment

Drug -allergy interactions

Correlation of availability of drugs(to avoid artificial shortage of drugs)

Clinical abuse/misuse.

All registered pharmacist can provide pharmaceutical care to patients in a community pharmacy or in home medication reviews. As per PPR 2015 regulations ,this is mandatory for all RPh to ensure patient safety.

Prof. Anantha Naik Nagappa
President, ACPI

Invited Editorial

The making of Indian Community Pharmacist 2023

V Gopal
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The power of community to create health is far greater than any physician, clinic or hospital – Mark Hyman

Among all the diseases, the credit goes to Covid 19, for making India focus back on health for all, in 2023. The dominating game changers of 2023 Indian health scenario are the human papillomavirus (HPV) and the flu vaccine, wearable gadgets for mental health, digital sleeping pills, discovering traditional health diet and renewed focus on preventive healthcare. The Indian public will be accessing these game changers through the community pharmacist, without the need of an appointment. The community pharmacist in India is transforming himself from a chemist to a pharmaceutical care provider with a help of a concoction of competence based learning and practical training in real job environment.

Ideally the six roles of community pharmacist are: 1. P**rocessing prescriptions, 2. checking for drug interactions, 3. dispensing medications with counselling, 4. disposing of medication, 5. providing appropriate health advice and 6. promotion of healthy lifestyle. But in India, largely, the community Pharmacist is seen focusing on dispensing medications. To play these six roles effectively, community Pharmacist need** 68 competences. The competencies required for community Pharmacist can be broadly classified into personal and patient- care competencies. The community Pharmacist derive their competencies from their education and experience. Competence frameworks are useful tools to monitor and improve performance. For making of Indian Community Pharmacist 2023, the Dreyfus model of skill acquisition needs to be adopted. It is a model of how learners acquire skills through formal instruction and practicing, used in the fields of education and operations research. Brothers Stuart and Hubert Dreyfus proposed the model in 1980 at the University of California, Berkeley. The model proposes that a student passes through five distinct stages viz: novice, competence, proficiency, expertise, and mastery. The Dreyfus model is based on four binary qualities: Recollection (non-situational or situational), Recognition (decomposed or holistic), Decision (analytical or intuitive), Awareness (monitoring or absorbed). Thus, competence-based learning following Dreyfus model is the need of the hour and would provide a sound foundation allowing pharmacy graduates to gather experience through practical training in the real job environment and play a vital role in achieving Health for all.

Review Article

Future Of Vitamin D In Cancer: Where Are We Today?

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ABSTRACT:
Vitamin D, an essential nutrient, is a precursor of a potent steroid hormone that regulates a broad spectrum of physiological processes. Vitamin D sufficiency is accessory with protection against malignancy in a number of tissues clinically, and a powerful body of evidence from animal and cell culture studies supports this protective role [22]. Numerous epidemiological, preclinical and cellular researches have revealed that vitamin D levels have an inverse relation with cancer mortality, while others have considered it a inherent risk factor [74]. There is increasing evidence linking the incidence and prognosis of certain cancers to low serum25 (OH) D3 levels. This article is a descriptive review of recent epidemiological findings regarding, serum 25-hydroxyvitamin D [25(OH)D] concentrations, vitamin D supplementation, and genetic variations in 25(OH)D concentration for incidence, progression, survival, and mortality rates of overall and breast, lung, colorectal, and Prostatic adenocarcinoma which include geographical ecological studies, observational studies associated with oral vitamin D intake and serum 25-Hydroxyl vitamin D [25(OH)D] concentrations, randomized Controlled trials (RCTs) of cholecalciferol supplementation, studies of genetic allele polymorphisms affecting 25(OH)D concentrations and mechanisms [75].Thus, all kinds of studies should be considered when assessing how vitamin D affects cancer. Therefore, using large observational claims, database, with real world unstructured treatment patterns, we qualitatively reviewed the epidemiological evidence within the oncology literature on the association between usage of vitamin D supplement and minimization of cancer risk with suggestions on how the evidence may be strengthened

Keywords— 25-Hydroxyl vitamin D, cancer, malignancy, epidemiology

I. INTRODUCTION

Cancer is a malignant disease characterized by rampant growth of body's cells which may escalate to other body parts. Vitamin D is a steroid hormone that has various physiologic effects in several tissue sand it is transformed through two hydroxylation reactions to its most active form (1,25-dihydroxyvitamin D) [85].The first observation of an inverse correlation between sunlight exposure and overall cancer incidence and mortality in North America was published almost 80 years ago. Thereafter, in 1980 and 1992, the initial epidemiological studies linking less sunlight subjection and high risk of colon and prostate cancers were proclaimed. Edward Gorham and colleagues carried out cohort and nested studies, including the first study that found an association of a serum vitamin D compound with reduced cancer risk [72].**William B. Grant** then meted out numerous ecologic studies that extended the vitamin D-cancer theory to other cancers [86].Several lines of population-based studies revealed an inverse correlation between serum 25-hydroxyvitamin D (25(OH)D) levels and soaring risk of gastric, colon, prostrate, breast, and other cancers. Moreover, there are strong evidences from several cell culture and animal studies to support the anti-tumorgenic effects of vitamin D[72].It is now becoming evident that deficiency of calciferol can contribute to the growth and progression of many forms of cancers, and thus maintenance of sufficient serum vitamin D levels might be beneficial for prevention and treatment of cancer.

II. DISCUSSION

Vitamin D has multiple anti-carcinogenic roles in cancer that are well-described at the molecular level and culminate in decreasing cancer cell proliferation and invasion potential and promoting apoptosis or cancer cell differentiation.

Vitamin D, Past, Present, Future

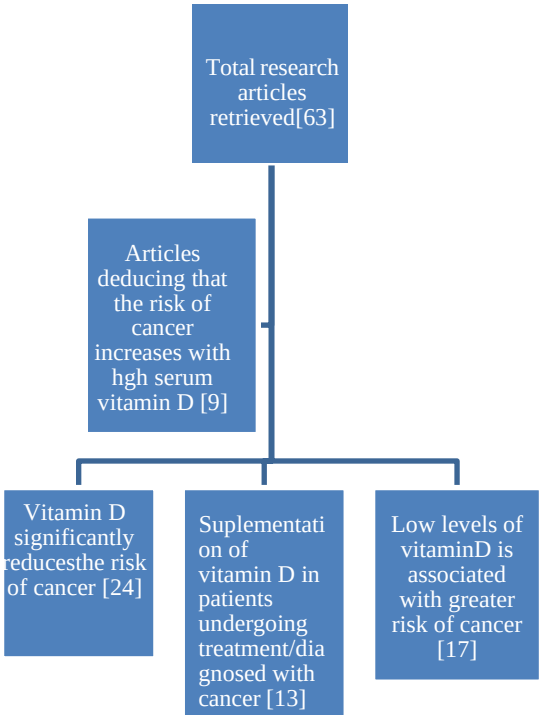
All In the last decade, abundance, as well as the allotment for vitamin D testing heightened substantially globally. The explosion of vitamin D utilization is result of many promising observational studies that have associated vitamin D concentration with health benefits in cardiovascular diseases, cancer, diabetes, fertility, and many others. The number of published papers on vitamin D, as well as diseases associated with its deficiency, upsurges daily [73]. Over the last 30 years, vitamin D metabolites have received, growing attention for their potential to prevent and/or retard cancer development. Laboratory studies have shown pleiotropic anti-cancer effects of the hormonal form of vitamin D, 1,25-dihydroxycholecalciferol (1,25(OH)2D), including control of cell differentiation, proliferation, and metastasis. Inter-relation between vitamin D and the innate history of cancer also have been detected in epidemiologic studies, which often anticipated the laboratory studies. Most sero-epidemiological studies have used measurements of the

pro- hormonal form of vitamin D, 25-hydroxyvitamin D (25- OHD), the accepted marker of an individual's vitamin D status.[11]

Vitamin D insufficiency has been categorized to be linked with an array of cancers, including breast cancer, colorectal cancer, multiple myeloma, and prostate cancer. Certain studies have shown vitamin D levels to have an inverse relation with cancer mortality, while others have considered it a potential risk factor. Elevated vitamin D concentrations are related with a 3- fold declined risk for pancreatic cancer (highest vs. lowest quintile, >26.2 vs. <12.8 mg/ml).[74]

Meta-analysis of prospective cohort studies suggest that vitamin D deficiency is associated with an increased risk of multiple types of cancer, including all cancers, colorectal cancer, bladder cancer, head and neck cancer, liver cancer and also death due to cancer. These associations have been explained by in vitro and in vivo effects of the active form of vitamin D (1,25 OH2 (dihydroxy) vitamin D), which promotes cellular differentiation, decreases cancer cell growth, stimulates cell death (apoptosis) and reduces angiogenesis.[1]

Despite the biological plausibility that vitamin D has an anticancer role, the literature on the relationship between cancer and 25(OH)D concentrations remains more controversial. The research findings evaluating the role of vitamin D as a possible preventive agent against cancer vary, and the optimal serum 25(OH)D concentration for cancer and other diseases prevention is still unknown. Overall, the results from a number of cell line experiments, mouse studies, ecological studies, observational studies and some clinical trials indicate that vitamin D has anticancer activity.[49]



Studies on serum vitamin D in Breast Cancer

Table I describes studies on serum vitamin D in patients with breast cancer. The studies are organized sequentially by the year of publication.

Imtiaz et al [65]carried out a case control study of Ninety breast cancer patients and equal number of age-matched healthy females for a period of 6 months to establish serum vitamin D levels in breast cancer patients and to evaluate its risk interconnection with grade and phase of the tumor. They notably found that the mean serum vitamin D level in the breast cancer patients was 9.3 ng/ml and in the control, group was 14.9 ng/ml (P value <0.001). Vitamin D deficiency was seen in 95.6% (86) breast cancer patients and in 77% (69) of the control group (P value <0.001). Among the breast cancer patients, the tumor characteristics did not show any significant associations with serum levels of vitamin D. Premenopausal breast cancer females had a mean serum vitamin D level of 10.5 ng/ml and postmenopausal females had a mean value of 13.5ng/ml (P value 0.015). Low BMD did not correlate significantly with vitamin D deficiency (P value 0.787).

Shaukat et al [52]performed a case control study which included 94 female patients (42 cases and 52 controls). They used the ELISA technique to study serum25-(OH) 2D levels in ng/ml and Vitamin D deficiency was considered at serum level less than 20ng/ml. They observed that Serum Vitamin D levels were significantly lower in cases (85.7%) than controls (55.8%) and the unadjusted and adjusted ORs for breast cancer in cases and controls showed a statistically significantly increased risk of breast cancer with low vitamin D concentration (p value0.003). They concluded that vitamin D deficiency was associated with risk of breast cancer.

O'Brien et al[71] studied the relationships between serum vitamin D, DNA methylation, and breast cancer using a case-cohort sample (1070 cases, 1277 in sub cohort) of non-Hispanic white women. They notably found that Of the CpGs in vitamin D-related genes, cg21201924 (RXRA) had the lowest p value for association with25 (OH)D ($p = 0.0004$). Twenty-two other candidates CpGs were associated with 25(OH)D ($p < 0.05$; RXRA, NADSYN1/DHCR7, GC, or CYP27B1). They also observed an interaction between

25(OH)D and methylation at cg21201924 in relation to breast cancer risk (ratio of hazard ratios = 1.22, 95% confidence interval 1.10–1.34; $p = 7 \times 10{-}5$), indicating a larger methylation-breast cancer hazard ratio in those with high serum 25(OH)D concentrations. Their findings suggested that 25(OH)D concentrations were associated with DNA methylation of CpGs in several vitamin D-related genes, with potential links to immune function-related genes and methylation of CpGs in vitamin D-

related genes may interact with 25(OH)D to affect the risk of breast cancer

Ismail et al [58] conducted a prospective study which included 50 Egyptian women with primary invasive, non-metastatic breast cancer. The serum level of 25(OH) D was measured by ELISA at diagnosis, before any cancer treatment. Vitamin D deficiency was defined as 25(OH) D<20 ng/ml. Patients were followed up for a median of 30 months (range: 18-48). They detected that the median level of 25(OH)D was 29.0 ng/mL (range: 10.0-55.0 ng/mL). Fifteen patients (30%) had vitamin D deficiency, which was positively associated with larger tumor size ($p < 0.001$), higher grade ($p = 0.014$), advanced stage ($p = 0.001$), lymph node positivity ($p = 0.012$), and HER2/Neu receptor expression ($p = 0.002$). It was also linked with worse overall survival (OS) and disease-free survival (DFS) ($p = 0.026$, and $p = 0.004$, respectively). On multivariate analysis, DFS was independently affected by vitamin D deficiency with an HR of 2.8 (95% CI: 1.6-7.0, $p = 0.022$) and advanced stage, i.e., stage II had worse survival compared to stage I with an HR of 4.8 (95%CI: 1.1-21.7, $p = 0.042$). They culminated that Vitamin D deficiency had a negative effect on overall and disease-free survival in breast cancer cases, being related to tumor size, stage, grade, nodal status and HER2/neu receptor expression.

They observed that 25OHD and 27HC levels were inversely correlated ($p = 7.0E{-}3$), Excluding two statistical outliers. Shamsi et al[49] examined the prevalence of vitamin D inadequacy and breast cancer in Pakistani women and observed that compared to patients with sufficient serum vitamin D (>30 ng/ml), women with serum vitamin D deficiency (<20ng/ml), had a higher risk of breast cancer (OR = 1.65, 95%CI: 1.10,2.50).

They also concluded that Women with history of vitamin D supplementation one year prior to enrollment, had significant protective effect against breast cancer (OR = 0.32, 95% CI: 0.24, 0.43). Their research implied that Serum vitamin D deficiency was associated with increased risk of breast cancer, while vitamin D supplementation was associated with decreased risk of breast cancer.

Going et al[70] measured27HC, 25-hydroxyvitamin D 25OHD), and 1,25(OH)2Din sera of 29 breast cancer patients before and after supplementation with low-dose (400 IU/day) or high-dose (10,000 IU/day) vitamin D in the interval between biopsy and surgery. They perceived a significant increase ($p = 4.3E{-}5$) in 25OHD and a decrease ($p = 1.7E{-}1$) in 27HC in high-dose versus low-dose vitamin D subjects.

Crew et al [59] reported that after a year of vitamin D3 20,000 IU/week in premenopausal women at high-risk of breast cancer, changes in mammographic density (MD) at 12 and 24 months were small and did not differ significantly between the active and placebo arms. Notably, compared to standard-dose vitamin D alone, the addition of vitamin D3 20,000 IU/week led to a significant increase in serum 25(OH)D, the main circulating form, and serum 1,25(OH)D, the activated form of vitamin D. There were also non-significant decreases in serum IGF-1 and IGFBP-3 at 12 months with vitamin D supplementation, which correlated with MD at 12 months. Cholecalciferol at a dose of 20,000 IU/week for a year was well-tolerated. Their studies suggested that there is insufficient evidence to support the use of vitamin D supplementation for breast cancer risk reduction among high-risk premenopausal women.

Table I: Studies on Serum Vitamin D in Breast cancer

First author, year, place (ref.)	Study design, Sample size	CANCER TYPE	AIM OF THE STUDY	RESULT OF THE STUDY	CONCLUSIONS
Noureen Shaukat, 2017, Pakistan (15)	A case control study. 42 cases and 52 controls	Breast	To determine the association between vitamin D deficiency and breast cancer.	They observed that Serum Vitamin D levels were significantly lower in cases (85.7%) than controls (55.8%) and the unadjusted and adjusted ORs for breast cancer in cases and controls showed a statistically significantly increased risk of breast cancer with low vitamin D concentration (p value0.003).	Vitamin D deficiency was associated with risk of breast cancer.
O'Brien, 2018, USA(64)	Cast control-cohort 1070 cases, 1277 in sub cohort.	Breast	To further investigate a possible link between vitamin D and DNA methylation.	An interaction was observed between 25(OH)D and methylation at cg21201924 in relation to breast cancer risk (ratio of hazard ratios = 1.22, 95% confidence interval 1.10–1.34; $p = 7 \times 10{-}5$), indicating a larger methylation-breast cancer hazard ratio in those with high serum 25(OH)D concentrations.	25(OH)D concentrations were associated with DNA methylation of CpGs in several vitamin D-related genes, with potential links to immune function-related genes. Methylation of CpGs in vitamin D-related genes may interact with 25(OH)D to affect the risk of breast cancer.

First author, year, place (ref.)	Study design, Sample size	CANCER TYPE	AIM OF THE STUDY	RESULT OF THE STUDY	CONCLUSIONS
Abeer Ismail, 2018, Egypt (35)	A prospective study, 50 women	Breast	To determine the frequency and prognostic significance of vitamin D deficiency in Egyptian women with breast cancer	The median level of 25(OH)D was 29.0 ng/mL (range: 10.0-55.0 ng/mL). Fifteen patients (30%) had vitamin D deficiency, which was positively associated with larger tumor size ($p < 0.001$), higher grade ($p = 0.014$), advanced stage ($p = 0.001$), lymph node positivity ($p = 0.012$), and HER2/Neu receptor expression ($p = 0.002$). It was also linked with worse overall survival (OS) and disease-free survival (DFS) ($p = 0.026$, and $p = 0.004$, respectively).	Vitamin D deficiency had a negative effect on overall and disease-free survival in our breast cancer cases, being related to tumor size, stage, grade, nodal status and HER2/neu receptor expression.
Catherine C. Going, 2020, USA (28)	A pilot breast cancer trial. 29 breast cancer patients.	Breast	To correlate if Vitamin D supplementation decreases serum 27-hydroxycholesterol.	A significant increase ($p=4.3E-5$) in 25OHD and a decrease ($p =1.7E-1$) in 27HC was observed in high-dose versus low-dose vitamin D subjects. Excluding two statistical outliers, 25OHD and 27HC levels were inversely correlated ($p = 7.0E-3$).	Vitamin D supplementation can decrease circulating 27HC of breast cancer patients, likely by CYP27A1 inhibition.

First author, year, place (ref.)	Study design, Sample size	CANCER TYPE	AIM OF THE STUDY	RESULT OF THE STUDY	CONCLUSIONS
Shamsi, 2020, Pakistan (105)	A multi-center case control study. 411 newly diagnosed,784 control.	Breast	To study the association of vitamin D with breast cancer among women in Karachi, Pakistan.	Compared to patients with sufficient serum vitamin D (>30 ng/ml), women with serum vitamin D deficiency (<20ng/ml), had a higher risk of breast cancer (OR = 1.65, 95%CI: 1.10,2.50). Women with history of vitamin D supplementation one year prior to enrollment, had significant protective effect against breast cancer (OR = 0.32, 95% CI: 0.24, 0.43).	Serum vitamin D deficiency was associated with increased risk of breast cancer, while vitamin D supplementation was associated with decreased risk of breast cancer.
Katherine D. Crew, 2020, USA (50)	Randomized Double-Blind Placebo Controlled Biomarker Modulation Study. 200 post-menopausal women.	Breast	To evaluate the effect of vitamin D supplementation on MD in premenopausal women at high risk for breast cancer, evaluate the effects of vitamin D 20,000 IU/week on blood-based biomarkers associated with breast cancer risk (IGF-1, IGFBP-3) and safety.	Comparing the active and placebo groups at 12 months, MD changes were small and did not significantly differ. Mean MD changes at 12 and 24 months were −0.3% and −1.2%, respectively, in the active arm and +1.5% and +1.6% with placebo ($p>0.05$), MD was positively correlated with serum IGF-1 and IGF-1/IGFBP-3 ($p<0.01$).	There is insufficient evidence to support the use of vitamin D supplementation for breast cancer risk reduction among high-risk premenopausal women.

Studies on serum vitamin D in Lung Cancer

Table II describes studies on serum vitamin D in patients with lung cancer. The studies are organized sequentially by the year of publication.

Hoffer et al [30]performed single arm open-label pharmacokinetic trial, where outpatients with advanced lung cancer consumed 20,000 IU vitamin D daily with the largest meal of the day for 2 weeks followed by 10,000 IU per day for another week. Plasma concentrations of 25-hydroxyvitamin D [25(OH)D], parathyroid hormone, calcium, vitamin C and C-reactive protein were analysed on code days 0, 14 and 21, and serum vitamin D binding protein (VDBP) concentrations on days 0 and 21. Of the 91 patients enrolled in the study, 85 % had hypovitaminosis D and 41 % had hypovitaminosis C e. Final plasma 25(OH)D concentrations were subnormal (<75 nmol/L) for 13 % of the patients

and sub-target (<120 nmol/L) for 44
% of them. In most cases, subnormal and sub-target These results suggest that a loading dose of 30,000 IU per day for 14 days would be safe and effective for patients who are obese or at risk of severe hypovitaminosis D. The preliminary nature of the study design, and the failure to achieve target 25(OH)D concentrations for a large proportion of the patients, do not allow any firm conclusion about the clinical effects of correcting hypovitaminosis D in this patient population. Nevertheless, no evidence was obtained that partial correction of hypovitaminosis D greatly improved mood, reduced distress or relieved cancer-related symptoms.

Feng et al [32]conducted meta-analysis based on 17 prospective cohort studies, with 138,858 participants with 4368 incident cases, this meta-analysis provides the most up-to-date epidemiological evidence supporting higher circulating 25- hydroxyvitamin D is helpful for lung cancer. They performed a dose–response analysis which revealed that increasing 10 nmol/L dose of circulating 25-hydroxyvitamin D was associated with an 8% reduction in the risk of lung cancer risk and a 7% reduction in the risk of lung cancer mortality. They deduced that their findings underscore the notion that higher vitamin D was significantly associated with lung cancer decrement.

Table II: Studies on Serum Vitamin D in Lung cancer

First author, year, place (ref.)	Study design, Sample size	CANCER TYPE	AIM OF THE STUDY	RESULT OF THE STUDY	CONCLUSIONS
L. John Hoffer, 2016, Canada (75)	A single arm open-label pharmacokinetic trial. 91 patients.	Lung	To assess appropriate vitamin D loading regimen for patients with advanced lung cancer.	The vitamin D load increased the average plasma 25(OH)D concentration to 116 ± 34 nmol/L (mean ± SD); the median concentration was 122 nmol/L (interquartile range103–134).	These results suggest that a loading dose of 30,000 IU per day for 14 days would be safe and effective for patients who are obese or at risk of severe hypovitaminosis D.
Qianqian Feng, 2017, China (38)	A dose–response meta-analysis of prospective cohort studies. 138,858 participants with 4368 incident cases.	Lung	To clarify and quantitatively assess the correlation between circulating 25-hydroxyvitamin D and lung cancer.	Higher circulating 25hydroxyvitamin D significantly decreased risk of lung cancer (relevant risk [RR]:0.84;95% confidence interval (CI): 0.74–0.95; P=.006.	The findings underscore the notion that higher vitamin D was significantly associated with lung cancer decrement.
Tadashi Akiba, 2018, Japan (30)	A Randomized, Double-Blind, Placebo-Controlled Trial. 155 patients.	Lung	To examine whether vitamin D supplementation can improve the prognosis of patients with non-small cell lung cancer.	The vitamin D group showed significantly better 5-year RFS (86% vs. 50%, P =0.04) and OS (91% vs. 48%, P = 0.02) than the placebo group. Relapse and death occurred in 40 (28%) and 24 (17%) patients, respectively.	In patients with NSCLC, vitamin D supplementation may improve survival of patients with early-stage lung adenocarcinoma with lower 25(OH)D levels.

Akiba et al [43]in a randomized, double-blind, placebo-controlled trial in patients with NSCLC found that, (1) vitamin D supplementation did not improve RFS and OS in the total study population, (2) patients with high 25(OH)D (20 ng/mL) before taking the supplement showed better OS than those with low 25(OH)D (<20 ng/mL), (3) In restricting the analysis to the subgroup with early-stage adenocarcinoma with low 25(OH)D, the vitamin D group showed significantly better 5-year RFS and OS than the placebo group, (4) Among the examined polymorphisms, 5-year RFS and OS were better in patients with DBP1 TT than in those with TG/GG genotypes, as well as in patients with CDX2 AA/AG than with GG genotypes, both of which remained significant even after adjustment by stage, adenocarcinoma, low 25(OH)D, and vitamin D supplementation. Through this they inferred that in patients with NSCLC, vitamin D supplementation

may improve survival of patients with early-stage lung adenocarcinoma with lower25(OH)D levels.

Studies on serum vitamin D in Colorectal and Prostate Cancer

Table III describes studies on serum vitamin D in patients with colorectal cancer (CRC) and prostate cancer. The studies are organized sequentially by the year of publication.

Wagner et al [18] executed a Double-blind randomized clinical trial which consisted of 66 subjects out of which, 63 completed the dosing protocol. They evaluated vitamin D metabolite levels and Ki67 labeling in surgical prostate tissue. Preventive measures, PTH, and prostate-specific antigen (PSA) were also evaluated. They noted that Prostate tissue and serum levels of vitamin D metabolites, including calcitriol, multiplied dose dependently (P < .03) and were substantially advanced in the 40 000-IU/d batch relative to each other dose group (P < .03). Prostate vitamin D metabolites corresponded productively with serum levels (P <.0001). Ki67 measures did not differ significantly among vitamin D dose groups. However, cross-sectional analysis indicated that the calcitriol level attained in prostate was inversely associated with Ki67 intensity and Ki67 (3+) percent positive nuclei in prostate cancer and benign tissue (*P* <.05). Safety measures did not change adversely with dosing. Compared with the 400-IU/d group, serum PTH and PSA were lower in the combined higher- dose groups at the end of the study (*P* <.02). they concluded that Oral vitamin D3 raised prostate calcitriol levels (level 1 evidence) and modestly lowered both PSA and PTH. Although Ki67 expression did not differ among dose groups, its levels correlated inversely with prostate calcitriol.

Baron et al [48] recruited patients with recently diagnosed adenomas and no known colorectal polyps remaining after complete colonoscopy. They randomly assigned 2259 participants to receive daily vitamin D3 (1000 IU), calcium as carbonate (1200 mg), both, or neither in a partial 2×2 factorial design. They notably discovered that participants who were randomly assigned to receive vitamin D had a mean net increase in serum 25-hydroxyvitamin D levels of 7.83 ng per milliliter, relative to participants given placebo. Overall, 43% of participants had one or more adenomas diagnosed during follow-up. The adjusted risk ratios for recurrent adenomas were 0.99 (95% confidence interval [CI], 0.89 to 1.09) with vitamin D versus no vitamin D, 0.95 (95% CI, 0.85 to 1.06) with calcium versus no calcium, and 0.93 (95% CI, 0.80 to 1.08) with both agents versus neither agent. They concluded that Daily supplementation with vitamin D3 (1000 IU), calcium (1200 mg), or both after removal of colorectal adenomas did not significantly reduce the risk of recurrent colorectal adenomas over a period of 3 to 5 years.

Santaland et al [19] performed a retrospective, cross-sectional, observational study to evaluate the relationship between prostate cancer and vitamin D levels and reduce the risk of the disease. They observed that the percentage of subjects with prostate cancer with vitamin D levels <75 nmol/L (1.6%) was significantly less than subjects with vitamin D levels ≥75 nmol/L (2.2%) (0.74; 95% CI = 0.58–0.93, p = 0.0103).

Wesselink et al[45] carried out a prospective cohort study which included 1733 colorectal cancer patients. They detected that After adjustment for other demographic and lifestyle factors 25(OH) D3 levels decreased 6.7 nmol/L (95 %CI -9.8; -3.8) more in patients receiving chemotherapy compared to patients who underwent surgery. They hypothesized that Vitamin D supplement use and treatment appear to be important determinants of 25(OH)D3 levels during the first six months after CRC diagnosis, although the difference in 25(OH)D3 levels was minor.

Table III: Studies on serum vitamin D in Colorectal and Prostate Cancer

First author, year, place (ref.)	Study design, Sample size	CANCER TYPE	AIM OF THE STUDY	RESULT OF THE STUDY	CONCLUSIONS
John A. Baron, 2015, USA(26)	A randomized, double-blind, placebo-controlled trial. 2813 participants	Colorectal	To study the comprehensive potential of higher intake and serum levels of vitamin D and calcium to reduce the risk of colorectal neoplasia.	The adjusted risk ratios for recurrent adenomas were 0.99 (95% confidence interval [CI], 0.89 to 1.09) with vitamin D versus no vitamin D, 0.95 (95% CI, 0.85 to 1.06) with calcium versus no calcium, and 0.93 (95% CI, 0.80 to 1.08) with both agents versus neither agent.	Daily supplementation with vitamin D3 (1000 IU), calcium (1200 mg), or both after removal of colorectal adenomas did not significantly reduce the risk of recurrent colorectal adenomas over a period of 3 to 5 years.
Marcus Stanaland, 2017, USA (27)	Retrospective, cross-sectional, observational study.	Prostrate	To evaluate the relationship between prostate cancer and vitamin D levels and reduce the risk of the disease.	The percentage of subjects with prostate cancer with vitamin D levels <75 nmol/L (1.6%) was significantly less than subjects with vitamin D levels ≥75 nmol/L (2.2%) (0.74; 95% CI = 0.58–0.93, p = 0.0103).	Among the documented risk factors for prostate cancer from the available data, age, military service, and race group were significantly associated with prostate cancer diagnosis.
E.Wesselink, 2020, Netherlands(47)	Prospective cohort study, 1733 CRC patients.	Colorectal	To investigate which clinical characteristics in conjunction with demographic and lifestyle factors, were associated with 25(OH)D3 levels at diagnosis and six months later.	After adjustment for other demographic and lifestyle factors 25(OH) D3 levels decreased 6.7 nmol/L (95 %CI -9.8; -3.8) more in patients receiving chemotherapy compared to patients who underwent surgery only.	Vitamin D supplement use and treatment appear to be important determinants of 25(OH)D3levels during the first six months after CRC diagnosis, although the difference in 25(OH)D3 levels was minor.

Studies on serum vitamin D in Multi-site Cancer.

Table IV describes studies on serum vitamin D in patients with other as well as multiple cancer sites. The studies are organized sequentially by the year of publication.

J-B Wang [13]performed a nested case–control study in the Lin Xian Nutrition Intervention Trials on participants developing incident liver cancer or dying from chronic liver disease over 22 years of follow-up. Standard serum 25(OH) vitamin D was analysed in 226 incident liver cancer cases, 282 incurable liver disease deaths and 1063 age-, sex- and trial-matched controls. The mean serum vitamin D level in controls was inadequate (20 nmol l–1). Compared with the lowest quartile, subjects in the fourth quartile had lower risk of chronic liver disease death (OR ¼ 0.34, 95% CI ¼ 0.21–0.55). Nonetheless, they interpreted that in a low vitamin D population, higher serum 25(OH) vitamin D concentrations were associated with significantly lower risk of chronic liver disease deaths, and among those with higher serum calcium, incident liver cancer.

Trude Eid Robsahm et al [11]investigated association of serum 25-hydroxyvitamin D (25-OHD) levels with cancer death, using repeated measurements of serum 25-OHD. Pre- diagnostic serum specimens were assorted in population health inspections in Norway (1973– 2004). individuals who thereafter developed cancer (1984– 2004) gave a second serum specimen at the time of cancer diagnosis. Reiterate samples existed from 37 colon cancers, 124 lymphomas, 193 lung cancers and 202 breast cancers. Serum 25-OHD was measured via competitive radioimmunoassay the median 25-OHD levels were 63.3 and 62.5 nmol/L, respectively. During follow-up, 313 cancer deaths occurred. Compared to low pre-diagnostic 25-OHD levels (<46 nmol/L), higher levels (≥46 nmol/L) had significantly lower HRs (39– 54%) of case fatality. Donors who had both samples at high (≥62 nmol/L) levels had 59% lower HR of case fatality, compared to those for whom both samples were at low levels (<46 nmol/L). Furthermore, versus a decline in serum 25-OHD (Median −22.4 nmol/L) from pre- diagnostic to diagnostic samples, a rise (median22.3 nmol/L) was associated with lower case fatality (HR 0.57, 95% CI 0.43−0.75). Their study demonstrates that 25-OHD levels <46 nmol/L, both several years prior to and at the time of cancer diagnosis, were associated with higher case fatality. They further deduced that lower hazards of case fatality in cases with rise in serum 25-OHD toward diagnosis, when the pre-diagnostic sample was collected ≥10 years prior to the diagnosis.

Fie Juhl Vojdeman et al [25] examined the association between serum levels of vitamin D and cancer incidence in the Capital Region of Denmark. The study population of 217,244 individuals had a median level of vitamin D of 46 nmol/L (IQR 27–67 nmol/L), a median age of 48.8 years (IQR 33.5–64.1 years), female predominance (65.3%), and a low comorbidity burden (Charlson Comorbidity Index of 0 in 79.5%) with pulmonary disease being the most frequent comorbidity. A total of 18,359 individuals were diagnosed with an incident cancer (8.5% of the population) during the follow-up period. Non-melanoma skin cancer (N = 5045) was the most frequent incident cancer followed by breast cancer (N = 2167), lung cancer (N = 1707), prostate cancer (N = 1470), and colon recto sigmoidal cancers (N = 1108) No associations were found between increments of 10 nmol/L vitamin D and incidence of breast, colorectal, urinary, ovary or corpus uteri cancer. However, higher levels of vitamin D were associated with higher incidence of non-melanoma (HR 1.09 [1.09–1.1]) and melanoma skin cancer (HR 1.1 [1.08–1.13]) as well as prostate (HR 1.05 [1.03–1.07]) and hematological cancers (HR 1.03 [1.01–1.06]), but with lower incidence of lung cancer (HR 0.95 [0.93– 0.97]). The median level of vitamin D differed depending on cancer type ranging from 47 nmol/L in individuals developing an incident lung or rectum cancer to 58 nmol/L in individuals developing a non-melanoma skin cancer. Their study concluded that vitamin D levels are not associated with the incidence of several major cancers such as breast, urinary and colon-recto sigmoidal cancers in a population from primary care in Denmark, but higher vitamin D levels are associated with a higher incidence of skin, prostate, hematological cancers, and non-Hodgkin lymphomas solely as well as a lower incidence of lung cancer. These results should be interpreted in the light of the representativeness of the cohort as well as the known limitation of registry studies in lack of information on potential confounding factors.

Acikgoz et al [9]carried out a nested case control to analyze the effect of serum 25- hydroxyvitamin D (25(OH)D) level on lung, breast, colorectal and prostate cancers in people aged 30+ years, they interpreted Serum 25(OH)D levels did not show a significant association with breast, colorectal and prostate cancers. There was an inverse association between 25(OH)D level and lung cancer risk, where the OR values for the first, second and third quartiles, compared with the fourth quartile (1.00), were 2.92 (CI: 0.82–10.35), 3.76 (CI: 1.14–12.37) and 3.55 (CI: 1.04– 12.08) respectively. Hence, they concluded that low 25(OH)D levels were associated with a greater than threefold increased risk of lung cancer;no

Table IV: Studies on serum vitamin D in Multi-site Cancer.

First author, year, place (ref.)	Study design, Sample size	CANCER TYPE	AIM OF THE STUDY	RESULT OF THE STUDY	CONCLUSIONS
J-B Wang, 2013, China (38)	A nested case–control study. 1063 subjects.	Multi-site cancer	To examine the association between serum 25(OH) vitamin D concentrations and subsequent risk of primary liver cancer incidence and chronic liver disease mortality	The median serum vitamin D level in controls was low (20 nmol l–1). Compared with the lowest quartile, subjects in the fourth quartile had lower risk of chronic liver disease death (OR¼0.34, 95% CI¼0.21–0.55).	In a low vitamin D population, higher serum 25(OH) vitamin D concentrations were associated with significantly lower risk of chronic liver disease deaths.
Trude Eid Robsahm, 2019, USA (3)	Prospective cohort studies. 556 cases.	Multi-site cancer	To investigate the association b/w Circulating 25-OHD and cancer mortality using repeated measurements of serum 25-OHD.	The median time between pre-diagnostic and diagnostic samples was 14.4 years. The median 25-OHD levels were 63.3 and 62.5 nmol/L, respectively. During follow-up, 313 cancer deaths occurred. Compared to low pre-diagnostic 25-OHD levels (<46 nmol/L), higher levels (≥46 nmol/L) had significantly lower HRs (39–54%) of case fatality.	The results suggest a causal relationship between vitamin D and cancer case fatality.

cancer.

First author, year, place (ref.)	Study design, Sample size	CANCER TYPE	AIM OF THE STUDY	RESULT OF THE STUDY	CONCLUSIONS
Fie JuhlVoideman, 2019, Denmark (34)	A population-based study. 217,244 individuals	Multi-site cancer	To examine the association between serum levels of vitamin D and cancer incidence.	No associations were found between increments of 10 nmol/L vitamin D and incidence of breast, colorectal, urinary, ovary or corpus uteri cancer. However, higher levels of vitamin D were associated with higher incidence of non-melanoma (HR 1.09 [1.09–1.1]) and melanoma skin cancer (HR 1.1 [1.08–1.13]) as well as prostate (HR 1.05 [1.03–1.07]) and haematological cancers (HR 1.03 [1.01–1.06]), but with lower incidence of lung cancer (HR 0.95 [0.93–0.97]).	Their study concluded that vitamin D levels are not associated with the incidence of several major cancers such as breast, urinary, and colon-recto sigmoidal cancers in a population from primary care in Denmark, but higher vitamin D levels are associated with a higher incidence of skin, prostate, haematological cancers, and non-Hodgkin lymphomas solely as well as a lower incidence of lung cancer.
Ayla Acikgoz, 2020, Turkey (46)	A nested case–control study. 606 persons (179 cases and 427 controls)	Multi-site cancer	To investigate prospectively the effect of serum 25 hydroxyvitamin D (25(OH)D) level on lung, breast, colorectal and prostate cancers in people aged 30+ years.	Serum 25(OH)D levels did not show a significant association with breast, colorectal and prostate cancers. There was an inverse association between 25(OH)D level and lung cancer risk, where the OR values for the first, second and third quartiles, compared with the fourth quartile (1.00), were 2.92 (CI: 0.82–10.35), 3.76 (CI: 1.14–12.37) and 3.55 (CI: 1.04– 12.08) respectively.	It was seen that low 25(OH)D levels were associated with a greater than threefold increased risk of lung cancer; no association was detected for breast, colorectal and prostate cancers

Association was detected for breast, colorectal

CONCLUSION: In our article we have comprehensively reviewed the prevalence of vitamin D in cancer. Most of the researches, case studies, randomized clinical trials were directed towards the significant reduction in risk of cancer through vitamin d supplementation, and other compelling effects of vitamin D in diagnosis of cancer. However, there are some possible restrictions of vitamin D based cancer therapy which should be considered to build better curative approaches. From a conceptual approach our review of observational studies should be considered with some exceptions as there were an array of analysis and clinical trials,

moreover, the studies were inquisitive and arbitrary, without confirmed results. Ideally, more unequivocal evidence of vitamin D on any cancer risk reduction should be obtained through large, population-based, longitudinal RCTs with adequate doses of vitamin D as

interventions. Unravelling such intricate networks involving cancer and vitamin D will contribute to the understanding of vitamin D in cancer and provide promising new opportunities for cancer management.

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Research Article

Drug Utilization and Evaluation Of Paclitaxel In Patients With Ovarian, Cervical And Breast Cancer

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ABSTRACT:

INTRODUCTION: Cancer is growing into a leading health and economic crisis worldwide causing over 10 million deaths in 2020.

AIMS AND OBJECTIVES:

- Assessment of treatment effectiveness of paclitaxel. (Primary objective)
- Assessing the drug utilization of paclitaxel in ovary, breast and cervical cancer.
- To determine the correlation between menarche and menopause with occurrence of cancer in women.
- To review and analyze the severity of drug associated ADRs

METHODS: Various methods were used to find out the objective of the study.

RESULTS: Out of 68 patients, 41 patients were having breast cancer, 22 patients with ovary cancer and 5 patients with cervical cancer.

CONCLUSION: Our study found that majority of the study population that is about 60% were affected by breast cancer, followed by 32% of population with the diagnosis of ovarian cancer and 7% with cervical cancer. The correlation of age at menarche and incidence of cancer in women showed the greater incidence of ovarian and breast cancer in women with early menarche. The ADR was analysed using naranjo's scale and CTCAE grading scale and most of them experienced drug induced burning or tingling sensation, peripheral neuropathy, myalgia and hypersensitivity reaction during the chemotherapy administration.

INTRODUCTION:

Cancer is growing into a leading health and economic crisis worldwide causing over 10 million deaths in 2020. The global cancer burden is estimated to have risen to 18.1 million new cases and 7.6 million deaths in 2018. One in 5 men and one in 6 women worldwide develop cancer during their lifetime and one in 8 men and one in 11 women die from the disease. Worldwide the total number pf people who are alive within 5 years of cancer diagnosis (5 years' prevalence) is estimated to be 43.8 billion. The increasing cancer burden is due to several factors including population growth and aging as well as the changing prevalence of certain causes of cancer linked to social and economic development. This is particularly true in rapidly growing economics, where a shift is observed from cancers related to poverty and infections to cancer associated with lifestyles more typical of industrialized countries. As per WHO Cancer is one of the leading causes of death globally. Especially in women, we have observed higher incidence of cervical & ovarian cancer over the years due to the unhealthy and unhygienic lifestyle.

Cancer being a dreadful disease in itself, the treatment is no less miserable. Over the years the incidence of cancer in women has skyrocketed to millions. Breast Cancer being one of the most common cancers has crossed the number of 2 million cases in the year 2020. With respect to Cervical cancer, it's observed in eight of ten and nine out of ten women die from the same condition especially in a moderate income surrounding like ours.

The treatment primarily aims to cure cancer or to considerably prolong life. There is, however a significant difference in the treatment approach between various countries based on favored protocol.

One among the treatment options which concerns us as pharmacists is Onco-Chemotherapy. Chemotherapy subdivided into Cytotoxic, Targeted and Hormonal domains of treatment. Cytotoxic drugs are in greater use, renowned for their fast and effective outcome in curbing cancer. Among all the different classes of

Cytotoxic drugs, Taxols have shown better effects in nominal doses.

Paclitaxel is prescribed in dose specific manner, based on either the BSA or BMI of Patient. Paclitaxel is prescribed either as a monotherapy or often combined with Carboplatin in various cancers more specifically breast and ovarian cancer. It's normally prescribed after an initial 4 cycles AC regimen and is also used in Adjuvant and Neo Adjuvant chemotherapy. Alongside the effects and pharmacological outcomes of Paclitaxel, it causes severe and often life threatening ADRs. Paclitaxel chemotherapy in a whole has benefited and also diminished quality of life in patients. Paclitaxel has been a remarkable source of healing in cancer patients but for a price of compromised quality of life. In this study, we are assessing the treatment efficacy and utilization evaluation by monitoring the health parameters.

MATERIALS AND METHODOLOGY:

Study site: Bharath hospital & institute of oncology, Mysuru.

Study design: This is a Prospective observational study

Study period: The study will be carried out for a period of **Six** months

Sources of data:

- Medical and Medication records of the patient.
- Interviewing patient and caretaker.
- Communicating with concerned clinicians and health care professionals.

Study criteria:

Inclusion criteria:

-Patients meeting study criteria.
-Patients with age from 18years.
-Patients diagnosed with ovarian, cervix and breast cancers.
-Patients receiving chemotherapy.

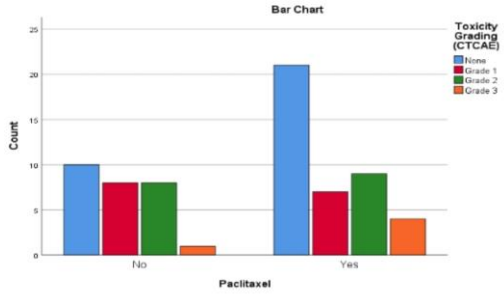
Exclusion criteria:

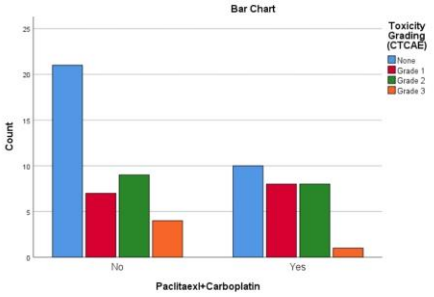
-Incomplete case sheets.
-Incomplete medical or medication information.
-Patients not willing to participate in the study.
-Patient who are non-adherent to treatment.

Experimental design:

- The study involved the following steps:
- Step 1: Preparation of Informed Consent form An ICF was suitably designed in both English (Annexure 2) and Kannada (Annexure 3) to obtain consent from patients (Fulfilling the study criteria) to be included into the study. The ICF was reviewed and approved by an Institutional ethics committee. The patient was thoroughly explained about the study in their regional languages and the consent was taken by taking their signature or thumb impression respectively.
- Step 2: Preparation of Data Collection Form A specially designed data collection form (Annexure 1) was devised for the study. The form included demographic details like name, age, gender, family history, social habits, address, contact number. Clinical data such as diagnosis, past medication history, co-morbidities, allergy status, therapeutic data such as name of the drug prescribed, dose, frequency, route and duration of administration, concurrent medications were taken. The same details were documented electronically in specially designed google forms (Link: https://docs.google.com/forms/d/e/1FAIpQLSdyzg7eXAriJs5VFdCPPWIy1Isfu2HidbRhq_RjL2vxT36gXg/viewform?usp=sf_link). To report, document and assess adverse drug reaction due to Paclitaxel, a standardized *Naranjo algorithm in English* (Annexure 4).
- Step 3: Patient enrolment: Patients fulfilling the study criterion were enrolled into the study after obtaining their informed consent after translating to their regional language/preferred language. Patients were enrolled during their outpatient visits. All the documents used in the study were translated to their regional language/preferred language
- Step 4: Data Collection: All relevant details of the enrolled patients were obtained from a fore mentioned data sources and documented in the data collection form (Annexure 1)
- Step 5: Statistical analysis Statistical analysis was performed by using SPSS Software for the evaluation of data. Descriptive statistics (Percentage, mean standard deviation, tables and graphs) is used to resemble the results.
- Step 6: Interpretation: The prescription audit of drugs was performed according to NCCN Guidelines and Adverse drug reaction due to Antipsychotics can be assessed by using *Naranjo algorithm*.

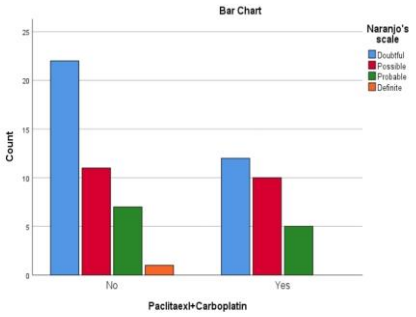
RESULTS:

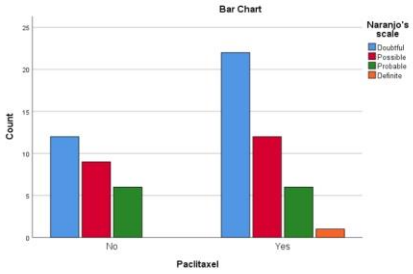




Distribution of CTCAE Grading:

Among 27 patients receiving chemotherapy of Paclitaxel+Carboplatin among the 68 of study population, 8 of them were computed to have grade 2 toxicity according to CTCAE toxicity grading. 8 patients were observed with grade 1 toxicity and only 1 patient with grade 3 toxicity according to CTCAE grading respectively.

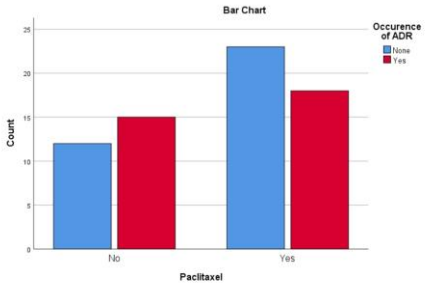


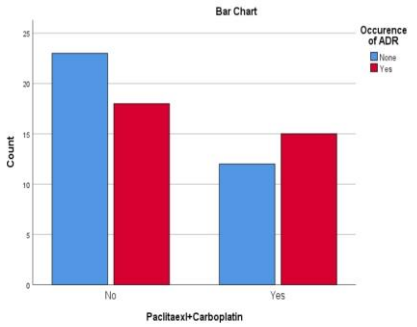


Naranjo's Scale Score:

Among the 27 patients receiving chemotherapy of Paclitaxel+Carboplatin in the study population of 68 patients, 12 were screened with doubtful ADRs and 10 with possible ADRs. 5 patients showed signs of probable ADRs and no patient was observed with definite ADRs as per the Naranjo's scoring.

Among the 41 patients receiving chemotherapy of Paclitaxel in the study population of 68 patients, 22 were screened with doubtful ADRs and 12 with possible ADRs. 6 patients showed signs of probable ADRs and only 1 patient was observed with definite ADRs as per the Naranjo's scoring.



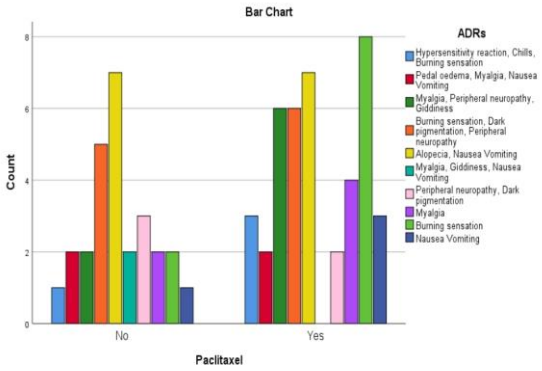


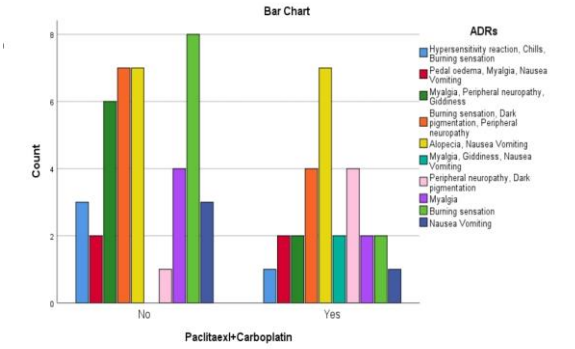
Among the 68 patients study population, among which 41 patients receiving Chemotherapy of Paclitaxel about 43.9% of them were observed with occurrence of ADRs (n=18). Whereas among the 27 patients receiving chemotherapy of Paclitaxel+Carboplatin about 55% of them were observed with the occurrence of ADRs.

Among 41 patients receiving chemotherapy of paclitaxel among the 68 of study population, 9 of them were computed to have grade 2 toxicity according to CTCAE toxicity grading(n=9). 7 patients were observed with grade 1 toxicity and 4 others with grade 3 toxicity according to CTCAE grading respectively.

6 of the patients were observed with peripheral neuropathy and pigmentation along with major complaint of burning sensation.6 other patients experienced myalgia and giddiness along with peripheral neuropathy. 3 of the patients

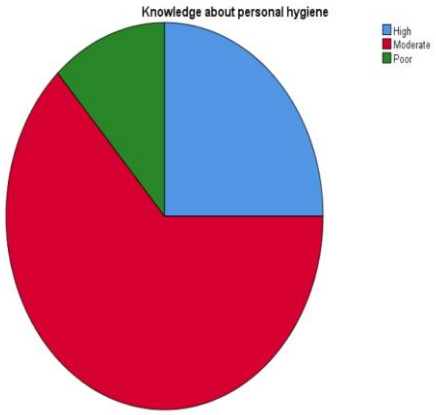
experienced hypersensitivity reaction and chills during the administration of the chemotherapy. Very few were observed with pedal oedema(n=2) and the others experienced one of the above mentioned ADRs (n=7).





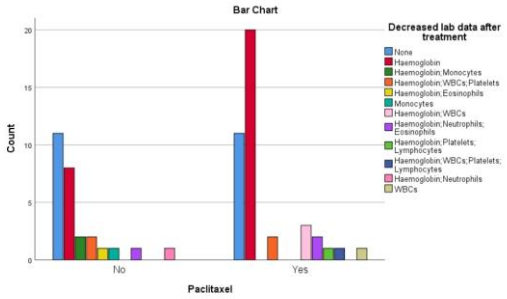
6 of the patients were observed with peripheral neuropathy and pigmentation along with major complaint of burning sensation.6 other patients experienced myalgia and giddiness along with peripheral neuropathy. 3 of the patients experienced hypersensitivity reaction and chills during the administration of the chemotherapy. Very few were observed with pedal oedema(n=2) and the others experienced one of the above mentioned ADRs (n=7).

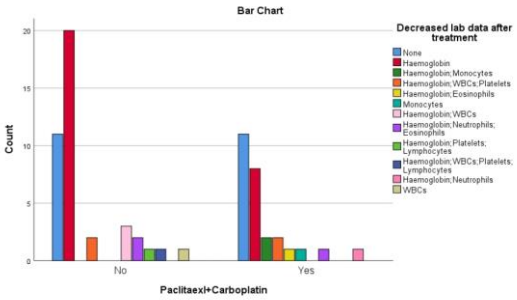
Among 27 patients receiving chemotherapy of Paclitaxel+Carboplatin among the 68 of the study population, Majority of them experience drug induced nausea and vomiting along with alopecia(n=7). Followed by several other experiencing burning sensation(n=4) and observed to have peripheral neuropathy and pigmentation(n=4).2 patients experienced myalgia and 2 others were observed with pedal oedema along with the above mentioned ADRs. Other patients experienced one of these ADRs only.



DISTRIBUTION OF KNOWLEDGE OF PERSONAL AND MENSTRUAL HYGIENE:

Among the women of our study about 63.2% of them had moderate level knowledge of menstrual and personal hygiene. A total of 25% high knowledge on menstrual hygiene and personal hygiene and practice. Only about 11.8% of women of the study had poor knowledge and understanding of hygiene.





Lab data variation:

In Patients receiving Paclitaxel and Pacli+Carbo chemotherapy there was considerable decrease in Haemoglobin levels. Followed by a gradual decrease in WBCs, Platelets, neutrophils, lymphocytes and eosinophils.

The chemotherapy induced anaemia was quite evident.

CONCLUSION:

Drug prescribing patterns of different regimens of Paclitaxel were observed for the varying effect on target patients. The individual patient response and also the possible ill-effects of a drug was analysed using standard scales such as CTCAE toxicity grade and Naranjo scale scores, in order to draw an inference on the fashion of adverse reactions and events occurring in study population. Along with this primary approach to study the evaluation of drug utilization and its beneficence, certain other correlations of menarche age and menopause age with diagnosis of cancer was strived to establish pertaining to some of the prominent factors of the considered study subject. Statistical analysis of each variable and data collected during the study and its accurate application into computing the results of the intended study, helps to validate and rely on the findings of the study. Thus, the performed research satisfactorily met the needs to understand the beneficence of chemotherapy of paclitaxel and its combination regimen by comparative and correlative approach.

ACKNOWLEDGEMENT:

The authors are thankful to our mentor Dr. Nagendra R, Associate professor, SVCP, Mysuru., and all the faculty members of the Department of Pharmacy Practice, SVCP, Mysuru. We also thank Dr. Hanumanthachar Joshi, Principal, SVCP, Mysuru, Dr. Nandhini, assistant professor, SVCP and Special thanks to Dr Vishveshwara MS, Medical superintendent, Bharath Hospital and Institute of Oncology, Mysuru.

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Research Article

A Cross-Sectional Knowledge Attitude Practice Study on Assessment Of Selfcare, Nutrition, Medication and Postpartum Care To Be Taken in Antenatal Period During Pregnancy

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ABSTRACT: Background: The primary goal of antenatal care is to ensure the health of both the mother and the baby. Maternal mortality is quite high, although it can be lowered via regular check-ups, early detection of pregnancy-related problems, and rapid treatment. The current study aims to analyse pregnant women's knowledge, attitude, and practice attending Seth Mohandas Tulsidas Maternity Hospital in Mysuru.

Methods: A cross-sectional study was conducted on 140 women for period of six months. Questionnaires documented electronically in Google-form, entered in MS-Excel sheet.

Results: A total of 79-[rural area], 61-[urban area]. Age group of patients were 42-[<20 years], 87-[21-30 years], 11-[<31 years]. Total of 42-high school education, 35 passed intermediate, 40-graduation and 23-illiterate. On validation overall, I-CVI(%)-95%, S-CVI(%)-95.85, 94.25,93.75,95.25% for relevance, clarity, simplicity, ambiguity. Cronbach's alpha coefficient-0.71, indicating questionnaire is accepted and validated. KAP results shows moderate knowledge practice(n=59,42.14%) (n=61,43.57%), good attitude (n=78,55.71%), 16.42%(n= 23) having poor overall KAP scores, age found to influence it.

Conclusion: Increase Education, awareness program to motivate women to utilize maternal care services. Government should provide easily accessible ANC facilities to all rural areas, to improve maternal health, resolve maternal-infant deaths in India.

Keywords: Antenatal care (ANC), pregnancy, maternal health, adolescent pregnancy rural-urban.

INTRODUCTION:

Antenatal care is considered as the backbone of obstetrical services and the health of pregnant women. It includes not only providing nutrition and care but also risk identifications and screening, prevention and management of maternal and foetal complications during ANC period.[1] Globally 80% of pregnant women receive at least one ANC visit with skilled person.[2] The World Health Organization (WHO) describes antenatal care (ANC) as the care provided by skilled health-care professionals to pregnant women and adolescent girls in order to ensure the best health conditions for both mother and baby during pregnancy. Antenatal Care is an opportunity to promote the benefits of skilled attendance at birth and to encourage women to seek postpartum care for themselves and their new-born. It is also an ideal time to counsel women about the benefits of child spacing. [1] Maternal health refers to the health of women throughout pregnancy, childbirth, and the postpartum period. [3]

Maternal mortality is one of the major causes of death among women between the age of 15 to 19 years. [4] Annually, 810 women die globally as a result of pregnancy and childbirth. [3] India has the highest number of maternal deaths in the world. [4] Nearly two-thirds of all maternal deaths are caused by serious complications, which include severe bleeding (typically after childbirth), infections, high blood pressure throughout pregnancy (pre- and eclampsia), problems during delivery, and botched abortions.[4,5] In India it is heartening to note that Maternal Mortality Ratio (MMR) has declined from 130/100,000 live births in 2014–16 to 113/100,000 live births in 2016-18.[4] 95% of

maternal death occur in low- income and lower-middle- income countries like India[5]. According to WHO guidelines there must be at least four ANC should be done [6]. The advice regarding nutrition, prevention of anemia, iron calcium and folic acid supplements, hygiene, physical activity, breastfeeding and social and emotional support are the parts of ANC. [7,8,9] Overall, these interventions result in healthy pregnancies and lower rates of maternal mortality. There are various obstacles that lower the quality of maternal health services, including ignorance, negligence, abuse in basic health facilities, hunger, poverty, and early marriages that exacerbate the problem [6].

Knowledge refers to a pregnant women's understanding of components of antenatal care which include registration of pregnancy, danger signs during pregnancy, intake of prophylactic Iron and Folic Acid tablets during pregnancy and adapting family planning methods. Attitudes are emotional, motivational, perceptive and cognitive beliefs that positively or negatively influence the behaviour or practice of an individual. A pregnant female's antenatal check-up, adapting family planning behaviour is influenced by her emotions, motivations, perceptions and thoughts [5]. Practice is defined as the observable actions of a pregnant women that could affect her to go to the hospital for an antenatal check-up, after knowing the danger signs during pregnancy, how she is making the arrangement to attend the hospital and how she had adapted to the family planning methods after marriage, in the previous and present pregnancy.[10] Better access to high-quality care prior to, during, and after childbirth can lower the risk of maternal death [5].

Most of the pregnant mothers were from rural areas and were young who did not know much about the importance of antenatal visits, screening for infectious diseases and advantages of taking supplements on time during pregnancy, so necessity of education, antenatal care and awareness program can resolve the current scenario of maternal and infant deaths in India. Current study was conducted in order to assess the knowledge, attitude, and practice related to ANC among the pregnant women attending antenatal clinic Seth Mohandas Tulsidas Maternity Hospital, Mysuru. This may be useful to further planning of health intervention program.

MATERIALS AND METHODOLOGY:

Study Setting: A study was conducted over six months among pregnant women aged between 18-36 years in Seth Mohandas Tulsidas Maternity Hospital, Mysuru.

Inclusion and Exclusion criteria: We randomly selected the respondents between 18-36 years of age and who were willing to participate in the study, were included after taking consent from them or their caretakers through the informed consent form. Whereas pregnant women who don't have relevant data were excluded from the study.

Ethical issues: written informed consent was taken from the individual subjects before the commencement of the study.

Sample size: Total number of subjects enrolled in the study: 140.

Selection of subjects: We randomly selected the subjects who met all the required inclusion and exclusion criteria.

Data collection: All the relevant information like demographic details, and medical and medication history of the patient were collected and documented using a suitable annexure.

Study Tools:

a. Informed Consent Form: Informed consent is a process by which a subject voluntarily confirms his/her willingness to participate in a particular trial, after having been informed of all aspects of the survey that are relevant to the subject's decision to participate. It is documented using a written, signed, and dated informed consent form.

b. KAP questionnaire: A Knowledge, Attitude, and Practices (KAP) survey is a quantitative method (predefined questions formatted in standardized questionnaires) that provides access to quantitative and qualitative information. It is a 40-point questionnaire with 10 knowledge-based questions, 6 attitude questions and 6 practice-based questions scored and analysed.

c. Patient Data collection Form: It included demographic details like name, age, gender, gestational period, weight, social history (education, place of residence, diet, parity, abortion, miscarriage, interpregnancy interval, smoking and alcohol), non-oral hormonal contraceptive, oral hormonal. contraceptive, regular menstrual cycle, history of anaemia before pregnancy, Hb (g/dl) level in 2 months of interval, past medical history, past medication history, present medical history and present medication history.

Analysis: The quantitative variables were described using their number and mean. Microsoft word and Excel have been used to generate graphs, tables etc. Chi-square test, mean and P-value were used in our study.

QUESTIONNAIRE:

To access the knowledge of pregnant women.

1. Is antenatal care essential for pregnant women?
   Yes (76) No (1) Don't know (63)
2. Is it necessary to do at least 4 visits to antenatal clinic?
   Yes (45) No (4) Don't know (91)
3. Is it necessary to give inj. TT during pregnancy?
   Yes (96) No (6) Don't know (38)
4. How many inj. TT should be given to the pregnant mother?
   1 (20) 2 (110) 3(4) Don't know (6)
5. Is it necessary for pregnant women to undergo screening for Hepatitis B, C, HIV, blood grouping and haemoglobin?
   Yes (58) No (4) Don't know (78)
6. Are you aware of the alarming signs during pregnancy?
   Yes (49) No (73) Don't know (18)
7. Do pregnant women need vitamin supplements, folic acid, and iron supplements during their pregnancy?
   Yes(82) No(6) Don't know(52)
8. Do you know milk and sunlight are good sources of calcium?
   Yes(46) No(6) Don't know(88)
9. Are you aware of any family planning methods?
   Yes (54) No(52) Don't know(34)
10. Are you familiar with breastfeeding concepts?
    Yes(73) No(51) Don't know(16)

To access Attitudes among pregnant women.

1. The First visit to the antenatal clinic must be done in the first trimester of pregnancy.
   Agree(81) Neutral(50) Disagree(9)
2. At least 4 visits are a must during pregnancy
   Agree(54) Neutral(16) Disagree(70)
3. Blood pressure should be monitored regularly during pregnancy
   Agree(78) Neutral(12) Disagree(50)
4. Dietary habits should be changed as advised by the doctor
   Agree(86) Neutral(22) Disagree(32)
5. Iron and folic acid supplements are a must for pregnant women during pregnancy
   Agree(83) Neutral(21) Disagree(36)
6. Antenatal follow-up is good for the mother and child's health
   Agree(111) Neutral(28) Disagree(1)

To access Practice among pregnant women

1. Are you regular for antenatal care visit schedule?
   Yes(92) No(48)
2. How many antenatal visits did you make?
   1(7) 2(40) 3(46) 4(44) >4(3)
3. Are you involved in any physical activities like walking, yoga, meditation, and exercise?
   Yes(85) No(55)
4. Are you taking supplements as prescribed by your doctor?
   Yes(87) No(53)
5. Do you take proper rest as advised by your doctor?
   Yes(102) No(38)
6. Did you make changes in your diet as advised by your doctor?
   Yes(74) No(66)

DEMOGRAPHIC DISTRIBUTION OF STUDY POPULATION:

Out of 140 subjects, 56.4% (79) and 43.5% (61) were from rural and urban areas respectively. 42 (30%) of pregnant women were from the age group of <20 years, 62.1% (87) from 21-30 years, and 7.8% (11) were from <31 years. 63 (45%) subjects were vegetarian and 77 (55%) were non- vegetarian. A total of 42 (30%) had got high school education, 35(20%) passed intermediate, 40(28.5%) had graduated, and 23(16.4%) were illiterate (Table 1)

Table 1: Demographic Distribution of Study Population

Demographics		Numbers (%) (n=140)
Age Group	<20 years 21-30 years >31 years	42 (30%) 87 (62.1%) 11 (7.8%)
Literacy	High school Intermediate (PUC) Degree Illiterate	42 (30%) 35 (25%) 40 (28.5%) 23 (16.4%)
Diet	Veg Non veg	63(45%) 77 (55%)
Residency	Rural Urban	79 (56.4%) 61 (43.5%)
Parity	1 2 3 >4	89(63.57%) 29(20.71%) 19(13.57%) 3(2.1%)

RISK FACTOR ANALYSIS BY USING OVERALL KAP SCORES:

The probable risk factors such as age, residency, parity and educational status were considered for risk factor analysis, the following results are shown in the following (Table 3)

Table 3: Details of risk factors analysis: influencing KAP

Factors		Overall KAP scores		Chi-square value	p-value
		0-20 (poor)	21-40 (good)		
Age	18-26	52	54	20.25	0.000434
	27-36	2	32		
Place of residency	Rural	38	41	7.9	0.088225
	Urban	15	46		
Parity	1	44	45	18.74	0.09656
	2	8	21		
	3	0	19		
	>4	2	1		
Literacy	High school	24	18	91.1	1.24
	Intermediate (PUC)	14	21		
	Degree	2	38		
	Illiterate	14	9		

RESULT:

A study includes 140 subjects. Out of these, 56.4% (79) and 43.5% (61) were from rural and urban areas respectively. 42 (30%) of pregnant women were from the age group of <20 years, 62.1% (87) from 21-30 years, and 7.8% (11) were from <31 years. A total of 42 (30%) had got high school education, 35(20%) passed intermediate, 40(28.5%) had graduated, and 23(16.4%) were illiterate. Knowledge-based questionnaires revealed that 76 of 140 subjects agree that receiving antenatal care is essential.

The remaining 64 subjects were teenagers from rural areas who were unaware of the benefits of antenatal care and it was their first visit. Out of which majority of the respondents (n=91) had little awareness of antenatal visits, and 45 of them agreed that at least four visits were required. Only 58 of the 140 applicants had knowledge of infectious disease screening. Multiparous subjects had an experience with prenatal care. 49 out of 140 subjects were aware of warning symptoms like vaginal bleeding, discharge, persistent weight loss, and excruciating abdominal pain throughout pregnancy. About 96 pregnant women agreed that injection of Tetanus Toxoid is required but was unaware of its importance during pregnancy. 82 subjects were aware of the intake of iron, folic acid, and vitamin supplements during pregnancy. Iron and folic acid were taken merely because of the doctor's advice. The majority of subjects (88) were unfamiliar that milk and sunlight are good sources of calcium. Only 54 multigravida subjects were aware of utilizing copper T for the inter-pregnancy gap and family planning methods. 73 subjects were cognizant of breastfeeding principles.

DISCUSSION AND CONCLUSION:

The study included 140 pregnant women who are visiting the Seth Mohandas Tulsidas Maternity Hospital, Mysore. Predominantly subjects were belonging to age group of 18-26 (75%) and other belongs to 27-36 (25%) age group. However, 16% (23) of pregnant women were illiterate and 30% (42) of them completed their High school education and 25% (35) of them completed their Intermediate and remaining are graduated. 61 (43%) subjects reside in urban areas while the remaining 79 (56%) reside in rural areas. According to studies 63% (89) possess first pregnancy and 51(36%) possess multi pregnancy. Whereas 45% of pregnant women following vegetarian diet and remaining 55% of them are following non-vegetarian diet. A study conducted by *Assefa Philipos kare et al*[1] share almost similar demographic details like age, literacy, place of residency.

Vuppu Sitalakshmi et al[11] conducted a study on KAP study on antenatal care among pregnant women attending antenatal tertiary care institution in which 20% of pregnant women completed 3 of their ANC visits. In our study 54% of subjects agreed that antenatal care is essential Similarly, 45% of also agreed to the necessity of at least 4 antenatal visits during their gestational period. Based on studies 57% of them visited the ANC clinic during their first trimester of pregnancy, 46% of pregnant women completed their 3rd ANC visit, 44% of pregnant women completed their 4th during their gestational period, and 79% of subjects are willing for further follow up for better mother and child health.

The study depicts that 68% of subjects are incognizant about TT injection (n=96) and 78% of them have knowledge about the number of TT injection that needs to be taken during pregnancy (n=110) which is similar to the study conducted by *Shahnaz Akhtar et al*[12] about KAP among pregnant women in the rural area of Lahore in which 51% of pregnant women agreed to take TT injection.

41% of pregnant women agreed to undergo a screening test for Hepatitis B, HIV, blood grouping and haemoglobin, which correlates with the study conducted by *Vuppu Sitalakshmi et al*[11] also, the study conducted by *Shahnaz Akhtar et al*[12] shows that 82% of pregnant women agreed to monitor Blood pressure regularly, which is similar to our study in which 55% of them were agreed to monitor Blood pressure during pregnancy.In our study 35% of subjects are sensible of alarming signs during pregnancy, which corelates with the study by *Abayneh Akililu Solomon et al*[13] in which 38% of pregnant women having knowledge about alarming signs during pregnancy.

Fida F et al[14] observational study on use of

dietary supplementation among pregnant women in the centre of Jordan in which 71% of subjects were taking iron supplements regularly. Comparably, in our study 82% of pregnant women having knowledge about need of vitamin, folic acid and iron supplements during pregnancy and also 83% of them agreed to take during gestational period and 62% of them are regularly intakes.In our study, 46% of subjects were aware of milk and sun light as a source of calcium, which is similar to study by *Zelalem Tenaw et al*[15] in which 82% of pregnant women were practicing regular milk intake for the source of calcium. Relatively 86% of pregnant women have a favorable attitude towards changing their dietary habits and also 74% of them practice proper diet guided by their doctors.

A study by *Jody R et al*[16] regards improving health literacy through group antenatal care, in which pregnant women have significant knowledge about breastfeeding (90% in group care and 66% in individual care). Equivalently 73% of pregnant women were familiar with the breastfeeding concept and 54% of them were familiar with family planning concept. 85% of pregnant women were practicing physical activities like yoga, meditation etc.

Most of the pregnant mothers were from rural areas and were young who did not know much about the importance of antenatal visits, screening for infectious diseases and advantages of taking supplements on time during pregnancy, so necessity of education, antenatal care and awareness program can resolve the current scenario of maternal and infant deaths in India. The study found that adolescent pregnancy was associated with a higher risk of late booking and fewer ANC visits, which could contribute to negative mother and birth outcomes. According to the information acquired from interviews, an adolescent's access to ANC services is restricted by the nurse's attitude, a fear of HIV testing, health system barriers, a lack of understanding, and financial barriers. A crucial component of the strategy would be to precisely identify the obstacles to individual counselling at the clinic level and implement suitable actions to guarantee that each pregnant woman's unique situation is addressed.

ACKNOWLEDGEMENT:

The authors are thankful to our mentor Dr. Davan B Bevoor, Associate Professor, SVCP, Mysuru., and all the faculty members of the Department of Pharmacy Practice, SVCP, Mysuru. We also thank Dr. Hanumanthachar Joshi, Principal, SVCP, Mysuru, Dr. Ravindra P Choudhary, assistant professor, SVCP and Special thanks to Dr Srinath, AMO, Seth Mohandas Tulsidas Maternity Hospital, Mysuru.

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Research Article

A Comparative Study on The Safety and Efficacy Of Intrathecal 0.5% Hyperbaric Bupivacaine Alone Versus Bupivacaine Along With Adjuvant Dexmedetomidine In Parturient Undergoing Cesarean Section – A Prospective Observational Study

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ABSTRACT: **AIM:** The aim of this study is to assess the efficacy and safety of 0.5% hyperbaric bupivacaine administered alone versus when given along with adjuvant dexmedetomidine in parturients undergoing LSCS.
METHOD: A hundred parturients of ASA grade II & III undergoing LSCS under spinal anaesthesia were randomly assigned into two groups of 50 each: group B received 0.5% hyperbaric bupivacaine (2ml) and group BD received 0.5% hyperbaric bupivacaine (1.9ml) with 10 mcg of dexmedetomidine (0.1ml). The onset and duration of sensory & motor block, intraoperative hemodynamic changes, and duration of analgesia were documented. No. of rescue analgesics given in the first 24 hrs were also noted.
RESULT: There was no significant difference between the onset of sensory and motor block. The mean duration of motor blockade in Group B was 107 ± 13.55 mins and in Group BD was 351 ± 57.36 mins. The mean duration of sensory blockade in Group B was 156.82 ± 24.75 mins and in Group BD was 415.94 ± 55.16 mins. The mean duration of analgesia in Group B was 182.86 ± 24.06 mins and in Group BD was 489.24 ± 64.76 mins. The no. of rescue analgesics consumed in group BD was less in 1st 24 hrs.
CONCLUSION: The findings of this study indicate that 10 mcg dexmedetomidine is more beneficial when used in conjunction with 0.5% hyperbaric bupivacaine compared to 0.5% hyperbaric bupivacaine used alone in parturients undergoing C-section under spinal anesthesia.
Keywords: Bupivacaine, Dexmedetomidine, LSCS, Spinal anesthesia.

INTRODUCTION:

The use of spinal anesthesia for cesarean delivery is preferred over general anesthesia, not only because it avoids the risks associated with general anesthesia, such as failed intubation, but also because it enables more effective pain control, early ambulation, and a faster return to daily activities for newly delivered mothers, thus improving their quality of life.[1]

Bupivacaine is an amide local anesthetic that produces significant sensory and motor blockade. Despite its advantages, bupivacaine can cause side effects. A disadvantage of using hyperbaric bupivacaine alone is its relatively short duration of action, which necessitates early analgesic intervention in the postoperative period.[2]

Postoperative pain management in cesarean cases is essential in order to

avoid adverse effects of pain on the mother. In addition, it facilitates the early recovery of the mother and the nursing of her newborn. Therefore, adding adjuvants to local anesthetic agents in spinal anesthesia is a sensible concept and choice.[3]

Dexmedetomidine is an $\alpha_2$receptoragonist, known to maintain hemodynamic stability, and provide good quality intraoperative and prolonged postoperative analgesia with minimal side effects when given along with hyperbaric bupivacaine. Also, dexmedetomidine has been widely used in different types of nerve blockade.[3]

MATERIALS AND METHODOLOGY:

A prospective observational study was carried out in Seth Mohandas Tulsidas Maternity Hospital, Mysuru for a period of 6 months from April 2022 to September 2022.

100 parturients undergoing Cesarean section were enrolled in the study after obtaining informed consent and were randomly divided into two groups of 50 each: **Group B** received 2 ml of 0.5% hyperbaric Bupivacaine alone for spinal anesthesia. **Group BD** received 1.9 ml of 0.5% hyperbaric Bupivacaine along with 0.1 ml of Dexmedetomidine as an adjuvant intrathecally.

Inclusion criteria:

- Women willing to participate in the study
- Women undergoing LSCS
- Age group between 18 to 40 years
- Parturients with Hb level > 10g/dl
- Parturient with singleton, without any complication
- Parturients of ASA physical status II, and III

After shifting the parturient to the operation theatre, standard monitors like NIBP, PR, MAP, and SpO_2 were connected and basal readings were noted. With the parturient in either a sitting position or left lateral position, spinal anesthesia was performed by using a 25G or 26G Spinal needle at L_2—L_3/ L_3—L_4 L4—L_5 intravertebral space by the anesthetist under aseptic circumspection.

After spinal anesthesia, the sensory blockade was measured every minute at the T10 dermatome. This is checked in the midaxillary line and considered ready for surgery after a loss of sensation to cold swabs. Every 3 minutes, the level of sensory blockade was assessed and the time from the completion of injection to the maximum level of sensory blockade was recorded.

The onset time of motor blockade (the interval from the process of injecting the drug to the occurrence of Modified Bromage scale 1 motor blockade) was noted using the Modified Bromage scale.

Hemodynamics such as NIBP, PR, MAP, and SpO2 were recorded intraoperatively at baseline, 1 minute after SAB, every 3 minutes for the first 15 minutes, every 5 minutes for the next 15 minutes, and every 10 minutes until the end of surgery.

The baby's delivery time, weight of the baby and neonatal outcome (APGAR score at 1 and 5 min) was recorded.

Intraoperatively, Bradycardia (R <60/min) was treated with Inj. Atropine 0.6 mg IV and Hypotension (MAP less than 20% of the baseline) were treated with Inj. Mephentermine 6 mg IV.

Postoperatively, all parturients were assessed by the investigators for the duration of motor blockade (from the time of injection of the drug till the patient regained complete motor power) and duration of sensory blockade (from the time of injection of the drug till the patient regained sensation at S2 dermatome) and duration of analgesia (from the time of injection of drug till the patient complain of pain at the incision site).

Inj. Diclofenac 75mg was given intramuscularly to the patient who complain of pain at the incision site with a VAS score $\geq$ 3. And the total consumption of analgesia within the first 24 hrs was noted.

All parturients were monitored post-operatively at 2 hrs, 4 hrs, 6 hrs, 12 hrs, and 24 hrs for vitals and post-operative pain (through the VAS scale). The time of the first rescue analgesic given is noted, and side effects were directly monitored by the investigators.

Then incidence of side effects was postoperatively recorded to check the efficacy and safety of spinal anesthesia in both groups.

Inj. Glycopyrrolate was given IV to treat post-operative Bradycardia; Inj. Tramadol and Inj. Chlorpheniramine maleate was given IM to treat post-operative shivering.

STATISTICAL ANALYSIS:

Statistical analysis was performed by using Microsoft Office Excel 2019 for the evaluation of data.

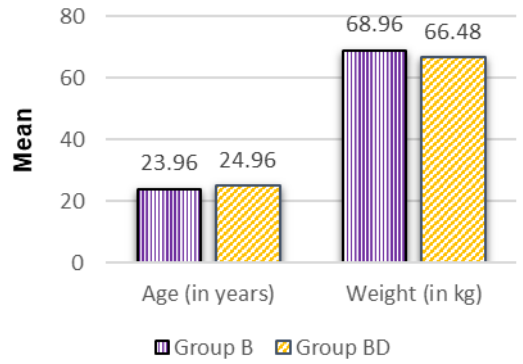
For nominal data Student t-test and categorical data chi-square test was used. The data were expressed as mean ± SD.

For categorical values, descriptive statistics were presented in the form of frequencies and percentages.
p-value < 0.05 was considered statistically significant.

OBSERVATION AND RESULTS:

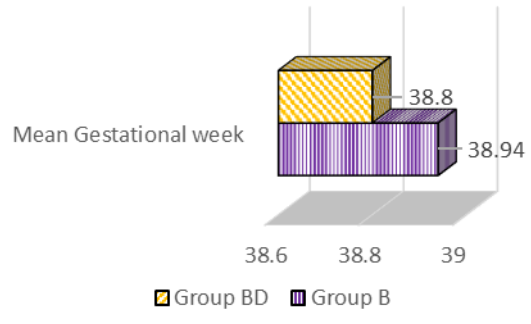
The mean age in group B was 23.96 ± 3.64 years and in group BD was 24.96 ± 3.71 years with a p-value of 0.177. The mean weight in group B was 68.96 ± 11.69 kg and in group BD was 66.48 ± 10.81 kg with a p-value of 0.273. Hence there were no statistically significant changes between the age and weight of parturients between the two groups. (Fig 1)

Fig 1: Age & Weight distribution between two groups



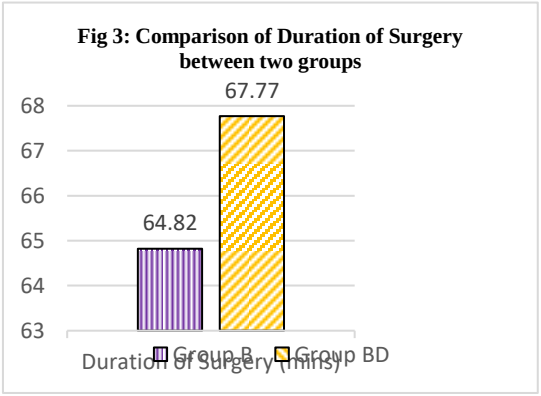
The mean gestational week in group B was 38.94 ± 1.11 weeks and in group BD was 38.8 ± 1.01 weeks with a p-value of 0.511. Therefore, the result was found to be statistically insignificant.

Fig 2: Comparison of gestational week between two groups



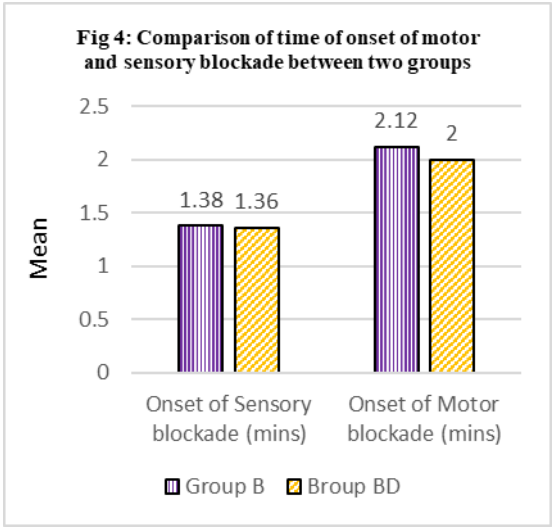
The mean duration of surgery in Group B was 64.82 ± 10.30 mins and in Group BD was 67.77 ± 15.52 mins with a p-value of 0.283. There was no significant difference in the duration of surgery between the two groups. (Fig 3)

Fig 3: Comparison of Duration of Surgery between two groups



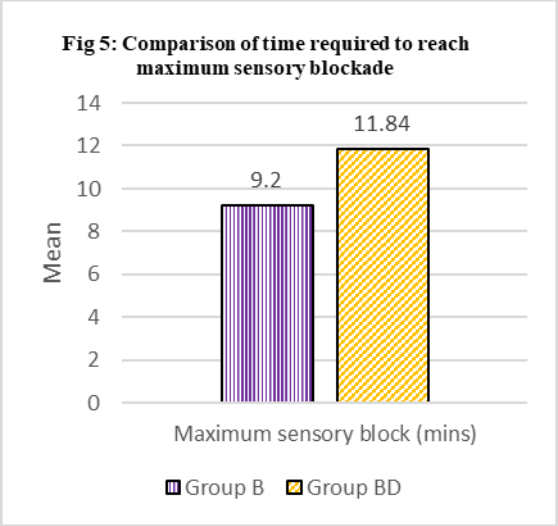
The mean onset of sensory blockade in Group B was 1.38 ± 0.49 mins and in Group BD was 1.36 ± 0.48 mins with p-value of 0.837. The mean onset time of motor blockade in Group B was 2.12 ± 0.52 mins and in Group BD was 2 ± 0.20 mins with a p-value of 0.131. Hence, there was no significant difference between onset of sensory blockade and motor blockade between two groups. (Fig 4)

Fig 4: Comparison of time of onset of motor and sensory blockade between two groups

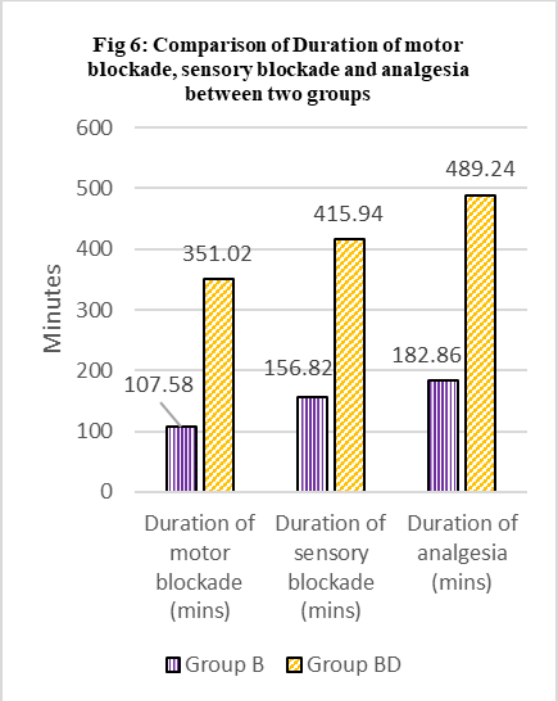


14 participants in Group B had T4 (28%) and 36 had T6 (72%) level of sensory block, where as in group BD all participants had a T4 (100%) level of sensory block with p-value < 0.0001 which was statistically significant.

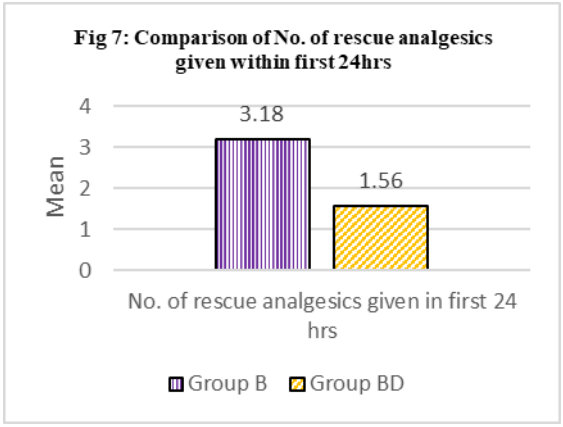
The mean time required for peak block height (maximum sensory blockade) in group B was 9.2 ± 1.42 mins and in Group BD was 11.8 ± 1.85 mins with p-value < 0.0001. Hence, the time required for maximum sensory blockade was statistically significant in both groups. (Fig 5)



The mean duration of motor blockade in Group B was 107 ± 13.55 mins and in Group BD was 351 ± 57.36 mins with p-value < 0.0001. The mean duration of sensory blockade in Group B was 156.82 ± 24.75 mins and in Group BD was 415.94 ± 55.16 mins with p-value < 0.0001. The mean duration of analgesia in Group B was 182.86 ± 24.06 mins and in Group BD was 489.24 ± 64.76 mins with p-value < 0.0001. Hence, the duration of motor blockade, sensory blockade, and analgesia were statistically significant. In Group B the mean no. of rescue analgesics consumed was 3.18 ± 0.48 and in Group BD was 1.56 ± 0.50 with p-value < 0.0001 which was statistically significant. (Fig 6)



In Group B the mean no. of rescue analgesics consumed was 3.18 ± 0.48 and in Group BD was 1.56 ± 0.50 with p-value < 0.0001 which was statistically significant. (Fig 7)



VAS score in group B was 2.42 ± 1.51, 1.88 ± 1.09, 2.88 ± 1.85, and in group BD was 0, 0, 0.38 ± 0.83 with p-value <0.001 which was statistically significant. At 12 hrs VAS score in group B was 2.48 ± 1.31 and in group BD was 2.44 ± 0.54, with a p-value of 0.842 which was statistically not significant. At 24 hrs VAS score in group B was 2.06 ± 1.47 and in group BD was 2.8 ± 0.90, with a p-value of 0.003 which was statistically significant. (Fig 8)

APGAR score was calculated to evaluate the health of new-born. There was no significant difference between the two groups in 1 minute and 5minute APGAR score. (Fig 9)

We observed shivering in 46% of participants in group B and 30% in group BD, Bradycardia in 2% of participants in group B and 10% of participants in group BD, hypotension in 4% of participants in group B, nausea was more frequent in group B (26%) than group BD (6%), vomiting was prevalent in group B, while headaches were reported by 22% in group B and 2% in group BD. There was no statistical difference between the two groups in terms of post-operative side effects. (Fig 10)

Fig 8: Comparison of VAS score between two groups

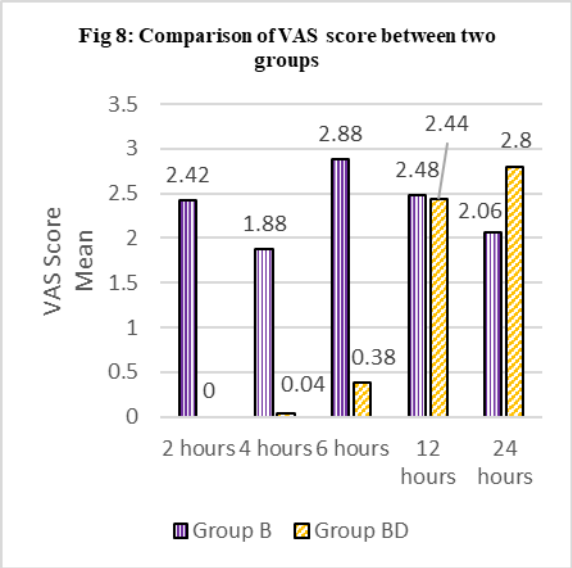
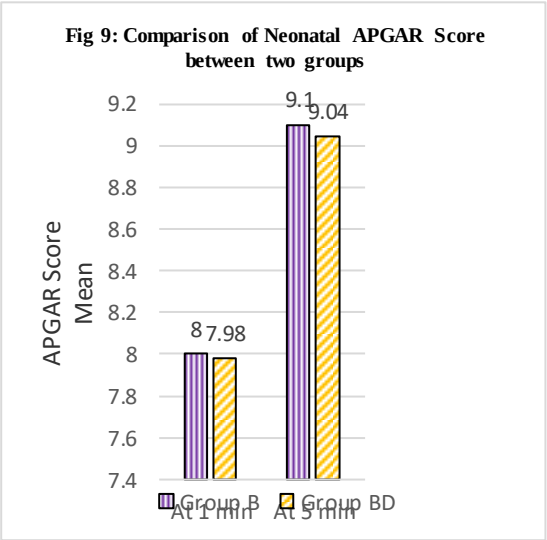


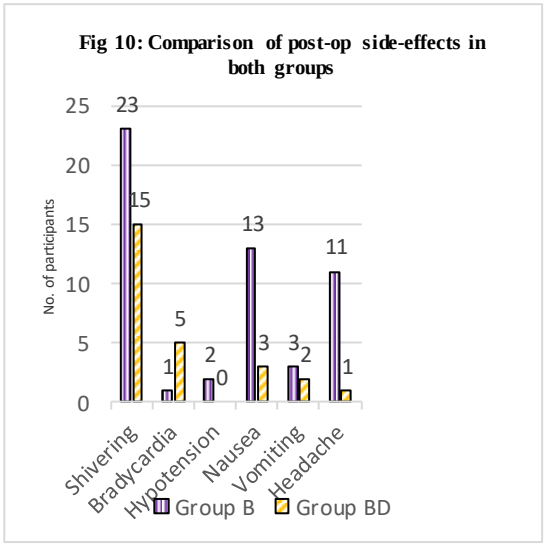
Fig 9: Comparison of Neonatal APGAR Score between two groups



DISCUSSION:

In our study, the mean onset of sensory blockade in Group B was 1.38 ± 0.49 mins and in Group BD was 1.36 ± 0.48 mins with a p-value of 0.837. The mean onset time of motor blockade in Group B was 2.12 ± 0.52 mins and in Group BD was 2 ± 0.20 mins with a p-value of 0.131. Hence, there was no significant difference between the onset of sensory block and motor block between the two groups. Thus, the time of onset of sensory block and motor block was comparable to the study conducted by M Azam et al [6].

Fig 10: Comparison of post-op side-effects in both groups



Hemodynamic changes:

Fig 11: Comparison of SBP between two groups

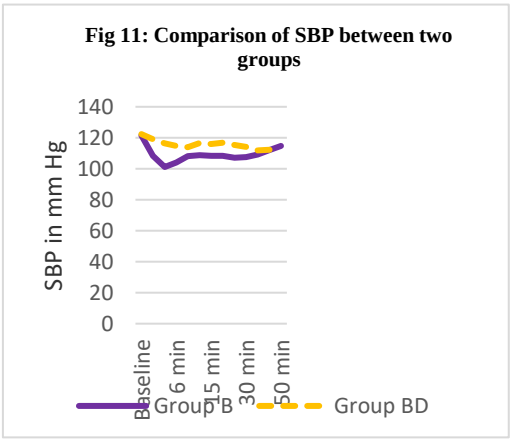
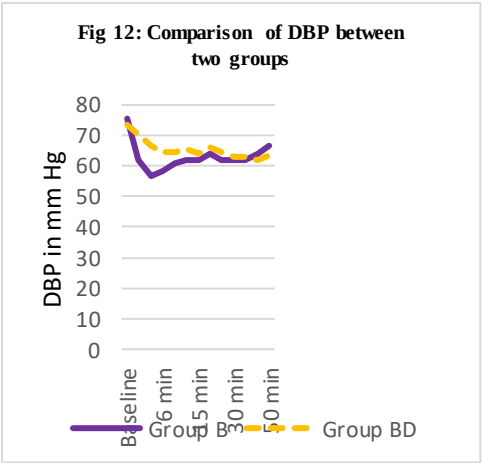
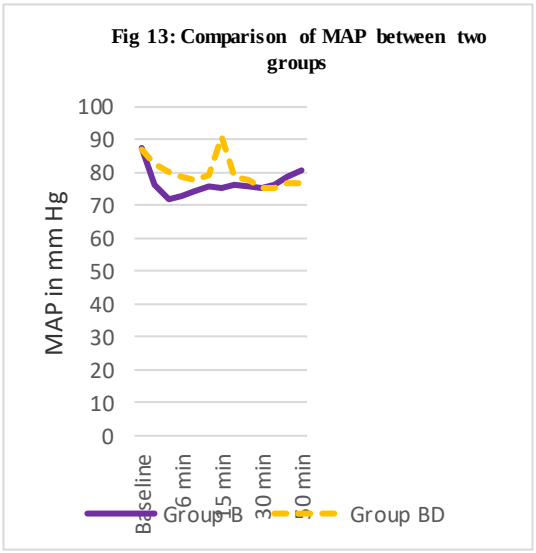
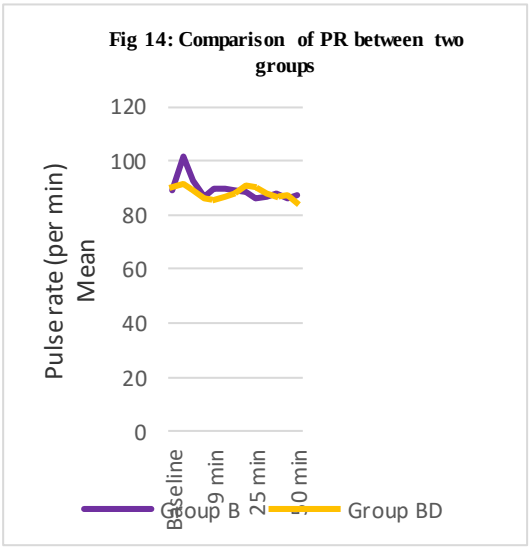


Fig 12: Comparison of DBP between two groups







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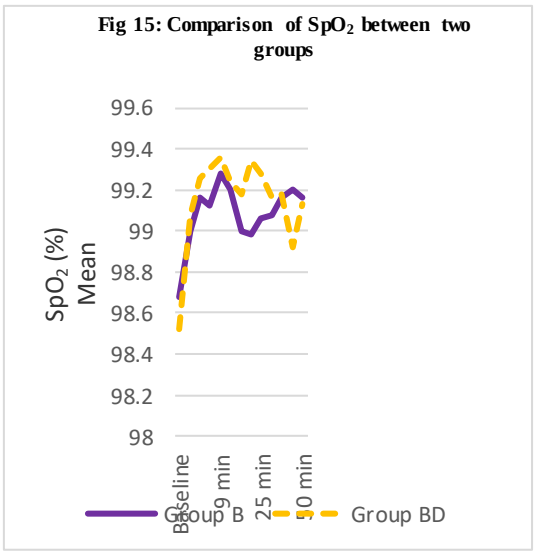

In our study, the peak sensory level achieved by group B was T_4 in 28% of participants and T_6 level in 72% which is consistent with the research result of Xiao-xiao Li et al [4] (peak sensory level at T_4 was 37% and T_6 was 61%). We found that the peak sensory level achieved by group BD in our study is T_4 in 100% of participants, this is in accordance with the study conducted by Chanda Salame et al [14].

In our study, the mean duration of motor block is found to be increased in group BD compared to group B (351 ± 57.36 mins **vs** 107 ± 13.55 mins). The mean duration of sensory blockade in Group B was 156.82 ± 24.75 mins and in Group BD was 415.94 ± 55.16 mins with a p-value < 0.0001. Hence, the duration of motor block and sensory block were statistically significant in our study. This was in accordance with the studies conducted by Rahul Rajan et al [5]., M Azam et al [6]., Sushruth MR et al [7]., Lin Liu et al [9]., Yong-Hong Bi et al [10]., and Chanda Salame et al [14]. Nasr I. A concluded that the duration of sensory and motor block is seen longer in the group of parturients, who were given with sufentanil or dexmedetomidine with hyperbaric bupivacaine as intrathecal spinal anesthesia. [8]

The mean duration of analgesia In Group B was 182.86 ± 24.06 mins and in Group BD was 489.24 ± 64.76 mins with a p-value < 0.0001. According to Ali M.S [15] in the dexmedetomidine group the mean postoperative duration of analgesia was 270.25±23.81 minutes, while in bupivacaine, the mean was found to be 140.46±10.38 minutes. Ali M.S concluded that women undergoing elective cesarean section with standard spinal anesthesia with dexmedetomidine have longer post operative analgesia duration compared to standard spinal anesthesia given alone.

In our study, the mean no. of rescue analgesics consumed in group B was 3.18 ± 0.48 and in Group BD was 1.56 ± 0.50 with a p-value < 0.0001. In the study conducted by Chanda Salame et al., the Bupivacaine group required 2-3 doses of Diclofenac and Dexmedetomidine required 1-2 doses of Diclofenac as a rescue analgesic in the first 24 hrs. [14]

Intraoperative side-effects:

The incidence of shivering is lower in group BD (2%) compared with group B (24%) in our study. It is comparable with the results of Sushruth MR [7]

and Karim Nasseri [11] who had found a lower incidence of shivering with the use of intrathecal dexmedetomidine.

In our study, the mean MAP was found significantly higher from 1 min after SAB to 6 mins in group BD compared to group B. 10% of participants in group B and 2% of participants in group BD developed hypotension. In the study conducted by M Azam et al [6]., 36.7% with bupivacaine and 13.3% with dexmedetomidine developed hypotension which was statistically different.

The pulse rate was significantly higher at 1 min after SAB from the baseline in Group B in our study. The incidence of bradycardia was not significant in our study. None in group BD and 2% of participants in group B developed bradycardia. Karim Nasseri [11] reported 8.33% with bupivacaine and 4% with dexmedetomidine developed bradycardia.

VAS score:

With regard to VAS score our study is comparable to studies conducted by Rahul Rajan et al [5] and Chanda Salame et al [14]. In our study, the VAS score was significantly higher in group B at 2 hrs, 4 hrs, and 6 hrs compared to group BD. At 12 hrs also VAS score was lesser in group BD but was not statistically significant.

Neonatal APGAR score:

There was no significant difference between the two groups at 1-minute and 5-minute APGAR scores ($p = 0.836$, $p = 0.549$, respectively). In the study by Houman Teymourain et al., [12] and Yong-Hong Bi et al [10]., it was shown that dexmedetomidine had no adverse effects on neonatal APGAR scores and no significant difference was seen in both groups.

Postoperative side-effects:

We observed shivering in 46% of participants in group B and 30% in group BD, Bradycardia in 2% of participants in group B and 10% of participants in group BD, hypotension in 4% of participants in group B, nausea was more frequent in group B (26%) than group BD (6%), vomiting was prevalent in group B, while headaches were reported by 22% in group B and 2% in group BD. There was no statistical difference between the two groups in terms of post-operative side effects.

Xia F et al [13] in their study observed 33.33% hypotension, 15.5% nausea and vomiting, and 20% shivering cases, whereas the dexmedetomidine group had 17.7% hypotension, nausea, and vomiting cases, 15.5% shivering cases, and 2.2% PDPH case.

CONCLUSION:

According to our findings, when dexmedetomidine is combined with hyperbaric bupivacaine, the following results can be achieved:

- Prolonged duration of sensory block
- Prolonged duration of motor block
- Hemodynamics were stable throughout the LSCS, except for Bradycardia in few patients post-operatively.
- Prolonged duration of analgesia
- The incidence of post-operative shivering was less
- Consumption of no. of rescue analgesics was less
- Incidence of intra-operative and postoperative side effects was less

Hence, the findings of this study indicate that dexmedetomidine is more beneficial and safer when used in conjunction with hyperbaric bupivacaine than when used alone Intrathecally in parturients undergoing C-section under spinal anesthesia.

ACKNOWLEDGEMENT:

The authors are thankful to the Department of Anaesthesiology, Seth Mohandas Tulsidas Maternity and Child Health Hospital, Mysuru for providing all the facilities to carry out this work.

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Research Article

Antioxidant Activity of a Popular Formulation Claimed By The Traditional Herbal Medicine Practitioners of Puducherry To Be Effective In Prophylaxis And Therapeutic Management Of Covid-19

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ABSTRACT: The aim of this research work is to evaluate the antioxidant activity of the hydroalcoholic extract of herbal formulation for COVID-19 by *in silico* and *in vitro* approach. The reported phytoconstituents of ingredients of herbal formulation were explored for molecular docking using Autodock Vina against the four targeted proteins such as lipoxygenase, NADPH oxidase, myeloperoxidase and xanthine oxidase. *In vitro* antioxidant activity was evaluated by DPPH radical scavenging and Hydroxyl Radical scavenging assay. The molecular docking study revealed that all phytoconstituents exhibited negative binding energy which indicates that they possess inhibitory activity. Among 157 phytoconstituents, Licorice-saponinA3 showed least binding energies such as-12.3Kcal/mol, -11.9Kcal/mol and -11.4Kcal/mol for the protein myeloperoxidase, NADPH oxidase, and xanthine oxidase respectively and 19-acetoxy-7, 9, 10 deacetyl-baccin VI showed least binding energy (-11.2Kcal/mol) for the protein lipoxygenase. The *in vitro* antioxidant activity revealed that the hydroalcoholic extract showed dose dependent scavenging activity and maximum activity at 1mg/ml concentration. Based on the results obtained it is concluded that herbal formulation possesses antioxidant activity.

Keywords: DPPH scavenging assay, hydroxyl scavenging assay, molecular docking and phytoconstituents.

INTRODUCTION:

COVID-19 (Corona Virus Disease -2019), a highly contagious respiratory disease which was first reported in Wuhan, China was caused by SARS CoV2 (Severe Acute Respiratory Syndrome Corona Virus-2) that lead to escalation of infection globally also death of million across the world[1,2]. SARS Cov-2 belonging to Beta coronavirus genera and subfamily ortho coronavirinae primarily causes respiratory and extra respiratory manifestation with varying severity[3].Depending upon one's age, health and comorbidities such as hypertension, diabetes etc, the severity of disease varies. Acute cardiac complication, ARDS and multiple organ dysfunction are some of the chronic condition in COVID-19 due to the response of immunological stress. This condition is due to activation of many inflammatory pathways and excess production of ROS. ACE2 receptor acts as the primary binding site for SARS CoV-2 spike protein which causes reduction of cleavage of AT II and hence its concentration increases in blood. This in turn activates MAP kinase , NF-kappa B and protein kinase C which results in NOX2 activation and upstream of cytokine and COX2. Activation of endothelial NOX2 causes excessive production of ROS resulting in oxidation of RNA, DNA and proteins which in turn signals the inflammatory response. Successively ensue in cell death and organ damage. Hence, in COVID-19 pathogenesis oxidative stress and ROS production play a major role[4]. This research work aims to explore novel herbal formulation for antioxidant activity through *insilico* and *invitro* approach.

Materials and Methods:

Insilico studies - Molecular docking:

Protein Preparation:

In the course of Arachidonic acid metabolism the enzymes such as myeloperoxidase, xanthine oxide, Lipoxygenase, NADPH oxidase and cytochrome P450 tend to rise the ROS generation which causes the oxidative stress and affects the redox homeostasis[5]. Hence these proteins serve as target for designing the drug for antioxidant property. The targeted proteins were downloaded

from protein data bank in PDB format and converted to PDBQT format using Autodock 4.2.6 software.

Ligand Preparation:

The reported 157 phytoconstituents of the formulation were downloaded from Pubchem in SDF format and converted to PDBQT format using open babel software.

Autodock Vina

Virtual screening was studied for the reorted phytoconstituents of herbal formulation using Autodock vina software where the protein ligand interaction for inhibition of protein is evaluated based on the their binding energy in comparison with standards such as zileuton, melatonin, dextromethorphan and febuxostat for the proteins lypoxygenase, myeloperoxidase, NADPH oxidase and Xanthine oxidase respectively. AutoDock vina generates 10 conformation for complex of ligand with target receptor. The active sites were predicted in protein ligand interaction profiler website.

In silico Studies

DPPH Radical Scavenging assay

The free radical scavenging potential of natural compounds is widely evaluated by DPPH radical scavenging activity. The antioxidant activity of herbal formulation was evaluated by DPPH radical scavenging assay according to Beatrice MG etal described method with slight modification[6].Briefly, 5 different concentration of hydroalcoholic extract of herbal formualtion (0.0625, 0.125, 0.25, 0.5,1 mg/ml) were prepared to 1ml with DMSO in triplicate. Same concentation of standard Ascorbic acid were prepared using DMSO. To this 3ml of 0.1mM DPPH solution was added and incubated for 20 minutes at room temperature in dark room. Blank was prepared with 1ml of DMSO and 3ml of 0.1mM DPPH solution. The absorbance of the reaction mixture is measured at 517nm using spectrophotometer. The percentage of scavenging activity was determined using the following formula:

$$\% \text{ of Radical Scavenging activity} = \frac{\text{Abs of control} - \text{Abs of Sample}}{\text{Abs of control}} \times 100$$

Hydroxyl Radical Scavenging activity

Hydroxyl radical scavenging activity of hydroalcoholic extract was evaluated according to Kalaisezhiyen et al with slight modification[7]. 5 different concentration of sample and standard (0.0625, 0.125, 0.25, 0.5,1 mg/ml) were prepared using DMSO. To this 1ml of 0.13% of ferrous ammonium sulphate (Iron EDTA solution), 0.5ml of 0.018% of EDTA and 0.5ml of 0.018% of EDTA and 0.5ml of 0.22% ascorbic acid were added. The test tubes were carefully heated in water bath at 80 to 90ºC for 15 minutes. To the above mixture ice cold 17.5% of TCA(1ml) was added to terminate the reaction and 3ml of nash reagent was added and incubated for 15 minutes at room temperature. The absorbance was measured at 412nm against the blank. triplicate of standard and test sample were prepared. The percentage of inhibition is determined by following formula:

$$\% \text{ of Radical Scavenging activity} = \frac{\text{Abs of control} - \text{Abs of Sample}}{\text{Abs of control}} \times 100$$

Statistical Method :

Mean±SEM was calculated followed by Student t test with two tailed distribution with unequal variance with p value less than 0.05

Results and Discussion

Molecular docking:

Molecular docking reveals that all phytoconstituents showed negative binding energy. The standand zileuton showed -7.5Kcal/mol against the targeted protein lypoxygenase and the binding energies of phytoconstituents were represented in figure1. The standard Melatonin showed binding energy -5.8Kcal/mol for the protein myeloperoxidae and the binding enegies for the phytoconstituents were represented in figure2. The standard dextromethorphan exhibited -7.4Kcal/mol for the protein NADPH oxidae and figure3 represent the binding energies of phytoconstitutents. The standard febuxostat exhibited -8.2Kcal/mol for the protein xanthine oxidase and the figure4 represent the binding enegies for the reported phytoconstituents. Among 157 phytoconstituents , the constituent 135 showed least binding energies for the protein targets myeloperoxidase(-12.3Kcal/mol), NADPH oxidase (-11.9Kcal/mol) and Xanthine oxidase (-11.4Kcal/mol) and the constituent 27 exhibited least binding energy for the protein lypoxygenase(-11.2Kcal/mol).

DPPH Radical Scavenging assay:

The principle behind the DPPH radical Scavenging assay is the acceptance of electron from antioxidant compound by DPPH radical which is indicated by colour change from violet to yellow followed by measurement of absorbance. The comounds which have the ability to carryout this reaction are considered as radical scavengers or antioxidants.

In vitro DPPH radical scavenging assay revealed the increased dose dependent scavenging activity for hydroalcoholic extract and maximum scavenging activity was observed for 1mg/ml. L-ascorbic acid (standard) exhibited higher scavenging activity than the extract. The results were represented in table 1 and figure 5.

Hydroxyl Radical Scavenging activity

Hydroxyl radical acts as potent oxygen reactive species in biological system. In hydroxyl radical scavenging assay ascorbic acid and iron EDTA generates hydroxyl radical by reacting with DMSO (oxidation reaction) which result in formation of formaldehyde, that helps in detection of hydroxyl radical when treated with nash reagent.

In vitro Hydroxyl radical scavenging assay revealed the increased dose dependent scavenging activity for hydroalcoholic extract and maximum scavenging activity was observed for 1mg/ml. Gallic acid (standard) exhibited higher scavenging activity than the extract. The results were represented in table 2 and figure 6.

Acknowledgement

The authors desire to acknowledge Dr.M.Arumugam, Associate Professor of CAS in Marine Biology, Annamalai University for allowing us to carry out invitro antioxidant activity in his laboratory.

Tables

Table 1 represent the scavenging activity of standard ascorbic acid and hydroalcoholic extract of herbal formulation by DPPH scavenging activity assay.

Table 1: Invitro DPPH scavenging activity of hydrochloric extract of herbal formulation.

Table1: Invitro DPPH scavenging activity of Hydroalcoholic extract of herbal formulation

Concentration in mg/ml	Percentage of Inhibition (in %)	
	L-ascorbic acid	Hydroalcoholic extract
0.0625	28.50±0.17	10.90±0.30
0.125	36.29±0.36	17.20±0.13
0.25	50.47±0.33	31.51±0.18
0.5	70.78±0.18	56.09±0.18
1	84.84±0.15	77.23±0.16

The values are expressed as mean±SEM

Table 2 represent the hydroxyl scavenging activity of gallic acid hydroalcoholic extract of herbal formulation

Table 2: Invitro hydroxyl scavenging activity of Hydroalcoholic extract of herbal formulation

Concentration in mg/ml	Percentage of Inhibition (in %)	
	Gallic acid	Hydroalcoholic extract
0.0625	24.36±0.13	18.99±0.20
0.125	39.62±0.29	33.73±0.10
0.25	57.63±0.13	47.38±0.17
0.5	68.98±0.12	59.56±0.13
1	82.93±0.07	73.09±0.20

The values are expressed as mean±SEM

Figures

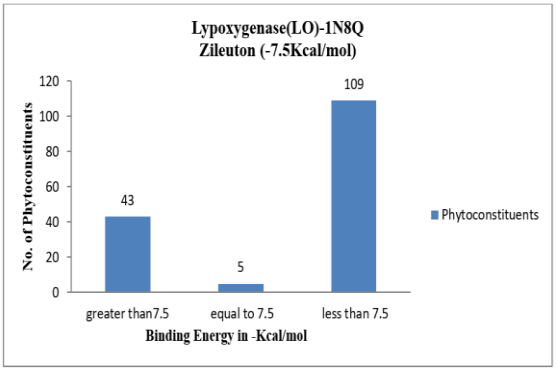

Figure1: Binding energies of phytoconstitutents against the protein lypoxygenase. The standard Zileuton showed binding energy – 7.5Kcal/mol. 109 phytoconstituents showed less binding energy than the standard which indicates that the possess better inhibitory activity than the standard.

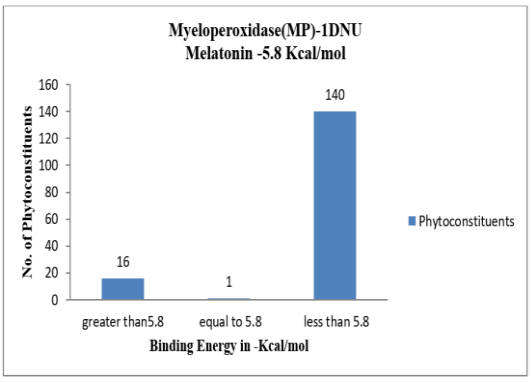

Figure2: Binding energies of phytoconstitutents against the protein myeleperoxidase. The standard Melatonin showed binding energy – 5.8 Kcal/mol. 140 phytoconstituents showed less binding energy than the standard which indicates that the possess better inhibitory activity than the standard.

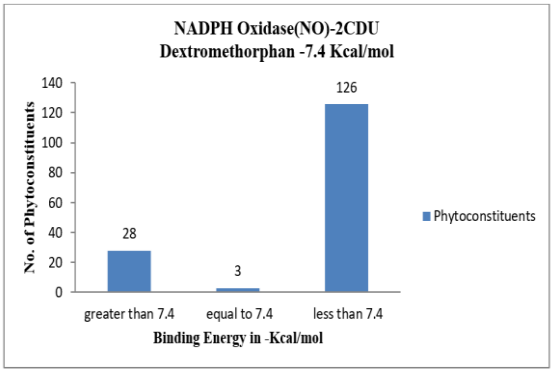

Figure3: Binding energies of phytoconstitutents against the protein NADPH oxidase. The standard dextromethorphan showed binding energy – 7.4 Kcal/mol. 126 phytoconstituents showed less binding energy than the standard which indicates that the possess better inhibitory activity than the standard.

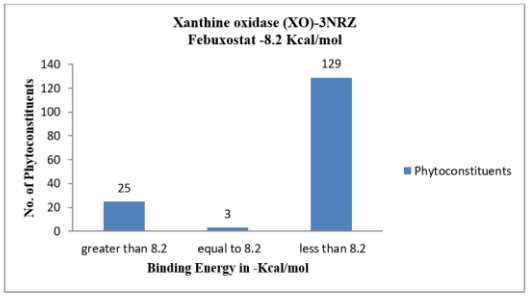

Figure4: Binding energies of phytoconstitutents against the protein Xanthine oxidase. The standard febuxostat showed binding energy -8.2 Kcal/mol. 129 phytoconstituents showed less binding energy than the standard which indicates that the possess better inhibitory activity than the standard.

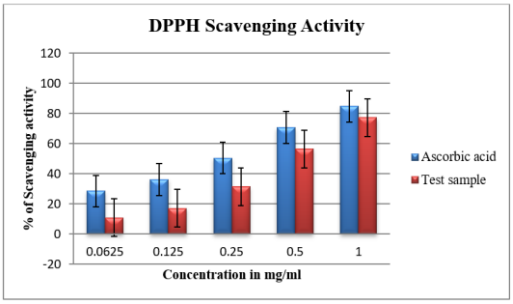

Figure5: In vitro DPPH scavenging activity of hydroalcoholic extract which is represented in mean±SEM and the values are not significantly different (p>0.05)

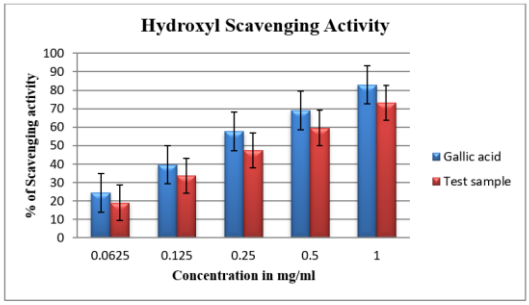

Figure6: In vitro Hydroxyl scavenging activity of hydroalcoholic extract which is represented in mean±SEM and the values are not significantly different (p>0.05)

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Review Article

Impact of Artificial Intelligence in Disease prediction and Biomedical Research Rising opportunities in Health care Industry

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ABSTRACT: Artificial intelligence has proved to play an important role in health care industry due to its primary capability behind development of precision medicine widely agreed to be direly needed advancements in care. Even though early efforts of providing diagnosis, management and treatment recommendations have proven challenging, the opportunities are high as AI shall ultimately master that domain as well. AI has proven to be very beneficial for radiological analysis of brain, speech and hearing, biomedical information processing, biomedical research, natural language processing, diagnosis and treatment of blood borne bacterial infections, bladder volume prediction, epileptic seizures, and management of dementia. It is interesting to understand that AI will not replace human clinicians completely, but may augment their efforts to take proper care of patients. In future, health care providers may move towards tasks and human skills that are required like empathy, persuasion and big picture integration, else they may lose their jobs over time, if do not work alongside artificial intelligence.

Key Words: Artificial Intelligence, Prediction, Machine learning, Biomedical research, Clinical design support

INTRODUCTION

Artificial intelligence (AI) is defined as the intelligence of machines, as opposed to the intelligence of humans or other living species [1-2]. AI can also be defined as the study of ‘‘intelligent agents”—that is, any agent or device that can perceive and understand its surroundings and accordingly take appropriate action to maximize its chances of achieving its objectives [3]. AI also refers to situations wherein machines can simulate human minds in learning and analysis, and thus can work in problem solving. This kind of intelligence is also referred to as machine learning (ML) [4]. Typically, AI involves a system that consists of both software and hardware. From a software perspective, AI is particularly concerned with algorithms. An artificial neural network (ANN) is a conceptual framework for executing AI algorithms [5]. It is a mimic of the human brain—an interconnected network of neurons, in which there are weighted communication channels between neurons [6]. One neuron can react to multiple stimuli from neighboring neurons and the whole network can change its state according to different inputs from the environment [7]. The goal for healthcare is to become more personal, predictive, preventative, and participatory, and AI can make major contributions in these directions. From an overview of the progress made, we estimate that AI will continue its momentum to develop and mature as a powerful tool for biomedicine.

AI for living assistance

In the area of assisted living for elderly and disabled people, AI applications using corresponding smart robotic systems are paving the way for improvements in life quality. An overview of smart home functions and tools offered for people with loss of autonomy (PLA), and intelligent solution models based on wireless sensor networks, data mining, and AI was published recently [8]. NNs can be trained with specific image-processing steps to recognize human facial expressions as commands. Furthermore, human–machine interfaces (HMIs) based on facial expression analysis allow people with disabilities to

control wheelchairs and robot assistance vehicles without a joystick or sensors attached to the body [9]. An ‘‘ambient intelligent system” called RUDO can help people who are blind to live together with sighted people and work in specialized fields such as informatics and electronics [10]. People who are blind can make use of multiple functions of this intelligent assistant through a single user interface. A ‘‘smart assistant” based on AI can help pregnant women with dietary and other necessary advice during crucial stages of maternity. It is capable of providing suggestions at ‘‘an advanced level” through its own intelligence, combined with ‘‘cloud-based communication media between all people concerned” [11]. A fall-detection system based on radar Doppler time–frequency signatures and a sparse Bayesian classifier can reduce fall risks and complications for seniors [12]. In fact, ‘‘smart communication architecture” systems for ‘‘ambient assisted living” (AAL) have been developed to allow AI processing information to be gathered from different communication channels or technologies, and thus to determine the occurrences of events in the network environment and the assistance needs of elderly people [13].

AI in biomedical information processing

Breakthroughs have been made in natural language processing for biomedical applications. In the area of biomedical question answering (BioQA), the aim is to find fast and accurate answers to user-formulated questions from a reservoir of documents and datasets. Therefore, natural language-processing techniques can be expected to search for informative answers [14]. To begin with, the biomedical questions must be classified into different categories in order to extract appropriate information from the answer. ML can categorize biomedical questions into four basic types with an accuracy of nearly 90% [15]. Next, an intelligent biomedical document retrieval system can efficiently retrieve sections of the documents that are most likely to contain the answers to the biomedical questions [16]. One novel scheme for processing one of the four basic types of BioQA—the yes-or-no answer generator, which originates from word sentiment analysis—can work effectively toward information extraction from binary answers [17].

AI in biomedical research

In addition to being able to act as an ‘‘eDoctor” for disease diagnosis, management, and prognosis, AI has unexplored usage as a powerful tool in biomedical research [18]. On a global scale, AI can accelerate the screening and indexing of academic literature in biomedical research and innovation activities [19-20]. In this direction, the latest research topics include tumor-suppressor mechanisms [21], protein–protein interaction information extraction [22], the generation of genetic association of the human genome to assist in transferring genome discoveries to healthcare practices [23], and so forth. Furthermore, biomedical researchers can efficiently accomplish the demanding task of summarizing the literature on a given topic of interest with the help of a semantic graph-based AI approach [24]. Moreover, AI can help biomedical researchers to not only search but also rank the literature of interest when the number of research papers is beyond readability. This allows researchers to formulate and test to-the-point scientific hypotheses, which are a very important part of biomedical research. For example, researchers can screen and rank figures of interest in the increasing volume of literature [25] with the help of an AI to formulate and test hypotheses.

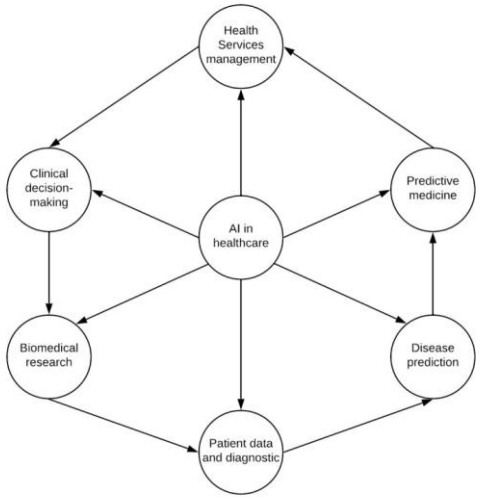
Disease diagnostics and prediction

The most urgent need for AI in biomedicine is in the diagnostics of diseases. A number of interesting breakthroughs have been made in this area. AI allows health professionals to give earlier and more accurate diagnostics for many kinds of diseases [26]. One major class of diagnosis is based on in vitro diagnostics using biosensors or biochips[27]. For example, gene expression, which is a very important diagnostic tool, can be analyzed by ML, in which AI interprets microarray data to classify and detect abnormalities (Fig. 1)

Healthcare

AI is now covering a wide range of healthcare applications [28]. In particular, it has been used for signal and image processing, and for predictions of function changes such as in urinary bladder control [29], epileptic seizures [30], and stroke predictions [31]. Below, we describe two typical case studies: bladder volume prediction and epileptic seizure prediction.

Figure 1: Dominant variables for AI in health care and biomedical research



Bladder volume prediction

When the storage and urination functions of the bladder fail as a result of spinal cord injury or because of other neurological diseases, health status, or aging, various complications occur in the patient's health conditions. Nowadays, partial restoration of bladder function in drug-refractory patients can be achieved using implantable neural stimulators. To improve the efficiency and safety of neuroprostheses through conditional neurostimulation [32], a bladder sensor that detects stored urine is required as a feedback device that applies electrical stimulation only when needed. The sensor can also be used to notify patients with impaired sensations in a timely manner when the bladder needs to be emptied or when an abnormally high residual postmicturition volume remains after an incomplete voiding. We have proposed new methods [33] and developed a dedicated digital signal processor (DSP) [34] for sensing both the pressure and its fullness in urine by using afferent neural activities from the regular neural roots of the bladder (i.e., mechanoreceptors), which depicts the changes during filling.

Epileptic seizure prediction

Epilepsy, a neurodegenerative disease, is one of the most common neurological conditions and is characterized by spontaneous, unpredictable, and recurrent seizures [35-36]. While first lines of treatment consist of long-term medications-based therapy, more than one third of patients are refractory. On the other hand, recourse to epilepsy surgery is still relatively low due to very modest success rates and fear of complications. An interesting research direction is to explore the possibility of predicting seizures, which, if made possible, could result in the development of alternative interventional strategies [27]. Although early seizure-forecasting investigations date back to the 1970s [37], the limited number of seizure events, the paucity of intracranial electroencephalography (iEEG) recordings, and the limited extent of interictal epochs have been major hurdles toward an adequate evaluation of seizure prediction performances.

AI in management of dementia

Machine learning models that can accurately distinguish those with symptomatic Alzheimer's dementia from those with mild cognitive impairment and normal cognition as well as predict progressive disease using relatively inexpensive and accessible ocular imaging inputs are impactful tools for the diagnosis and risk stratification of Alzheimer's dementia continuum [38]. If these machine learning models can be incorporated into clinical care, they may simplify diagnostic efforts. Recent advancements in ocular-based machine learning efforts are promising steps forward [39].

DISCUSSION

Artificial intelligence (AI) generally applies to computational technologies that emulate mechanisms assisted by human intelligence, such as thought, deep learning, adaptation, engagement, and sensory understanding [40-41]. Some devices can execute a role that typically involves human interpretation and decision-making [42-43]. These techniques have an interdisciplinary approach and can be applied to different fields, such as medicine and health. AI has been involved in medicine since as early as the 1950s, when physicians made the first attempts to improve their diagnoses using computer-aided programs [44-45]. Interest and advances in medical AI applications have surged in recent years due to the substantially enhanced computing power of modern computers and the vast amount of digital data available for collection and utilization [46]. AI is gradually changing medical practice. There are several AI applications in medicine that can be used in a variety of medical fields, such as clinical, diagnostic, rehabilitative, surgical, and predictive practices. Another critical area of medicine where AI is making an impact is clinical decision-making and disease diagnosis. AI technologies can ingest, analyse, and report large volumes of data across different modalities to detect disease and guide clinical decisions [42]. AI applications can deal with the vast amount of data produced in medicine and find new information that would otherwise remain hidden in the mass of medical big data [47–49]. These technologies can also identify new drugs for health services management and patient care treatments. The technology will potentially reduce care costs and repetitive operations by focusing the medical

profession on critical thinking and clinical creativity. The AI perspective is exciting; however, new studies will be needed to establish the efcacy and applications of AI in the medical field [50].

Conclusions

It is very evident that on AI strategies for healthcare from the accounting, business, and management perspectives. Structured literature review (SLR) method was employed for its reliable and replicable research protocol [51] and selected bibliometric variables as sources of investigation. Bibliometric usage enables the recognition of the main quantitative variables of the study stream [52]. This method facilitates the detection of the required details of a particular research subject, including field authors, number of publications, keywords for interaction between variables (policies, properties and governance) and country data [53]. It also allows the application of the science mapping technique. The investigation offers potentials insights for future researchers and practitioners.

ACKNOWLEDGEMENTS

Authors are thankful to Principal, The National Institute of Engineering, Mysuru and department of Electronics and Communication Engineering, NIE, for the encouragement and support.

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- To organize into an association of all persons engaged in, interested in or connected with community pharmacy.
- To elevate and establish a standard of competence for community pharmacy.
- To develop and promote standards of education and training for community pharmacy.
- To develop and promote short term informal training programs for individuals interested in community pharmacy.
- To educate hospital trustees, Board of Directors, Board of Visitors and the public to understand that the practice of community pharmacy calls for special training and experience.
- To serve as a forum for exchange of ideas and experiences, and collection and dissemination of information in general community pharmacy.
- To spread the knowledge on the principles, practices, techniques and methods concerning community pharmacy.
- To promote and safeguard the status and the interest of community pharmacy and the interests of those engaged in it.
- To promote sponsor, submit, memorandums, petitions and representations to local, state, union and other authorities for better laws, and influence legislations which affect hospitals and other community pharmacy organizations.
- To organize conferences, seminars, meetings and discussions for the promotion and furtherance of the aims and objects of the ACPI.
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