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Dear Readers,

It is with great pride and enthusiasm that I welcome you to this issue of the *International Journal of Pharmacy Practice*. As the Chief Editor, I am delighted to present a diverse collection of articles that underscore the evolving role of pharmacy practice in improving healthcare systems worldwide.

Pharmacy practice continues to expand and adapt to meet the needs of a rapidly changing healthcare environment. The integration of pharmacists into multidisciplinary healthcare teams, the adoption of evidence-based practices, and the use of innovative technologies are just a few examples of how our profession is shaping the future of healthcare delivery. This issue highlights the pivotal contributions of pharmacists in various areas, from optimizing medication use to advancing public health initiatives.

Our current edition includes a range of thought-provoking studies, reviews, and commentaries from experts around the world. Key highlights include:

- **Innovations in Clinical Pharmacy Practice:** Articles exploring advancements in clinical services, medication safety, and therapeutic drug monitoring.
- **Pharmacists as Public Health Advocates:** Research on the impact of pharmacist-led health promotion campaigns, vaccination efforts, and chronic disease management.
- **Global Perspectives on Pharmacy Education:** Insights into the evolution of pharmacy curricula and the development of competency frameworks to prepare future pharmacists.
- **Technological Transformations:** Discussions on the role of digital health tools, artificial intelligence, and tele pharmacy in enhancing pharmacy practice.

As we navigate these exciting changes, the journal remains committed to being a platform for sharing groundbreaking research, fostering collaboration, and inspiring innovation. To our readers, contributors, and reviewers, thank you for your unwavering support and dedication to advancing the practice of pharmacy. Your contributions are invaluable to our shared mission of improving healthcare outcomes.

Finally, I encourage all of you to continue engaging with the journal. Whether by submitting your research, providing constructive peer reviews, or simply sharing our content with colleagues, your involvement is crucial to our success.

Thank you for joining us on this journey to advance the science and practice of pharmacy. Together, we can build a healthier and more equitable world.

Sincerely,

Hanumanthachar Joshi
Editor in Chief
International Journal of Community Pharmacy

Review Article

A SYSTEMATIC REVIEW OF PHARMACOVIGILANCE AND ADVERSE DRUG REACTION

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ABSTRACT:

The history of pharmacovigilance started back 169 years ago with the death of a 15- year-old girl, Hannah Greener. However, the Thalidomide incident of 1961 brought a sharp change in the pharmacovigilance process, with adverse drug reaction reporting being systematic, spontaneous, and regulated timely. Therefore, continuous monitoring of marketed drugs was essential to ensure the safety of public health. Any observed adverse drug reaction detected by signals was to be reported by the health profession. Moreover, signal detection became the primary goal of pharmacovigilance based on reported cases. Among various methods used for signal detection, the Spontaneous Reporting System was most widely preferred; although, it had the limitation of "under-reporting". Gradually, the World Health Organization Collaborating Centre and "Uppsala Monitoring Centre" were established in 1978 for international monitoring of drugs. The center was responsible for operating various databases like vigiflow, vigibase, vigilyze, and vigiaccess. Recently, huge data could be generated through spontaneous reporting linked with computational methods, such as Bayesian Framework, E-Synthesis. Furthermore, drug safety surveillance at an early stage prior to the official alerts or regulatory changes was made possible through social media. In addition, India created a National Pharmacovigilance Program, and Schedule Y of the Drug and Cosmetic Act 1945 was reviewed and amended in 2005.

Keywords: Pharmacovigilance, Adverse drug reactions, Uppsala Monitoring Centre, World Health Organization (WHO).

INTRODUCTION

The challenge of maximizing drug safety and maintaining public confidence is indeed complex. Pharmaceutical and biotechnology companies have the responsibility to monitor and proactively assess and manage drug risks throughout a product's lifecycle, from development to post-market. This involves implementing robust pharmacovigilance systems to identify and evaluate potential risks, conducting clinical trials to gather safety data, and adhering to regulatory guidelines and requirements. (1) Indeed, pharmacovigilance plays a crucial role in drug regulation systems, public health programs, and clinical practice. It encompasses the science and activities involved in detecting, assessing, understanding, and preventing adverse effects of drugs or any other potential drug- related problems. By actively monitoring and evaluating the safety profile of drugs, pharmacovigilance helps identify and mitigate risks, ensuring the overall safety and effectiveness of medications. It also facilitates the collection and analysis of data on adverse drug reactions, enabling regulatory authorities, healthcare professionals, and patients to make informed decisions regarding drug use. Ultimately, pharmacovigilance contributes to the improvement of patient safety and the optimization of healthcare outcomes. (2)

According to the World Health Organization (WHO), pharmacovigilance is defined as the science and activities involved in the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related drawbacks, particularly the long-term and short-term adverse effects of medicines. The term "pharmacovigilance" has its roots in the Greek word "Pharmakon," meaning "drug," and the Latin word "vigilance," meaning "to keep watch." It is important to note that pharmacovigilance is not a new concept in many Asian countries and has, in fact, been ongoing since 1998. This demonstrates the recognition of the importance of monitoring and ensuring the safety of medicines in these regions for over two decades. (3) When Asian nations decide to join the Uppsala Centre for Adverse Event Monitoring, they gain access to an important tool for gathering safety data through spontaneous reporting of adverse drug reactions and adverse events. This method allows for early detection of potential risks associated with drugs. While clinical trials are essential for establishing the safety and efficacy of a drug before it is commercially marketed, they do have limitations. Strict inclusion and exclusion criteria limit the generalizability of trial results to a selective group of patients. Special populations such as children, pregnant women, and elderly individuals are often not included in these trials, and factors like genetic variations, environmental influences, and

drug- drug interactions may not be fully studied during the clinical trial phase.

By actively monitoring and analyzing data on adverse events, pharmacovigilance enhances the understanding of drug safety profiles and helps improve patient care by providing valuable information for drug prescribing and regulatory decision-making (4) You are correct that adverse drug reactions (ADRs) can have significant negative impacts on patients, including increased suffering, morbidity, and mortality. These ADRs also impose a financial burden on society. The estimated overall incidence of ADRs in hospitalized patients is approximately 6.7%. Data suggests that patients who experience ADRs have a 19.18% higher death rate and an 8.25% longer hospital stay compared to those without ADRs. Additionally, the total medical cost for patients with ADRs is increased by an average of 19.86%. These statistics highlight the importance of effective pharmacovigilance and proactive management of drug risks to minimize the occurrence and impact of ADRs, ultimately improving patient outcomes and reducing healthcare costs. (5)

Its stated objectives were:
It is support and strengthen consumer reporting ofsuspected ADRs.
It expands the role and scope of national pharmacovigilance centers to identify,analyze and prevent medication errors.
It is promoted better and broader use of existing pharmacovigilance data forpatient safety.
It is developing additional pharmacovigilance methods to complement data fromspontaneous reporting systems.
The work was organized into four main themes:
Increasing patient reporting of problems associated with the use of medicines.
Collection by national pharmacovigilance centers of reports of medication errors.
Improving the use of available pharmacovigilance data for identifying drug dependence,
counterfeit and sub-standard medicines, and for clinical risk estimation.
Development of active and targeted spontaneous pharmacovigilance activities.

HISTORY OF PHARMACOVIGILANCE IN ASIAN NATION:

Table No.01 : Sequential Pharmacovigilance development with special reference to India (6)

Year	Developments
1747	Very first known clinical trial by James Lind, proving usefulness of lemon juice in preventing scurvy.
1937	Death of more than 1000 children due to toxicity of Sulphanilamide.
1950	Aplastic anaemia reported due to Chloramphenicol toxicity.
1961	Worldwide tragedy due to thalidomide toxicity.
1963	16th World Health congregation recognize significant to rapid action on AdverseDrug Reactions.
1968	WHO research project for International drug monitoring on pilot scale.
1996	Global standards level clinical trials initiated in India.
1997	India attached with WHO Adverse Drug Reaction Monitoring Program.
1998	Initiation of PV In India.
2002	67th National Pharmacovigilance Centre established in India.
2004-05	India launched National PV Program.
2005	Accomplishment ofstructured clinical trials in India.
2009-10	PVPI started.

The sequential pv developments shown in the above table.
In 1986, pharmacovigilance (PV) was initiated in an Asian nation with the establishment of twelve regional centres, each covering a population of 50 million. However, the progress made in developing a proper adverse drug reaction (ADR) monitoring system was not significant. In 1997, Bharat (India) joined the World Health Organization (WHO) and attempted to implement an ADR surveillance program based in two urban centres, but it was not successful. Subsequently, in 2005, the WHO provided support and the World Bank funded the National PV Program (NPVP) of Bharat, which became operational. This initiative aimed to strengthen the pharmacovigilance system in the country and improve the monitoring and management of adverse drug reactions. (7,8,9,10).

STEPS IN PHARMACOVIGILANCE PROGRAMME:

1. Finding the risk of drug
2. Clinical trials
3. Pharmaco epidemiological study
4. Case report
5. Developing case series
6. Analysis of case series
7. Use of data mining to identify product-event combination

PARTNERS IN PHARMACOVIGILANCE:

You are correct in highlighting the complex and vital relationship that exists between various partners involved in drug safety monitoring. Collaboration and commitment among these partners are indeed crucial for effectively addressing future challenges in pharmacovigilance and ensuring its continued development and success. This includes close collaboration between pharmaceutical companies, regulatory authorities, healthcare professionals, patients, and other stakeholders. By working together, sharing information, and pooling resources, these partners can enhance the detection, assessment, and prevention of adverse drug effects.

- Government
- Industry
- Hospitals and academia
- Medical and pharmaceutical associations
- Poisons information centres
- Health professionals
- Patients
- WHO

METHODOLOGY:

PHARMACOVIGILANCE IN INDIA:

In a country as vast as India, with a population of over 1.2 billion and significant ethnic and socioeconomic diversity, it is indeed crucial to have a standardized and robust pharmacovigilance (PV) and drug safety monitoring program (SMP) in place. The pharmaceutical industry in India is valued at $18 billion and is growing at a rate of 12-14% annually, with approximately 40% of generic medicines being exported worldwide. India is also emerging as a hub for global clinical research and drug discovery and development, with outsourced projects in pharmacovigilance.

The Central Drugs Standard Control Organization (CDSCO) in New Delhi has witnessed a significant increase in the total number of applications received and processed, doubling from 10,000 in 2005 to 22,806 in 2009. This reflects the introduction of new chemical entities (NCEs) into the country. Given the diverse disease prevalence patterns and the practice of different systems of medicine in India. By implementing such a program, India can ensure the timely detection, assessment, understanding, and prevention of adverse drug reactions and other drug-related problems. This will help safeguard the health and well-being of its population and contribute to the overall growth and development of the pharmaceutical industry in the country. (11)

History of PV in India:

Traditionally, there was no emphasis on monitoring the safety of medicines in the country. However, it is important to note that pharmacovigilance (PV) is not entirely new to India. In 1986, a group of physicians, primarily from academic institutions, recognized the need for increased attention to potential adverse effects of prescription medicines and rational prescribing practices. As a result, the first ADR monitoring program was established, consisting of 12 regional centres, each covering a population of 50 million. However, it is acknowledged that this initial program faced challenges and was not successful in achieving its objectives. Despite this setback, efforts have been made to strengthen pharmacovigilance in India over the years. The establishment of the Pharmacovigilance Programme of India in 2010, in collaboration with the WHO, has been a significant step towards improving ADR monitoring and reporting in the country.

While pharmacovigilance in India may still be considered in its infancy, ongoing efforts are being made to enhance the system and promote a culture of ADR reporting among healthcare professionals and the general public. These initiatives aim to ensure the safe and effective use of medicines and contribute to the overall improvement of public health in India. (12)

The establishment of the WHO ADR Monitoring Program in India in 1997 marked a significant step towards pharmacovigilance, aiming to monitor adverse drug reactions (ADRs) associated with medicines marketed in the country. However, despite the identification of three monitoring centres, including the National Pharmacovigilance Centre at AIIMS, New Delhi, and WHO special centres in Mumbai and Aligarh, the initiative faced challenges.

One of the main issues was the non-functionality of these centres, attributed to a lack of awareness among prescribers about the need to report ADRs and a general lack of information about the functions of the monitoring centres. Additionally, inadequate funding from the government contributed to the unsuccessful implementation of the program.

Recognizing the shortcomings, a renewed effort was made to strengthen pharmacovigilance in India. From January 1, 2005, the WHO-sponsored and World Bank-funded National Pharmacovigilance Program for India was made operational. This initiative aimed to enhance the monitoring of ADRs, improve reporting mechanisms, and address the challenges that hindered the earlier program's success.

The implementation of the NPVP reflected a commitment to safeguarding public health by systematically monitoring and addressing adverse reactions to medicines. Ongoing efforts in pharmacovigilance contribute to a safer and more effective use of medications in India. (13) The National Pharmacovigilance Program established in January 2005 in India had a comprehensive structure with the National Pharmacovigilance Advisory Committee overseeing its operations at the CDSCO. The program included zonal centres, regional centres, and peripheral centres to collate and report information on adverse drug reactions from across the country. Despite its well-defined structure and objectives, the program faced challenges. The program had three broad objectives:

1. Short-term Objective: Foster a reporting culture.
2. Intermediate Objective: Involve a large number of healthcare professionals (HCPs) in information dissemination.
3. Long-term Objective: Establish the program as a benchmark for global drug monitoring. The current PV program in India:

The decision to restart and revamp the National Pharmacovigilance Program in India was a crucial step in enhancing drug safety and monitoring adverse drug reactions (ADRs). The initiative took shape during a brainstorming workshop jointly organized by the Department of Pharmacology at AIIMS and CDSCO in late 2009. The outcome of this collaborative effort was the formulation of a new and revised program, now known as the Pharmacovigilance Programme for India.

The revamped PvPI aimed to address the shortcomings of its predecessor and overcome the challenges that hindered the effective implementation of the NPVP. The program was officially operational from mid-July 2010, signifying a renewed commitment to pharmacovigilance and drug safety in the country.

Key features and improvements in the Pharmacovigilance Programme for India may have included:

1. Enhanced Awareness and Training: Efforts were likely made to increase awareness among healthcare professionals about the importance of reporting ADRs. Training programs may have been implemented to equip healthcare professionals with the knowledge and skills needed to actively participate in pharmacovigilance activities.
2. Streamlined Reporting Structure: The reporting structure may have been optimized to ensure efficient collection and analysis of ADR data. This could involve a clearer delineation of responsibilities among various levels of the reporting network, including zonal and regional centres.
3. Increased Stakeholder Involvement: Collaboration between regulatory bodies, healthcare institutions, and other stakeholders may have been strengthened to ensure a more comprehensive and coordinated approach to pharmacovigilance.
4. Improved Communication Channels: Efforts to improve communication channels for disseminating information about ADR reporting, program objectives, and updates may have been a focus, addressing one of the challenges faced by previous programs.
5. Strategic Partnerships: Collaborations with international pharmacovigilance organizations, such as the Uppsala Monitoring Centre in Sweden, might have been reinforced to leverage global best practices.

The renaming of the program to PvPI might have signalled a fresh start and emphasized the commitment to building a robust pharmacovigilance framework in India. Continuous monitoring, evaluation, and adaptation based on real-world experiences are crucial for the sustained success of such programs. (14)

The Union Ministry of Health in India has appointed the Indian Pharmacopoeia Commission as the new National Coordinating Centre for PvPI. This change signifies a strategic decision to involve the IPC in the leadership role, highlighting its responsibility to oversee and coordinate pharmacovigilance activities across the country.

The main aim of the NCC at IPC is to generate independent data on the safety of medicines. This data generation is crucial for assessing the benefit-risk profiles of medications and ensuring that the safety monitoring standards align with global benchmarks. By appointing the IPC as the NCC, there is likely an emphasis on maintaining transparency, credibility, and international compliance in the pharmacovigilance processes.

Key responsibilities of the NCC at IPC may include:
1. Data Collection and Analysis: Systematically collect, analyse, and evaluate data on adverse drug

reactions (ADRs) from various sources to assess the safety of medicines.
2. Reporting to Regulatory Authorities: Provide timely and accurate reports on ADRs to regulatory authorities, contributing to evidence-based decision-making.
3. Collaboration with Stakeholders: Foster collaborations with healthcare professionals, institutions, and international pharmacovigilance organizations to enhance the efficiency and effectiveness of the program.
4. Training and Awareness: Conduct training programs and awareness campaigns to engage healthcare professionals and the public in pharmacovigilance activities.

METHODS OF CAUSALITY ASSESSMENT:

Assessing and categorizing ADRs is a complex process that involves the use of various criteria and methods to establish a relationship between the administration of a drug and the occurrence of an adverse event. Some of the commonly used criteria and methods include:
1. Temporal Relationship
2. Dose-Response Relationship
3. DE challenge and Challenge
4. Exclusion of Other Causes
5. Confirmation by In Vivo or In Vitro Tests
6. Literature Review and Previous Reports
7. Known Pharmacological Effects
8. Expert Consensus

By combining these criteria and methods, researchers aim to categorize ADRs into different classes of causality, such as certain, probable, possible, unlikely, or unrelated. This comprehensive assessment helps healthcare professionals, regulatory authorities, and researchers make informed decisions regarding the safety of drugs and patient care. (15)

However, researchers and healthcare professionals commonly use three broad classes of approaches for relation assessment:

1. Professional Judgment:
Professional judgment involves the subjective assessment of healthcare professionals, often relying on their clinical experience and expertise.
Pros: This approach allows for the incorporation of nuanced clinical knowledge and contextual information. Experienced clinicians may use their judgment to weigh various factors in determining the likelihood of a causal relationship.
Cons: Subjectivity can lead to variability between different assessors, and it may be influenced by individual biases. Lack of standardized criteria can make it challenging to replicate assessments.

2. Algorithms:
Algorithms involve the use of predefined sets of criteria and rules to systematically assess the relationship between drug exposure and ADRs. These criteria may include factors like temporal relationship, DE challenge, challenge, and exclusion of other causes.
Pros: Algorithmic approaches aim to provide a more standardized and reproducible method of assessment. They can be applied consistently across different cases.
Cons: Algorithms may not capture the full complexity of clinical scenarios, and their rigidity might overlook unique aspects of individual cases. They may also need periodic updates to reflect advances in medical knowledge.

3. Probabilistic Approaches:
Probabilistic approaches involve the use of statistical methods to quantify the probability of a causal relationship between drug exposure and ADRs. Bayesian reasoning is often employed in these approaches.
Pros: Provides a quantitative measure of the likelihood of causality. Can account for uncertainties and incorporate evolving evidence over time.
Cons: May require access to comprehensive and accurate databases for prior probabilities. The complexity of statistical methods may limit their application in routine clinical practice. (16)

PHARMACOVIGILANCE IN DRUG REGULATION:

Pharmacovigilance programs made strong by links with regulators. Regulators understand that PV plays a specialized and pivotal role in ensuring ongoing safety of medicine products. Clinical trial regulation involves the rules, standards, and processes set by regulatory authorities to ensure the ethical conduct, safety, and quality of clinical trials. These regulations are designed to protect the rights and well-being of study participants, maintain the integrity of trial data, and facilitate the development of safe and effective medical interventions. The specific regulations can vary by country, but they generally cover several key aspects: 1. Ethical Considerations:
Regulatory frameworks require that clinical trials adhere to ethical principles, including informed consent, voluntary participation, and respect for the rights and privacy of participants.
2. Good Clinical Practice (GCP):
GCP guidelines provide an international ethical and scientific quality standard for designing, conducting, recording, and reporting clinical trials.
3. Protocol Design and Approval:

Regulatory authorities typically require a detailed and well-structured protocol for each clinical trial. The protocol outlines the objectives, design, methodology, statistical considerations, and participant eligibility criteria.
4. Informed Consent:
Regulations mandate that participants provide informed consent voluntarily after receiving comprehensive information about the trial, its risks and benefits, and their rights. 5. Safety Reporting and Monitoring:
Adverse events and safety information must be collected, documented, and reported to regulatory authorities as specified in the regulations. Continuous monitoring of participant safety during the trial is essential, and mechanisms for reporting and managing adverse events are established.
6. Data Integrity and Recordkeeping:
Rigorous recordkeeping is required to ensure the integrity of trial data. Regulations specify the documentation and data management practices that must be followed.
7. Investigator Responsibilities:
Investigators conducting the trial must meet certain qualifications, adhere to the protocol, and ensure compliance with regulatory requirements.
8. Regulatory Submissions and Approvals:
Before initiating a clinical trial, sponsors typically need to submit applications to regulatory authorities for review and approval.
9. Post-Marketing Surveillance:
After a drug or medical intervention is approved, post-marketing surveillance requirements may be in place to monitor its safety and effectiveness in real-world conditions.

Post marketing safety drug monitoring:

Post-marketing safety drug monitoring, also known as pharmacovigilance, is a crucial aspect of ensuring the ongoing safety of pharmaceutical products once they are approved and available in the market. The primary goal is to detect and assess adverse drug reactions (ADRs) and other safety-related information that may not have been apparent during pre-marketing clinical trials. Here are key components of post-marketing safety drug monitoring:
1. Adverse Event Reporting:
Healthcare professionals, patients, and drug manufacturers are encouraged to report any adverse events or suspected side effects associated with a drug to regulatory authorities. 2. Signal Detection:
Signal detection involves the systematic analysis of reported adverse events to identify potential safety concerns or signals associated with a particular drug.
3. Risk Assessment and Management:
Risk management strategies may include updates to product labelling, communication of safety information to healthcare professionals, or, in extreme cases, withdrawal of the drug from the market.
4. Periodic Safety Update Reports (PSURs):
Marketing authorization holders are often required to submit PSURs to regulatory authorities at defined intervals. PSURs provide a comprehensive overview of the safety profile of a drug, including any new safety concerns and relevant risk-minimization measures.
5. Risk Communication:
Transparent communication of safety information to healthcare professionals, patients, and the public is a crucial component of pharmacovigilance.
6. Registry Studies and Observational Research:
Post-marketing studies, including registry studies and observational research, may be conducted to further evaluate the long-term safety and effectiveness of a drug in real-world settings.
7. Collaboration and Information Sharing:
Global databases and networks, such as the WHO Global Individual Case Safety Reports database, facilitate international collaboration in pharmacovigilance.
8. Continuous Benefit-Risk Assessment:
The benefit-risk balance of a drug is continuously assessed based on emerging safety data and evolving clinical knowledge. Decisions regarding labelling updates, risk minimization measures, or regulatory actions are made to ensure the ongoing safety of patients.

Pharmacovigilance in national drug policy and disease control public health program

Pharmacovigilance plays a crucial role in the development and implementation of national drug policies. National drug policies encompass a set of strategies, regulations, and guidelines established by a country to ensure the safe, effective, and rational use of pharmaceuticals within its healthcare system.
1. Monitoring and Surveillance:
Pharmacovigilance contributes to the monitoring and surveillance of ADRs and other safety related issues associated with pharmaceutical products.
2. Ensuring Drug Safety:
National drug policies often include provisions for ensuring the safety of medicines throughout their lifecycle.
3. Regulatory Decision-Making:
Pharmacovigilance data influence regulatory decision-making processes related to the approval, labelling, and post-marketing monitoring of drugs.
4. Incorporation into Healthcare Systems:
National drug policies often incorporate pharmacovigilance into the overall healthcare system, defining the roles and responsibilities of

healthcare professionals, regulatory agencies, and other stakeholders. This integration ensures that pharmacovigilance activities are seamlessly woven into routine healthcare practices.

5. Capacity Building:

National drug policies may include provisions for building and strengthening pharmacovigilance capabilities within the country. This involves training healthcare professionals, establishing reporting systems, and enhancing the capacity of regulatory agencies to conduct pharmacovigilance activities effectively.

6. Post-Marketing Surveillance:

Pharmacovigilance contributes to post-marketing surveillance efforts outlined in national drug policies. Continuous monitoring of the safety of marketed drugs allows for timely detection and response to emerging safety concerns.

7. International Collaboration:

Many national drug policies recognize the importance of international collaboration in pharmacovigilance. Countries often participate in global pharmacovigilance networks, share information, and collaborate on safety assessments to benefit from broader experiences and perspectives.

MEDICATION ERRORS:

Questionnaire on Medication Error Monitoring:

Designing a questionnaire on Medication Error Monitoring involves considering various aspects related to the identification, reporting, and prevention of medication errors. Below is a sample questionnaire that can be used as a starting point for gathering information on this topic. Adapt and modify the questions based on the specific context and objectives of your Medication Error Monitoring program.

Section 1: Respondent Information

1. Name (Optional):
2. Role/Position:
3. Healthcare Organization:
4. Years of Experience:

Section 2: General Understanding

5. How would you define an error in your practice?
6. How significant is the issue of medication errors in your healthcare setting? Section 3: Identification and Reporting
7. Are there established procedures for identifying and reporting medication errors in your healthcare facility?
8. Who is responsible for reporting medication errors in your healthcare setting? 9. What methods or systems are in place for reporting medication errors? Section 4: Analysis and Investigation
10. Is there a systematic process for analysing and investigating medication errors in your facility?
11. What factors are typically considered during the analysis of a medication error? Section 5: Prevention Strategies
12. What strategies or interventions are in place to prevent medication errors in your healthcare setting?
13. How often are staff members educated or trained on medication safety practices? Section 6: Suggestions for Improvement
14. Do you have any suggestions for improving the Medication Error Monitoring process in your healthcare facility?

THE ROLE OF PHARMACIST IN DRUG SAFETY:

Pharmacists play a crucial role in drug safety throughout the entire medication use process. Their responsibilities extend beyond dispensing medications to include various aspects of drug safety, patient education, and collaboration with other healthcare professionals. Here are some key aspects:

1. Medication Dispensing:

Ensuring Accuracy: Pharmacists are responsible for accurately dispensing prescribed medications, checking for drug interactions, contraindications, and ensuring the correct dosage.

2. Patient Counselling:

Education: Pharmacists educate patients on how to take their medications, including proper administration, potential side effects, and any necessary precautions. Addressing Concerns: Addressing patient concerns, questions, and providing guidance on the safe use of medications.

3. Medication Therapy Management:

Reviewing Medication Regimens, Monitoring Adherence

4. Medication Safety Monitoring:

ADR Monitoring: Pharmacists play a role in monitoring and reporting adverse drug reactions to relevant authorities. Identifying Medication Errors: Detecting and preventing medication errors, including incorrect doses, drug interactions, or other safety concerns.

5. Collaboration with Healthcare Providers:

Communication: Collaborating with physicians, nurses, and other healthcare professionals to ensure coordinated and safe patient care.

Consultation: Providing consultations to healthcare providers on medication-related issues and contributing to interprofessional discussions about drug therapy.

6. Pharmacovigilance:
Reporting Adverse Events: Actively participating in pharmacovigilance activities by reporting adverse events and contributing to the monitoring of drug safety on a broader scale. Risk Management: Implementing risk management strategies to minimize potential harm associated with medications.

7. Drug Information and Patient Advocacy:
Providing Information: Offering accurate and up-to-date drug information to both healthcare professionals and patients to support informed decision-making.
Advocacy: Advocating for patient safety and participating in initiatives to improve medication safety practices within healthcare organizations.

8. Continuous Professional Development:
Staying Informed: Keeping abreast of developments in pharmacology, drug safety, and best practices through continuous education and professional development.
Training and Education: Providing training to pharmacy staff and students on medication safety and adherence.

9. Community Engagement:
Public Awareness: Engaging with the community to raise awareness about safe medication practices and promoting the role of pharmacists in ensuring drug safety. Health Promotion: Contributing to health promotion initiatives, such as vaccination campaigns, to enhance public health and prevent diseases.

ADVERSE DRUG REACTION (ADRs):
Adverse Drug Reactions refer to unintended and harmful responses to a medication that occur at doses normally used for treatment. These reactions can range from mild to severe and may occur immediately after a drug is administered or after prolonged use.(17,18,19) 1. Types of Adverse Drug Reactions:
Type A (Augmented): Predictable and dose-dependent reactions that are an extension of a drug's pharmacological effects. Examples include gastrointestinal disturbances or bleeding associated with aspirin use.
Type B (Bizarre): Unpredictable reactions that are not related to the known pharmacological actions of the drug. These reactions are often idiosyncratic and may involve the immune system, leading to allergic reactions or hypersensitivity.
Type C (Chronic): Reactions that occur with long-term use, such as drug-induced endocrine or metabolic disorders.
Type D (Delayed): Reactions that manifest after a delay, often involving cumulative drug exposure over time.
Type E (End of Use): Reactions that occur upon discontinuation of a drug, such as withdrawal symptoms.
2. Factors Contributing to ADRs: Patient-related factors, Drug-related factors, Environmental factors, idiosyncratic reactions.
3. Common Adverse Drug Reactions:
4. Serious and Life-Threatening ADRs:
5. Monitoring and Reporting ADRs:
6. Prevention and Management:
7. Regulatory Actions:
Patient safety is at the forefront of ADR management and prevention strategies.

Table No.2:- Drug and its Adverse effect (20)

DRUGS	ADVERSE DRUG REACTION
Thalidomide	Phocomelia, Multiple Defects.
Methotrexate	Multiple defects, Fetal death.
Androgen	Virilization of limb, esophageal, cardiac defects.
Progestin	Virilization of female fetus
Stilbesteron	Vaginal carcinoma in teenage female offspring
Tetracycline	Discolored or deformed teeth, retarded bone growth
Warfarin	nose, eye and hand defects, growth retardation
Phenytoin	Various malformations
Lithium	Fetal goiter, cardiac and other abnormalities
Aspirin/Indomethacin	Premature closer of ducts arteriosus
Quinidine	Ringing in ear
Alcohol	Low IQ baby, growth retardation
Carbamazepine	Neural tube defects

Rifampicin	Orange color urine
Chloramphenicol	Grey baby syndrome.
Anticancer Drugs	Cleft palate, multiple defects.
Valproate Sodium	Spina bifida, limb abnormalities.
Isotretenoin	Heart and CNS defects.

Documentation of ADRs:
Documentation of Adverse Drug Reactions (ADRs) is a crucial aspect of pharmacovigilance to ensure systematic recording, monitoring, and analysis of adverse events associated with medication use. Proper documentation helps healthcare professionals, regulatory authorities, and pharmaceutical companies track and assess the safety of drugs. Here are key considerations for the documentation of ADRs(21):
1. Adverse Event Reporting Form:
2. Patient Information:
3. Suspected Medication(s):
4. Concomitant Medications:
5. Healthcare Professional Information:
6. Severity and Outcome:
7. Causality Assessment:
8. Follow-Up Information:
9. Regulatory Reporting Requirements:
10. Documentation System:

PROCEDURE FOR REPORTING ADRs:
It is the first duty of any pharmacovigilance centre to report all suspected adverse events of the drug if found. Information regarding ADRs that should be reported and tabulated.

Monitoring of ADRs:
The monitoring of Adverse Drug Reactions is a critical component of pharmacovigilance, aiming to systematically collect, assess, and analyse information about adverse events associated with the use of medications. Here are key elements involved in the monitoring of ADRs: (22)

Spontaneous Reporting Systems: Healthcare Professionals and Consumers: Encourage healthcare professionals and consumers to report suspected ADRs voluntarily to national pharmacovigilance systems or regulatory authorities.

Active Surveillance Systems: Database Surveillance: Utilize electronic health records, claims databases, and other healthcare databases to actively monitor and identify potential safety signals. Signal Detection Tools: Implement data mining techniques, statistical algorithms, and other tools to identify patterns and trends that may indicate potential ADRs.

Periodic Safety Update Reports: Regulatory Requirement: Prepare and submit PSURs to regulatory authorities at defined intervals, providing a comprehensive review of the safety profile of a drug. Updated Safety Information: Include information on new ADRs, changes in the frequency or severity of known ADRs, and any relevant risk minimization measures.

Risk Management Plans: Risk Identification and Mitigation: Develop RMPs to proactively identify, assess, and minimize risks associated with a drug.
Clinical Trials: Adverse Event Monitoring: Systematically collect and report adverse events during the conduct of clinical trials to assess the safety profile of investigational drugs.

Pharmacovigilance Agreements and Collaborations: International Collaboration: Engage in collaborations and information-sharing agreements between regulatory authorities, pharmaceutical companies, and international pharmacovigilance networks. Global Data Sharing: Share safety data globally to enhance the identification of ADRs and facilitate a coordinated response.

Literature Surveillance: Scientific Literature Review: Regularly review published scientific literature for new information on ADRs and safety concerns.
Integration with Pharmacovigilance Databases: Integrate findings from literature surveillance with data from pharmacovigilance databases for a comprehensive analysis.

Benefit-Risk Assessment: Regular Evaluation: Conduct regular benefit-risk assessments to evaluate the overall safety profile of medications in comparison to their therapeutic benefits. Decision-Making: Use benefit-risk assessments to inform regulatory decisions, labelling updates, and communication strategies.

Public Communication: Safety Alerts and Communication: Disseminate safety alerts and information to healthcare professionals and the public to enhance awareness of potential ADRs. Educational Initiatives: Develop educational materials to inform healthcare providers and patients about the importance of reporting and monitoring ADRs.

Serious Adverse Event:

A serious adverse event (SAE) in human drug trials are defined as any untoward medical occurrence that is caused at any dose

(a) Results in death

(b) Is life threatening

(c) Require in-patient hospitalization

(d) Prolongation of existing hospitalization

(e) Causes congenital anomaly/birth defect(23).

Research suggests that these events are often inadequately reported in publicly available reports(24).

Different regulatory agencies:

1. Drug Controller General of India (DCGI)
2. Central Drugs Standard Control Organization (CDSCO)
3. Indian Council of Medical Research (ICMR)
4. Ministry of Environment & Forests (MOEF)
5. Central Bureau of Narcotics (CBN)
6. Ministry of Health and Family Welfare (MHFW).(25)

Conclusion:

The result is that there is currently no widely accepted technique for ADR casualty evaluation. Pharmacovigliance is the science and spectrum of methods involved in detecting, evaluating, understanding, and preventing side effects or any other drug-related issue. The best way to understand adverse drug reactions, or ADRs, is through

There are other approaches, such as spontaneous reporting, careful observation, and database research.

After forty years, pharmacovigilance remains a vibrant area of clinical and scientific research. It is still essential to address the major challenges posed by the ever-increasing variety and potency of drugs, all of which carry an inevitable and sometimes unforeseen risk of harm. It is imperative to declare any negative consequences and toxins that.

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Research Article

FORMULATION AND EVALUATION OF DENTAL GEL USING LANTANA CAMARA LINN.

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ABSTRACT

The aim of this study is to develop and evaluate a herbal gel containing Lantana leaf extract. Plant extracts were placed in the gel matrix and their pH, viscosity, diffusivity, etc. Physicochemical properties such as were determined. Physicochemical tests of the samples showed no agglomeration, uneven color and no fibers or particles. It also features easy cleaning and good conduction. The aim of this study is to investigate the antibacterial and antifungal properties of Lantana (Verbenaceae) leaf extract. Analysis of methanol extract of Lantana camara (MELC) for acetic acid production, hot plate analgesic activity, and anti-inflammatory activity in carrageenan and histamine-induced foot edema. The results showed that the leaves and bark of MELC (100 mg/kg and 200 mg/kg) had significant anti-inflammatory properties, and the 200 mg/kg dose of MELC leaves and bark showed greater activity than the 100 mg/kg dose. Preliminary phytochemical analysis has revealed the presence of various phytochemicals that may be responsible for its anti-inflammatory and antibacterial properties. The results show that MELC has a good ability to reduce inflammation and prevent infection and may be useful for treatment.

KEYWORDS
Lantana Camara, Herbal gel, Analgesic activity, Anti-inflammatory activity.

1. INTRODUCTION:

Many countries have used this plant as traditional medicine for thousands of years. Many systems in India (Ayurveda, Unani and Siddha) use medicinal plants and their extracts to treat various ailments. [1] The chemical diversity of plants makes them important for the isolation of active substances. Pain is usually treated with opioids and nonsteroidal anti-inflammatory drugs (NSAIDs). Both classes of drugs can cause serious side effects, including kidney damage, stomach upset, and difficulty breathing. Plants are always used for many purposes. [2,3] Although there are many types of analgesic and anti-inflammatory drugs on the market, the search for new effective drugs from plants to eliminate their side effects still continues. [4] There are approximately 150 species of Lantana camara from more than 50 countries. It is an evergreen plant commonly known as wild sage and lantana plant. For many years, various forms of Lantana have been used to treat and treat ailments such as stomach ulcers, cuts, tumors, and eczema. [5] Many plants have been reported for their medicinal properties such as anti-lymphocyte and anti-inflammatory, hepatoprotective, anti-peristaltic, anti-filarial, in vivo cytotoxic and antibacterial activities. A large number of medicinal plants in India possess many photochemical substances and therefore have many pharmacological activities. Opioids, or nonsteroidal anti-inflammatory drugs, are commonly used to relieve many types of pain, but they can have serious side effects, such as rash and itching. Therefore, it seems necessary to find a better way.

Gel formulations are used for topical and oral application due to their ease of use, increased contact time, and fewer side effects than other topical and oral applications. Lantana plant has been found to be used traditionally for its many medicinal properties such as anti-cancer, oral health, anti-inflammatory, antioxidant activity, dermatological study and wound healing. [6] On the basis of above findings, the present work was performed to formulate the herbal dental gel of analgesic and anti-inflammatory potential of L. camara leaves methanol extract.

MATERIALS AND METHODS

Plant Materials:
Leaves of Lantana Camara were collected from the residential areas of Saswad, Pune, Maharashtra, India.

Preparation of Plant extract:
Shade drying was done for almost a month as to avoid chemical degradation due to sunlight. Grinding of the dried material was done, with the aid of a grinder and converted into coarse powder. The powder was sieved. 50 gm defatted powdered; material was extracted at 50°C with a volume of 500 ml aqueous methanolic (70:30 methanol: water) in the Soxhlet apparatus.
Chemicals: Lantana camara extract, Carbapol940, Polyethylene glycol, Glycerin, Methyl Paraben, Propyl Paraben , Honey, Distilled Water.
Apparatus: Apparatus such as beaker, glass slide, measuring cylinder, test tube, volumetric flask
Instruments: pH meter, Mechanical stirrer, Viscometer

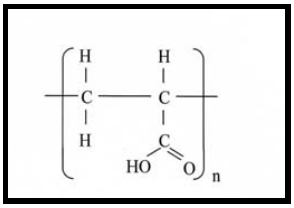
Figure 2: Ingredients for Formulation

Formulation Table:
Table no.1: Formulation Table

Sr.no.	Materials	Quantity	Functions
1	Lantana Camara Extract	1ml	Active Pharmaceutical Ingredient
2	Carbopol 940	0.3gm	Gelling Agent
3	Methyl Paraben	0.18gm	Preservatives
4	Propyl Paraben	0.02gm	Preservatives
5	Propylene Glycol	5ml	Co- Solvent
6	Glycerin	5ml	Drug Solubiliser
7	Triethanolamine	0.5ml	Neutralizer
8	Honey	1ml	Sweetening agent
9	Distilled Water	q.s	Vehicle

Excipient profile:

1)Carbapol940:
Carbopol940 polymer is a white powder, crosslinked polyacrylic acid polymer. It is an extremely efficient rheology modifier capable of providing high viscosity and forms sparkling clear gels or hydro-alcoholic gels and creams. Its short flow, non-drip properties are ideal for applications such as clear gels, hydroalcoholic gels, and creams.
Structure:

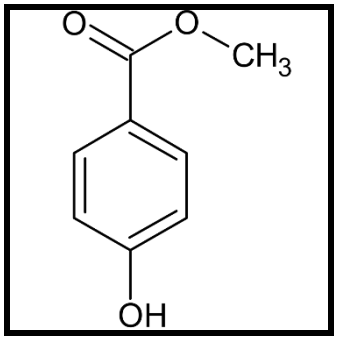


IUPAC Name: Poly (acrylic acid)
Other Names: PAA, PAAC, Acrysol, Acumer.
Chemical Formula: (C3H402)
Molar Mass: variable
Uses: Polyacrylic acid and its derivatives are used in disposable diapers ion exchange resins and adhesives. They are also popular as thickening,

dispersing suspending and emulsifying agents in pharmaceuticals.

2) Methyl Paraben:
Methylparaben is a 4-hydroxybenzoate ester resulting from the formal condensation of the carboxy group of 4-hydroxybenzoic acid with methanol. It is the most frequently used antimicrobial preservative in cosmetics. It occurs naturally in several fruits, particularly in blueberries. Structure:

Structure:



IUPAC Name: Methyl 4hydroxybenzoate
Other Names: Methyl Paraben
Chemical Formula: C8H803
Molar Mass: 152.15g mol-1
Uses: Methyl paraben is an antifungal agent often used in a variety of cosmetics and personal care products.

3) Propylene glycol:
Propylene glycol is a viscous, colorless liquid, which is nearly odorless but possesses a faintly sweet taste. Its chemical formula is CH_3CHCH_2OH. Containing two alcohol groups, it is classed as a diol. It is miscible with a broad range of solvents, including water, acetone, and chloroform.
Structure:

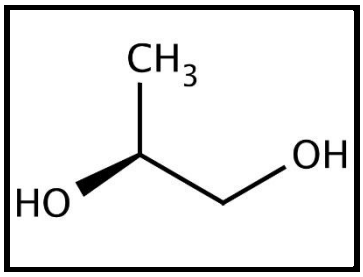


Figure 5: Structure of Propylene glycol

IUPAC Name: propane-1,2-diol
Other Names: 1,2-dihydroxypropane, 1,2-propanediol, methyl glycol, and trimethyl glycol
Chemical formula: C3H8O2
Molar mass: 76.09 g/mol
Uses: It is used to absorb extra water and maintain moisture in certain medicines, cosmetics, or food products. It is a solvent for food colors and flavors, and in the paint and plastics industries. Propylene glycol is also used to create artificial smoke or fog used in fire-fighting training and in theatrical productions.

4) Propyl paraben:
Propylparaben is the benzoate ester that is the propyl ester of 4-hydroxybenzoic acid. Preservative typically found in many water-based cosmetics, such as creams, lotions, shampoos and bath products. Also used as a food additive.
Structure:

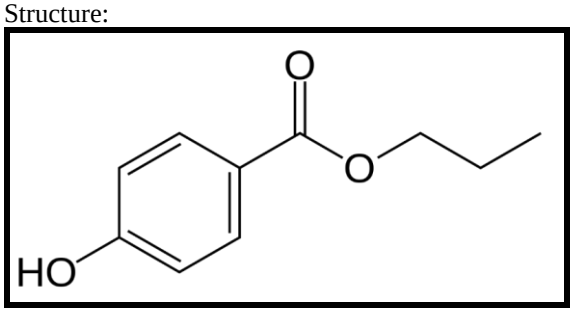


Figure 6: Structure of Propyl paraben
IUPAC Name:4-hydroxybenzoic acid
Other Name: n-propyl paraben, isopropyl paraben
Chemical formula:C10H12O3
Molar Mass:180 gm/mol
Uses: It is widely used as preservatives by pharmaceutical and cosmetics industry. They are effective. These compounds and their salts are used mainly for their antifungal and antibacterial properties.

5) Glycerin:
Glycerol, also called glycerine or glycerin, is a simple triol compound. It is a colorless, odorless, viscous liquid that is sweet-tasting and non-toxic. The glycerol backbone is found in lipids known as glycerides.
Structure:

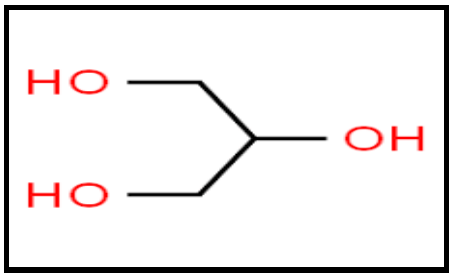


Figure 7: Structure of Glycerin
IUPAC Name: propane-1,2,3-triol
Other Name: Glycerol.
Chemical formula: C3H8O3
Molar Mass: 92.09 gm/mol
Uses: In addition to being a humectant, glycerin is used in a variety of food and drink products, including various beverages, nutrition and energy bars, cake icings, soft candies, chewing gum, condiments, creams, diet foods, dried fruits, fondant, fudge and marshmallows.

Procedure for the preparation of dental gel:

1)Soaking: Soaked carbapol 940 in water.
2) Neutralization: Neutralize with triethanolamine to pH 9.4.
3) Addition of preservative: Addition of propyl and methyl Paraben.
4) Addition of co-solvent and API: Addition of propylene glycol and clove oil in another test tube.
5) Addition of sweetener: Finally, honey is added.
6) Stirring: Stirring is done until a homogeneous product is formed. [19]

Evaluation Parameters:

Appearance:

All the formulations of lantana gel were pale yellow in colour.

Consistency:

The consistency was checked by applying on skin.

Greasiness:

The greasiness was assisted by the application on to the skin.

Determination of pH:

pH of gel was determined using digital pH meter by dipping the glass electrode completely into the gel system.

Determination of viscosity:

Viscosities of the formulated gels was determined using Brooke field viscometer, spindle no. 7 and spindle speed 60 rpm at 25-C was used gels, the corresponding dial reading on the viscometer was noted**.**

Determination of spreadability:

Spreadability was measured by this method on the basis of the slip and the drug characteristics of the gel put on the ground slide and the excess gel (approximately 2 g) under analysis. The gel was then placed between the slides and 200 g weighted for 5 minutes was placed on the top of 2 slides to expel air to provide a uniform gel film between the slides where excess gel was scrapped off the edges. The time noted by the top slide (in seconds) to cover a distance of 7.5 cm must be noted. Spreadability was determined using following formula,

S=M.L/T

Where M = Wt. tied to upper slide

L = Length of glass slides

T = Time taken to separate the slides

Determination of extrudability:
It was determined by sign a tube filled with the gel having a tip of sim opening and by measuring the amount of gel that extruded through the tip when a pressure was applied on the tube was noted down.

Stability study:
Physical stability study tests of the formulation was carried for one weeks at temperature of 37℃. The formulation was found to be physically stable at temperatures of 37℃. Within one weeks [18]

RESULT AND DISCUSSION:

Evaluation of Herbal gel
All results of different parameters of evaluation are recorded. The physical parameter such as color, appearance, feel on application are observed and shown in Table 2. The color of prepared herbal gels was yellowish. The color of extracts was greenish yellow. Appearance of gel was translucent and it was smooth on application. So, it shows significant physical evaluation parameters. The subjective properties mention in Table 2 such as consistency was good and texture of prepared herbal gel was found to be smooth. All the prepared herbal gel formulations show desirable spreadability values.

Observation table of Evaluation Parameter:

Table No.2 Physicochemical characteristics of Lantana Gel:

Sr.no	Parameters	Result
1	Appearance	Pale Yellow
2	Odour	Characteristics
3	Taste	Sweet
4	PH	6.72
5	Spreadability	17.30 g_cm
6	Extrudability	93.40%
7	Homogeneity	Very Good

Table No.3 Stability study (Evaluation Test After One Week):

Sr.no	Parameters	Result
1	Appearance	Pale Yellow
2	Odour	Characteristics
3	Taste	Sweet
4	PH	6.72
5	Spreadability	17.4 g_cm
6	Extrudability	93.58%
7	Homogeneity	Very Good

CONCLUSION

It is concluded, on the basis of the results obtained in the present analysis, that the herbal formulation of Lantana Camara extracts gel shows satisfactory physicochemical parameters. Herbal products are assumed to be safe for longer periods of time. However, quality control for efficacy and safety of herbal products is of paramount importance; and quality control tests must therefore be carried out for these preparations. The extract of this plant shows analgesic as well as anti-inflammatory properties. A study on the effects of formulated gels has shown that further studies are needed to confirm the role of each of these phytoconstituents activity. Thus, our research shows that herbal gel has good analgesic and anti-inflammatory activity.

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Review Article

COLORECTAL CANCER REVIEW

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ABSTRACT

Cancer had become a common disease worldwide and cancer related death is also increasing in various parts of the world in spite of increased screening and diagnostic facilities available with effective treatment modalities and modern technologies. The prevalence of different type of cancer varies with variation in the living environment, differences in the ethnicity, diet and life style. Early detection of cancer and availability of advanced health care system makes it possible to reduce cancer related mortalities. Life style modification, sedentary life style, processed food and fast-food consumption, lack of fibre rich food in the diet, stress causes alteration in the microenvironment of the cells leading to genetic changes and mutation. Mutation in the cellular level becomes the primary reason for the development of cancer cells. Colorectal cancer prevalence, risk factors for the development of colorectal cancer, pathogenesis, diagnosis and various treatment modalities available are discussed in this article.

KEY WORDS: Cancer, colorectal cancer, chemotherapy, biological agents.

INTRODUCTION:

Cancer is defined as abnormal division of cells. Uncontrolled cell division in the region of colon or rectum it is called as colorectal cancer (CRC). The colon, rectum and anus make up the large intestine which is the final segment of the gastrointestinal system. Large intestine absorbs water and minerals and eliminates waste. The first part of the large intestine is colon which is about 1.5 meters in length and 5 cm diameter. Colon is divided into 4 regions such as ascending colon, transverse colon, descending colon and the sigmoid colon. Colorectal cancer is caused by eating low fibre and high fatty food. Study says too much consumption of alcohol, smoking and sedentary life style can increase the risk of CRC. Presentation of Inflammatory bowel disease, a family history of colorectal cancer can also be a risk factor for the development of colon cancer. A polyp is a small growth in the lining of the colon which can develop into an adenomatous (precancerous) polyps over time. Colorectal cancers begin as small precancerous polyps which grows slowly without causing much symptoms until they become large or cancerous. Screening of these polyps at the right time can aid in the removal of them and preventing its growth into cancer. Polyps undergo various mutation in the cellular DNA and gets converted in a cancerous out growth[1].

MATERIALS AND METHODS:

Prevalence:

Colorectal cancer is the third most common type of cancer worldwide amongst men and second most common type of cancer amongst women. Almost 2 million cases were diagnosed in the year 2020. It is the second most common cause of cancer related deaths, almost 1 million deaths per year happened in the year 2020 according to WHO statistics. The burden of colorectal cancer is highest amongst Asians. More than half a million new cases and more than 280,000 deaths reported annually in China. Second highest number of deaths from colorectal cancer, almost 60,000 per year was reported by Japan[1].

Highest incidence rates have been identified in regions of North America, Europe, Australia, New Zealand, South Korea, Japan. 45% of incidence have been identified amongst low and middle-income countries [LMICs] accounting to 52% of death in these regions. Increased incidence in the number of cases and death has been observed in regions of Eastern Europe, China and South America. Decreased incidence observed in regions of South Asia and Africa. The differences observed in these regions may be due to limitation in screening or access to early detection and health care[2].

The incidence rates for colorectal cancer among Indian population were 4.4 per 100000 population. More than 1.4 million new cancer cases are being identified every year amongst the Indian sub-population[3].

Five-year survival rate for stage 4 colorectal cancer at the time of diagnosis was less than a 10% which might be due to the ineffectiveness of current treatment regimens.

Worldwide, an estimated 1,931,590 colorectal cancer were newly identified during the year 2020. Incidence of CRC varies as much as six-times in different regions globally. Southern European region has the highest estimated rates (per 100,000 population, 40.6 in men and 24.5 in women), as compared to the lowest levels in south-central Asia (per 100,000 population, 6.6 in men and 4.4 in women).

Worldwide, CRC had caused around 935,173 deaths during the year 2020, leading to 9.4% of CRC related mortality overall. As with incidence rates, mortality rates worldwide vary six-fold, with the highest estimated mortality rates at the eastern and central Europe (14.5 / 100,000), and the lowest in the regions of south-central Asia (3.2 per 100,000 population) [4].

Anatomy:

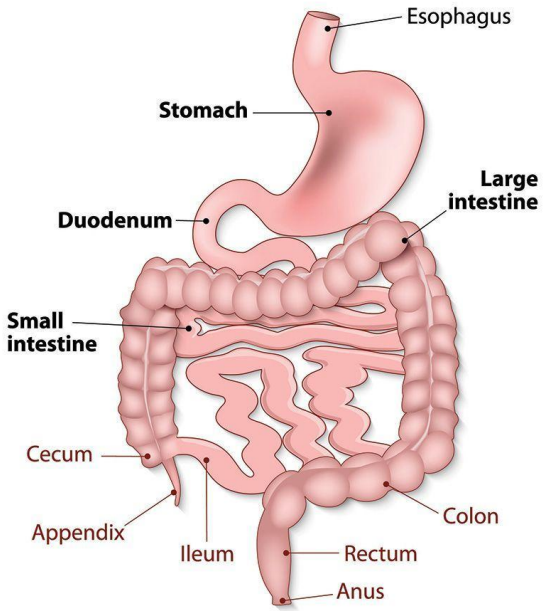


Fig 1: Gastrointestinal tract

Risk factors:
Some of the major risk factor for the development of colorectal cancer are: having a family history of colorectal cancer among the first-degree relative, increase in age. A personal history of colorectal adenomas, ovarian cancer. Hereditary conditions like familial adenomatous polyposis and Lynch syndrome. History of chronic ulcerative colitis or Crohn's disease. Excessive alcohol consumption, cigarette smoking, obesity, being an African-American can have a risk for the development of CRC[5].

Etiology:
AGE: Majority of CRC occurs in people above the age of 50, though it is found amongst younger adults also. The incidence had declined in older adults due to early detection and screening. But the incidence has increased in younger adults below 50 for unknown reasons.

Genetics: Mutation of APC gene results in Familial Adenomatous Polyposis (FAP) which can develop into CRC and have a 100% risk. Hereditary non-polyposis colon cancer syndrome (HNPCC) has 40% risk of development for CRC.

Race: Black people have a higher risk and incidence in US and also increased death rate.

Gender: Men have higher in the incidence rate than women.

Family History: About 6% have an association with inherited genetic mutation.

Rare Inherited Conditions: Lynch syndrome, Familial adenomatous Polyposis, attenuated familial adenomatous polyposis, Gardner syndrome, Juvenile polyposis syndrome, Muir-Torre syndrome, MYH associated polyposis, Peutz-Jeghers syndrome, Turcot syndrome.

Adenomatous Polyps: Presentation of adenoma in the colon has high risk of developing into a CRC[6].

Diet: Diet rich in animal fat, red meat is linked with the development of CRC. Also diet with low fibre, low fruits and vegetable intake can also progress to CRC.

Life Style: Obesity, smoking, consumption of alcohol, excessive consumption of sweetened beverages, sedentary life style has increased the risk of development of CRC.

Inflammatory Digestive Tract: Presentation of IBD like Ulcerative colitis, Crohn's disease increases the risk of CRC.

Signs and symptoms:
Iron-deficiency anaemia, rectal bleeding, abdominal pain, change in bowel habits, intestinal obstruction or perforation.
Physical findings:

Early Disease: Fatigue, weight loss.

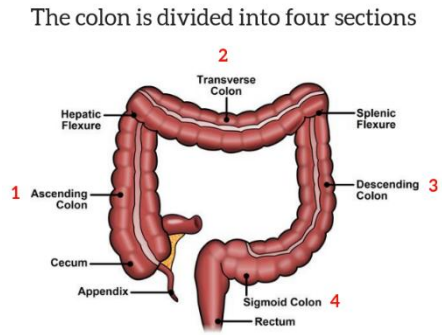
Advanced Disease: Abdominal tenderness, macroscopic rectal bleeding, palpable abdominal mass, hepatomegaly, ascites.

Diagnosis: Diagnosis of CRC can be done by performing a complete blood count test, liver function tests, serum carcinoembryonic antigen.

Imaging Studies: Imaging studies include chest radiography, chest computed tomography, abdominal barium study, abdominal/pelvic CT, contrast ultrasonography of the abdomen and liver, abdominal/pelvic MRI, Positron emission tomography, including fusion PET-CT scan.

Other Procedures: Other procedures which can help in providing conclusive evidence for the presentation of CRC are Colonoscopy, Sigmoidoscopy, Biopsy of suspicious lesions, Double-contrast barium enema[7].

Pathophysiology: Molecular Pathway for Colorectal Cancer



Conventional Pathway: More than 80% CRC cases are caused due to chromosomal instability pathway, which is initiated by APC mutation, followed by mutations in KRAS, PIK3CA and SMAD4, loss of heterozygosity of chromosome 18 (LOH 18q) and TP53 mutation. Colorectal cancer progression through conventional chromosomal instability pathway is associated with high levels of CIN (CIN+++), microsatellite stability (MSS) and very low levels of the CpG island methylation pathway (CIMP–).

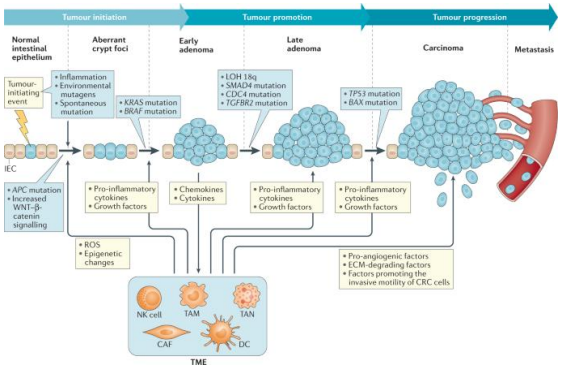


Fig 2: Large Intestine

Fig 3: Tumour pathogenesis

Serrated Pathway: Around 20% of CRC cases develop cancer through the serrated pathway. Serrated pathway can be divided into CIMP^{low} MSS tumours (*KRAS* mutations), *BRAF*-mutant CIMP^{high} MSS tumours or *BRAF* mutant CIMP^{high} microsatellite instability (MSI) tumours. Serrated tumours are mostly associated with silencing of *MGMT*, *CDKN2A* or *MLH1*.

MSI pathway: CRC cases are development due to dysfunctional DNA mismatch repair genes[8].

Premalignant Adenoma: Premalignant adenoma undergoes genetic transformation and results in adenocarcinoma which can be invasive. Mutation takes place in the adenomatous polyposis gene (APC), activating oncogene c-MYC and cyclin D1 resulting in the progression towards malignancy.

KRAS mutation: KRAS (Kirsten rat sarcoma viral oncogene), belongs to the RAS family genes associated with tumour. KRAS binds to guanosine 5′ -triphosphate (GTP), and gets activated and is involved in the process of cell signal transduction for the regulation of cell proliferation and differentiation.

When mutations happen in the KRAS gene, the responsiveness to GAPs gets altered. Mutation results in rapid exchange for GTP, uncontrolled cell division, growth, transformation and metastasis. This also results in the development of resistance to chemotherapy and EGRF targeted therapy. KRAS mutations lead to unusual signal activation of the RAS/ RAF/MEK/ERK signalling pathway and promotes liver metastasis. KRAS mutation enhances angiogenesis by activating Vascular endothelial growth factor. KRAS mutation also affects the tumour microenvironment by increasing the glucose uptake of the tumour cells, alter glutamine metabolism and elevate autophagy. KRAS mutations causes elevated levels of glycolysis and protein expressions and metabolic alterations [9].

DNA mismatch repair: Deficient DNA mismatch repair results in the development of CRC. Mutations of MSH2, MLH1, and PMS2 gene results in high frequency microsatellite instability resulting in the development of hereditary nonpolyposis colon cancer syndrome.

Epigenetics: Abnormalities in the tumour suppressor genes or activation of oncogenes results due to abnormal DNA methylation, this can compromise the genetic balance of the cell and results in malignant transformation.

Staging:
Stage 0 is the very early stage of cancer, this is followed by stage I, II, III, IV. Lower the number in the stage, lesser the cancer spread.

The American Joint Committee on Cancer (AJCC): TNM system of cancer staging: TNM

system staging of cancer is based on the size and spread of the cancer cells.

Size of tumour (T): Growth of the cancer cells in the region of the colon or rectum. This includes different layers like mucosa, muscular mucosa, submucosa, muscularis propria, subserosa and serosa.

Spread to lymph nodes (N): The growth and spread of cancer cells to the nearby lymph nodes.

Distant metastasis (M): Cancer cells travel along the lymph nodes and reach distant organs like liver, lungs, kidney, brain and cause cancer in those organs, this is called as distant metastasis[10].

MANAGEMENT:

Localized cancers can be completely removed by surgical procedures. Name of the surgical procedure varies based on the location of the lesion in the colon region like: right hemicolectomy (cecum, right colon), extended right hemicolectomy (proximal or middle transverse colon), left hemicolectomy (splenic flexure and left colon), sigmoid colectomy (sigmoid colon lesions), total abdominal colectomy with ileorectal anastomosis.

Other therapeutic options:

Cryotherapy involves application of extreme cold or freezing of the cancer tissue, causing death of the cells. Radiofrequency ablation is a technique by which high frequency radiation are passed on the affected tissue and causes destruction of the cells, hepatic arterial infusion of chemotherapeutic agents directly to liver cells for colorectal liver metastasis. Adjuvant therapy is used in selected patients who are at high risk for recurrence of tumour cells.

Systemic chemotherapy:

5-fluorouracil (5-FU) is an antimetabolite drug widely used in the treatment of colorectal cancer. 5-FU exerts its anticancer effects through inhibition of thymidylate synthase (TS) and incorporation of its metabolites into RNA and DNA[11].Topoisomerase inhibitors are chemotherapeutic agents interfering with the topoisomerase enzymes I and II, which regulates the change in the structure of the DNA. Topoisomerase inhibitors block the ligation step of the cell cycle, which generates DNA single and double-strand breaks, leading to apoptotic cell death[12]. The platinum-containing agent oxaliplatin, and the 5-FU prodrug capecitabine are the first line drugs in the treatment of colorectal cancer[13]. The combination therapies, using FU/leucovorin and oxaliplatin and 5-FU/leucovorin and irinotecan, have become established as efficacious cytotoxic regimens for the treatment of metastatic CRC, resulting in overall survival times of approximately 2 years[14].

Biologic agents:

Biological agents are substances made from living organisms used in the treatment of cancer. Biological agents like Bevacizumab, a humanized monoclonal antibody that targets vascular endothelial growth factor. Cetuximab, Panitumumab, monoclonal antibodies against the epidermal growth factor. Ipilimumab a CTLA-4 immune checkpoint inhibitor. Cytotoxic T lymphocyte-associated antigen (CTLA-4) is a coinhibitory transmembrane protein which binds to the B-71 and B7-2 ligands on antigen presenting cells[15]. Nivolumab is a human immunoglobulin (Ig) G4 anti-PD-1 monoclonal antibody. By binding to PD-1, an inhibitory co-receptor expressed on antigen-activated T cells, thus preventing interaction with PD-L1, resulting in the loss of inhibitory signals in T cells, and tumour recognition by cytotoxic T cells and thus restoring T-cell function[16]. Pembrolizumab is also an anti-PD-1 antibody which stimulates the body to act against the cancer cells. Ramucirumab is a monoclonal antibody against VEGFR2, it has antiangiogenic activity preventing formation of new blood vessels. It also has an inhibitory effect on the cell cycle progression[17].

CONCLUSIONS:

A family history of colorectal cancer in the first degree relative has a highest risk factor for the development of colorectal cancer with the increase in age. 80% CRC cases are caused due to chromosomal instability pathway, which is initiated by APC mutation. If cancer is localized, it can be completely removed by surgical procedures. To stop the growth and progression of the tumour cells, chemotherapeutic agents are used. Treatment option becomes more advanced with the introduction and utilization of biological agents which acts on various growth factor and interrupts the growth cycle. Targeted drug delivery system has gained more importance in recent times which has an effective means of drug delivery making the treatment more precise and limiting the toxicity.

LIST OF ABBREVIATIONS:

CRC: Colorectal cancer
CT: Computerized Tomography
MRI: Magnetic resonance imaging
PET: Positron emission tomography,
PET-CT: positron emission tomography-computed tomography
FAP: Familial Adenomatous Polyposis.
HNPCC: Hereditary non-polyposis colon cancer syndrome
WHO: World Health Organization

MSS: Microsatellite Stability
CIMP: CpG island methylation pathway
5-FU: 5-Fluorouracil
DNA: Deoxyribonucleic acid
RNA: Ribonucleic Acid
LMICs: Low and Middle-Income Countries
IBD: Inflammatory Bowel Disease
AJCC: The American Joint Committee on Cancer
KRAS: Kirsten rat sarcoma viral oncogene
EGRF: Epidermal Growth Factor Receptor
TNM: Tumour, Nodes and Metastases
Ig: Immunoglobulin
TS: Thymidylate Synthase
APC: Adenomatous Polyposis Gene
CTLA-4: Cytotoxic T lymphocyte-associated antigen
VEGFR2: Vascular endothelial growth factor receptor 2
PD-1: Programmed cell death protein 1
GTP: Guanosine 5′ -Triphosphate

CONFLICT OF INTEREST:

The author has no conflicts of interest in this review**.**

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Research Article

COMPARATIVE STUDY OF PERCEPTION AND AWARENESS ABOUT GENERIC VS BRANDED MEDICINES IN RURAL AND URBAN AREAS OF KOLHAPUR

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ABSTRACT

Typically, pharmaceutical companies create two different drugs from a single ingredient. One product, known as branded medicine, is heavily advertised and supported by doctors, retailers, and chemists. Another option, known as generic medicine, is not advertised or promoted.. So the Government of India is taking lot of steps to promote the availability of generic medicines both in rural and urban areas and also taking steps to aware people that it is equally safe and effective as that of branded medicines. The survey is about perception towards generic medicines and branded medicines and current scenario of branded and generic medications in rural and urban areas of Kolhapur. This study was conducted to find out the different factors that could influence the use of generic and branded medicines among people from rural and urban areas of Kolhapur. The study was carried out among 100 people from rural areas and 100 from urban areas of Kolhapur. From the above survey it is found that Branded medicines from each category were widely used in Rural and Urban areas of Kolhapur compare to the Generic medicines. People found less aware about the difference between the Generic and branded medicines in Rural area than the Urban area.

KEYWORDS

Branded medicines, Generic medicines, perception, Urban and Rural areas

INTRODUCTION

Nowadays, Pharmacists' responsibilities extended beyond the usual preparation and dispensing of pharmaceuticals by additionally influencing the prescribing procedure and providing pharmaceutical care services, which has increased their involvement in patient care. Prior definitions of the duty of the chemist have included "the responsible provision of medication for the aim of achieving definite outcomes to enhance patients' quality of life" (Hepler & Strand, 1990). Pharmacy professionals have the knowledge and abilities to identify, address, and prevent drug-related issues. Additionally, according to Merten et al. (2013), chemists can advise patients on pharmacological therapy and suggest cost effective treatments.

• **Drug:** A drug is defined as "A substance recognized by an official pharmacopoeia or formulary, intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease."

• **Generic drugs**: A generic drug is a medication created to be the same as an already marketed brand name drug in dosage form, safety, strength, route of administration, quality, performance characteristics, and intended use. In other words, you can take a generic medicine as an equal substitute for its brand name.

• **Branded drugs**: A drug sold by a drug company under a specific name or trademark and that is protected by a patent. Brand name drugs also known as innovator drugs.

The Indian government is doing a lot to increase the accessibility of generic medications in both urban and rural areas, as well as to educate the public about their safety and efficacy on par with that of branded medications. Generic medications are produced by a large number of pharmaceutical businesses and distributed through retail retailers. E-pharmacies are operating and distributing generic medications to customers' homes. The government has established thousands of Pradhan Mantri Bhartiya Janaushadhi Kendra's (PMBJK) all over the nation where people can obtain generic medications for a much reduced price.

Typically, pharmaceutical companies create two different drugs from a single ingredient. One product, known as branded medicine, is heavily advertised and supported by doctors, retailers, and chemists. Another option, known as generic

medicine, is not advertised or promoted. Interesting fact: Similar molecules are used to create both medications. As a result, although the two medications' formulas are comparable, the price of the branded drug is significantly greater. This survey is based on the current scenario of branded and generic medications. To learn more about their understanding of generic and branded medications, a survey was conducted to Kolhapur residents in both urban and rural areas. In terms of the quantity of medications exported, the Indian pharmaceutical industry is ranked third. India is referred to as the "pharmacy of the world" by other nations because it exports a significant amount of medications to different regions of the globe.

Similarity between generic and branded drugs –

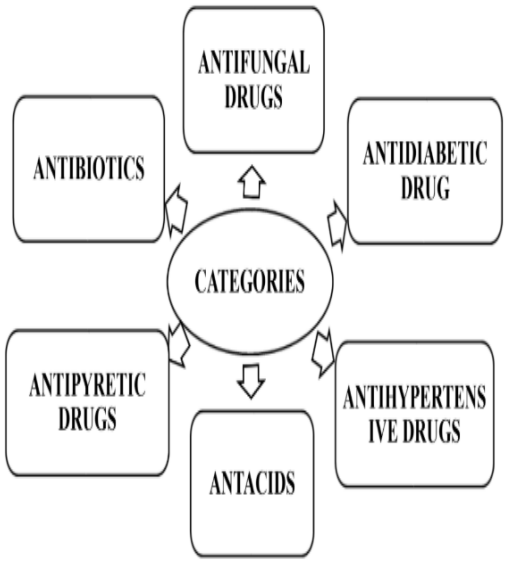
- It must have the same active ingredients.
- The dose form must be the same.
- Their performance and quality are comparable.
- Its administration method must be consistent.
- Generic medications are just as safe as branded ones.
- Its bioavailability is exactly the same.

Differences between generic and branded medicines

PARAMETER	BRANDED MEDICINES	GENERIC MEDICINES
Patents	Patent protected	Off-patent
Trade name	Marketed under a unique proprietary name given by the company	Marketed under the generic name of the drug
Manufactured by	Developed and manufactured by an innovator company	Manufactured by several pharmaceuticals' companies after patents expiration of the relevant brand name drug
Name variation	Same or different brand names in different countries	Same generic drug name in any country
Cost/price	Higher in cost	Lower in cost
Appearance/look	Drugs are standard in size, colour, packaging etc.	Packaging and the drug itself may look different
Excipients	Uses acceptable excipients	Same or altered but acceptable excipients

Table no. 01 : Difference between generic and branded medicines

Drug categories we selected:
Fig no. 01: Drug categories we selected



Material and Methods This is an observational study. we conducted a pilot survey of 200 people 100 from Rural and 100 from urban area of Kolhapur district. Survey research may use a variety of data collection methods with most common being questionnaire and interviews. The data was collected during the year 2022-2023.

Study population: Various people from rural and urban areas of Kolhapur from the villages like Kalambe, Bhamate, Kale and urban areas like Mangalwar peth, Mahalaxmi Nagar, Jawahar nagar, etc in Kolhapur are selected and interviewed. Sample size: Total 200 people were surveyed. In which 100 people were from urban areas and 100 from rural areas of Kolhapur.

Study design: This cross sectional study was conducted among various people of rural and urban areas of Kolhapur. Each individual patient was provided with questionnaire regarding generic and branded medicines. Everyone was asked information on health condition, their perception and use of generic and branded medicines, its differences and similarities, etc.

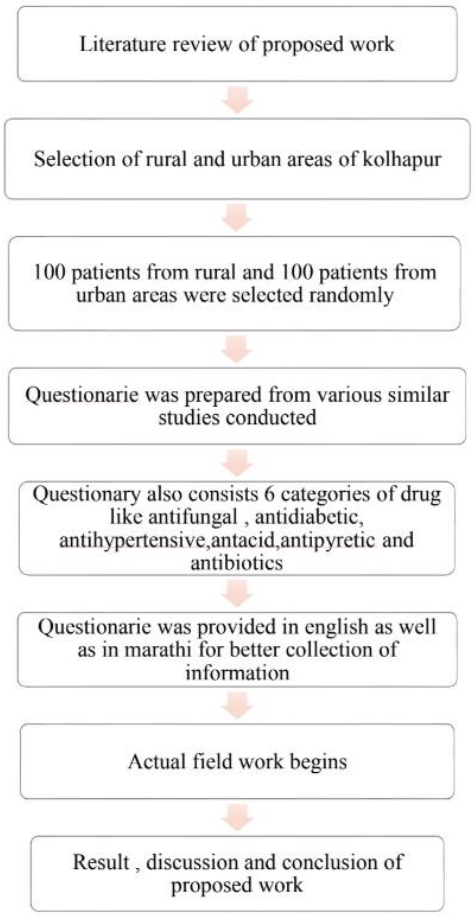
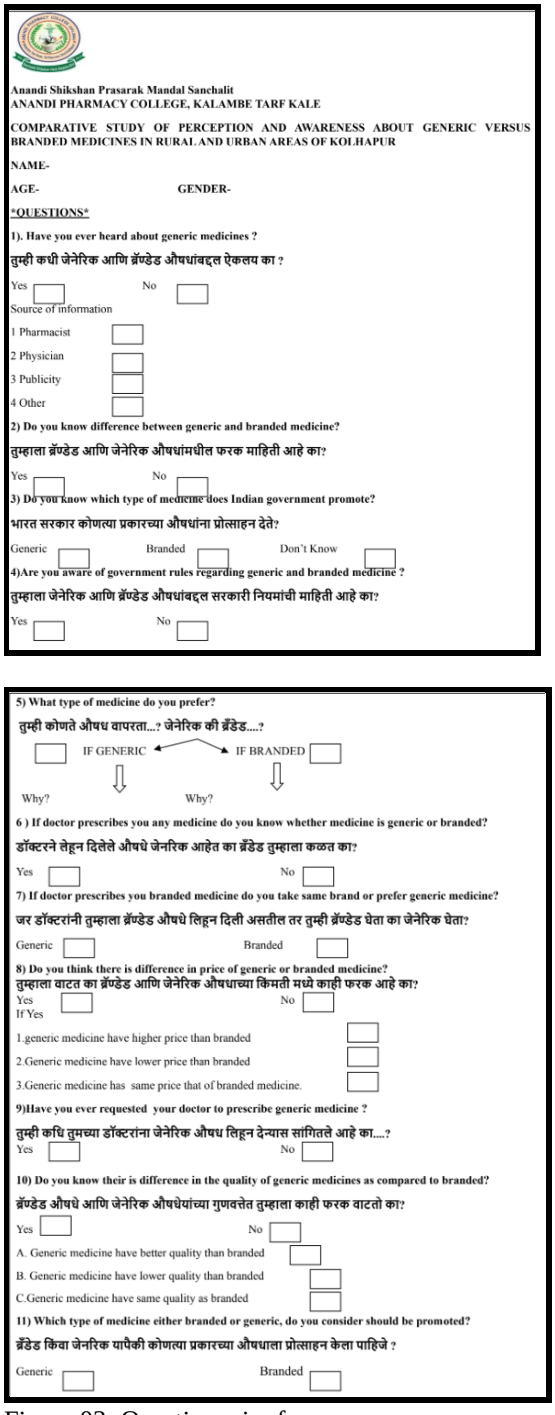


Fig no. 02: Methodology

The questionnaire was collected. The data obtained was subjected to statistical analysis using appropriate method.

Scope of design: The result obtained will help to create awareness about use of generic and branded medicines and its knowledge among people from urban and rural areas of Kolhapur. Data obtained will help to compare how much percent of people from urban and rural areas are aware about knowledge regarding generic and branded medicines and their use. And it will help to awareness among them by such program.

Collection of data: Collection of data done through door-to-door visit



Anandi Shikshan Prasarak Mandal Sanchalit
ANANDI PHARMACY COLLEGE, KALAMBE TARF KALE

COMPARATIVE STUDY OF PERCEPTION AND AWARENESS ABOUT GENERIC VERSUS BRANDED MEDICINES IN RURAL AND URBAN AREAS OF KOLHAPUR

NAME-

AGE- GENDER-

QUESTIONS

1). Have you ever heard about generic medicines ?

तुम्ही कधी जेनेरिक आणि ब्रॅण्डेड औषधांबद्दल ऐकलय का ?

Yes ☐ No ☐

Source of information

1 Pharmacist ☐
2 Physician ☐
3 Publicity ☐
4 Other ☐

2) Do you know difference between generic and branded medicine?

तुम्हाला ब्रॅण्डेड आणि जेनेरिक औषधांमधील फरक माहिती आहे का?

Yes ☐ No ☐

3) Do you know which type of medicine does Indian government promote?

भारत सरकार कोणत्या प्रकारच्या औषधांना प्रोत्साहन देते?

Generic ☐ Branded ☐ Don't Know ☐

4)Are you aware of government rules regarding generic and branded medicine ?

तुम्हाला जेनेरिक आणि ब्रॅण्डेड औषधांबद्दल सरकारी नियमांची माहिती आहे का?

Yes ☐ No ☐

5) What type of medicine do you prefer?

तुम्ही कोणते औषध वापरता...? जेनेरिक की ब्रँडेड....?

☐ IF GENERIC ⇦ ⇨ IF BRANDED ☐

Why? ⇩ Why? ⇩

6) If doctor prescribes you any medicine do you know whether medicine is generic or branded?

डॉक्टरने लेहून दिलेले औषधे जेनरिक आहेत का ब्रँडेड तुम्हाला कळत का?

Yes ☐ No ☐

7) If doctor prescribes you branded medicine do you take same brand or prefer generic medicine?

जर डॉक्टरांनी तुम्हाला ब्रॅण्डेड औषधे लिहून दिली असतील तर तुम्ही ब्रॅण्डेड घेता का जेनेरिक घेता?

Generic ☐ Branded ☐

8) Do you think there is difference in price of generic or branded medicine?

तुम्हाला वाटत का ब्रॅण्डेड आणि जेनेरिक औषधाच्या किंमती मध्ये काही फरक आहे का?

Yes ☐ No ☐

If Yes

1.generic medicine have higher price than branded ☐
2.Generic medicine have lower price than branded ☐
3.Generic medicine has same price that of branded medicine. ☐

9)Have you ever requested your doctor to prescribe generic medicine ?

तुम्ही कधि तुमच्या डॉक्टरांना जेनेरिक औषध लिहून देन्यास सांगितले आहे का....?

Yes ☐ No ☐

10) Do you know their is difference in the quality of generic medicines as compared to branded?

ब्रॅण्डेड औषधे आणि जेनेरिक औषधेयांच्या गुणवत्तेत तुम्हाला काही फरक वाटतो का?

Yes ☐ No ☐

A. Generic medicine have better quality than branded ☐
B. Generic medicine have lower quality than branded ☐
C.Generic medicine have same quality as branded ☐

11) Which type of medicine either branded or generic, do you consider should be promoted?

ब्रँडेड किवा जेनरिक यापैकी कोणत्या प्रकारच्या औषधाला प्रोत्साहन केला पाहिजे ?

Generic ☐ Branded ☐

Fig no.03: Questionnaire for survey

Some Examples of Generic and Branded medicines available in Market: Table no. 02: Some Examples of Generic and Branded medicines available in Market Drug Category : **ANTI-HYPERTENSIVE**

Category	Branded	Generic
Amlodipine	Amlokind/Amlosafe/Amlovas/ Amlogard/Amodep	Amlip/Lupidip /Amlotex/Tenlodip

Telmisartan	Telmikind/Telma/ Telista/Tazloc/ Temsan	Telsun/Telgo/Steltan /Dazteli
Enalapril	Envas/ Enam / napril / Nuril	Vasopril/Lepril/ Anapril/Enaril- s
Rosuvastatin	Rosuvas/Roseday/ Novastat/Rozat/ Rozavel	Rosumit/Rosta-f/Rosuline/Rosudoz
Atorvastatin	Storvas/Atorva/Aztor/Atocor/Stator	Atrovin/Peditor/ Atrovast/Lipvas

Drug Category : **ANTACID**

Category	Branded	Generic
Pantaprazole	Pantin/Pan/Glanpan / Nicopenta	Pantosec/Paneath/ Emtop/
Omeprazole	Omez/ Ocid- IT / Omicap	Omzid/Aciphex/Omee/ Omelezo
Esomeprazole	Esoz/Nexpro/Esomac	ES-Od / Esomroz / Esodol
Rabeprazole	Cyra/Rekool/Rabemac/Rabekind	Rubyzol / Remitrx 20/ Rabidiv/Rablist

Drug Cartegory :**ANTI-FUNGAL**

Category	Branded	Generic
Clotrimazole	Candid/Canesten / Candiderma/Cwin	Clocip/Widezole/ Clomits/Rizole-DS
Ketoconazole	Ketostar /Zykt /Kz/Keraglo	Ketoactive/ketokem/Ketocip/Ketolechem
Fluconazole	Zocon/Onecan	Flucos /Flumet /Flulor-B/Fluka
Itraconazole	Candiforce/Itrasys/Syntran/IT-Mac	Itrado-200/Itranaz/Mouzol/Necitra
Terbinafine	Terbicip/Terbifinaforce/Terbinol/ TRFY	Terbifex /Trenol /Termax/Terbicrom

Drug category : **ANTI-DIABETIC**

Category	Branded	Generic
Metformin	Glyciphage/Glycomet/Glimy/ Glimet-DS	Okamet-500/Fortamet-500/Wellmet 500
Glimipride	Tribet-2/Amaryl-1/GP-1	Zesky-m1/Glimics
Sitagliptin	Januvia-100mg/ Janumet-100mg/ Istavel-100mg	Glipsi-50 / Salvaglip-50 /Sitaliptin-50
Glipizide	Glucotrol/Minodiab/Glynase	Acitizide-M/Bimode-M/ Biacon-M
Voglibose	Vobosee-0.2/Vogo 0.2/Volibo-0.3	Vogliboz/Amibose/Kardem-0.2

Drug Category : **ANTIPYRETIC**

Category	Branded	Generic
Paracetamol	Dolo / Crocin /Fepanil / Doliprane	Paracip / Mepar
Ibuprofen	Imol / Combiflam /Ibugesic / Brufen	Ibruwell /Brufex
Diclofenac	Dynapar/ Voveran/Enzoflam/ Diclomol	Diclogen/ Reactin/Dolofresh/ Omnee
Nimesulide	Nise / Nobel / Sumo	Nicip / Nimket /NP-425/Nodard

Tramadol	Ultracet / Tramazac/ Megaflam/ Zerodol-PT	Ultramed

Drug Category : **ANTIBIOTICS**

Category	Branded	Generic
Azithromycin	Azee/ Azithral/ Zathrin/ATM	Azicip / Zubithro /Azilay/ Aziryl
Amoxillin	Novamox/Blumox/ Mox	Omniclav / Saltip/Merryclav
Cefixime	Zifi/taxim o / Cefolac/Safexim	Cefix / Amicefi /Cefrax / Cefex
Doxycycline	Doxt/ Minicycline/Microdox/ Doxicip	Doxisept LB/ Welldox/ Doxicip /Doxyplus
Moxifloxacin	Moximac / Mahaflox /Miliflox/ Moxif	Moxiyst/Eustomox/Radixme/Moxiflox

Observations and Results -
The survey is conducted in people from rural and urban areas of Kolhapur in order to check the perception and knowledge about generic and branded medicines. The information obtained from survey has been tabulated as follows:

Observation obtained from Rural and Urban areas of Kolhapur :
In present study 100 people from rural area and 100 people from urban area of Kolhapur were participated in survey.

Table no 04 observations obtained from rural and urban areas of Kolhapur QUESTION 01

Have you ever heard about generic medicines ?	**YES**	**NO**
RURAL	56%	44%
URBAN	80%	20%

QUESTION 02

Do you know difference between generic and branded medicine?	**YES**	**NO**
RURAL	41%	59%
URBAN	66%	34%

QUESTION 03

Do you know which type of medicine does Indian government promote?	**GENERIC**	**BRANDED**	**DON'T KNOW**
RURAL	30%	13%%	57%
URBAN	52%	5%	43%

QUESTION 04

Are you aware of government rules regarding generic and branded medicines?	**YES**	**NO**
RURAL	07%	93%
URBAN	15%	85%

QUESTION 05

What type of medicine do you prefer?	**GENERIC**	**BRANDED**
RURAL	15%	85%
URBAN	30%	70%

QUESTION 06

If doctor prescribes you any medicine do you know whether medicine is generic or branded?	**YES**	**NO**
RURAL	25%	75%

URBAN	49%	51%

QUESTION 07

If doctor prescribes you branded medicine do you take same brand or prefer generic medicine?	**GENERIC**	**BRANDED**
RURAL	18%	82%
URBAN	29%	71%

QUESTION 08

Do you think there is difference in price of generic or branded medicine?	**YES**	**NO**
RURAL	68%	32%
URBAN	70%	30%

QUESTION 09

Have you ever requested your doctor to prescribe generic medicine?	**YES**	**NO**
RURAL	11%	89%
URBAN	24%	76%

QUESTION 10

Do you know there is difference in the quality of generic medicines as compared to branded?	**YES**	**NO**
RURAL	52%	48%
URBAN	56%	44%

QUESTION 11

Which type of medicine either branded or generic, do you consider should be promoted?	**GENERIC**	**BRANDED**
RURAL	47%	53%
URBAN	41%	59%

As per Question No. 05 reasons to use generic / branded medicines in urban and rural areas of Kolhapur:

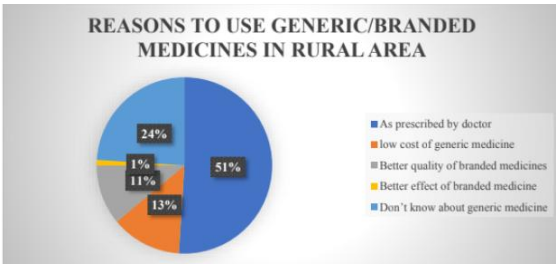


Fig no.06 Reasons to use generic/branded medicines in rural area

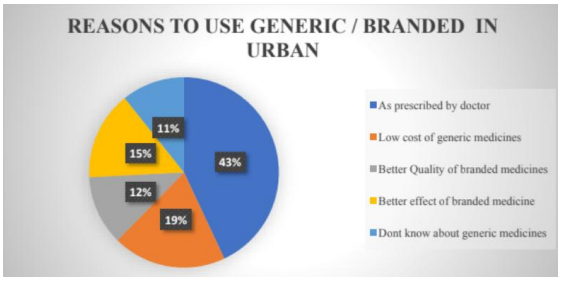


Fig no.07 Reasons to use generic/branded medicines in urban area

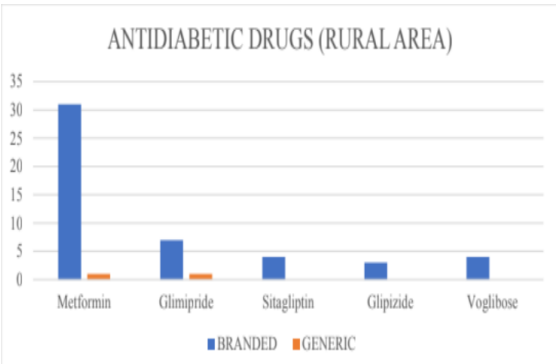


Fig no. 08 Use of Antidiabetic drug in rural area

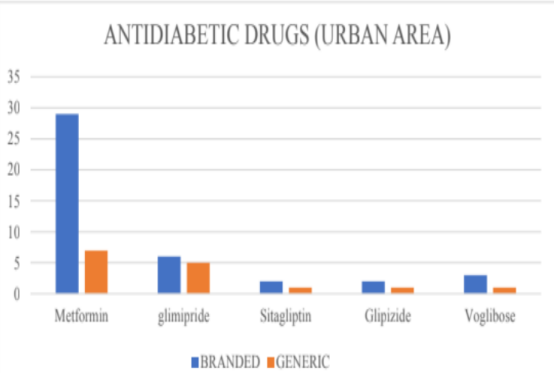


Fig no. 09 Use of Antidiabetic drug in urban area

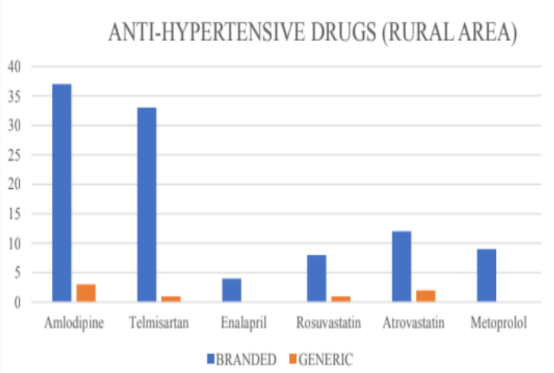


Fig no. 10 Use of Anti-hypertensive drug in rural area

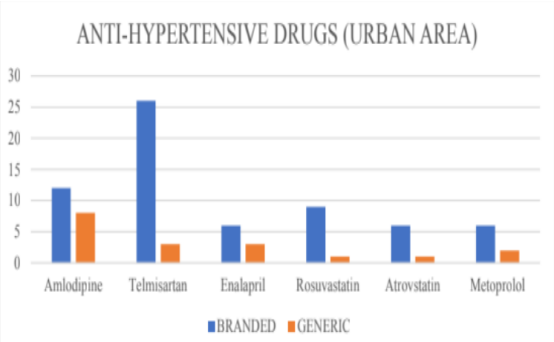


Fig no. 11 Use of anti-hypertensive drug in urban area

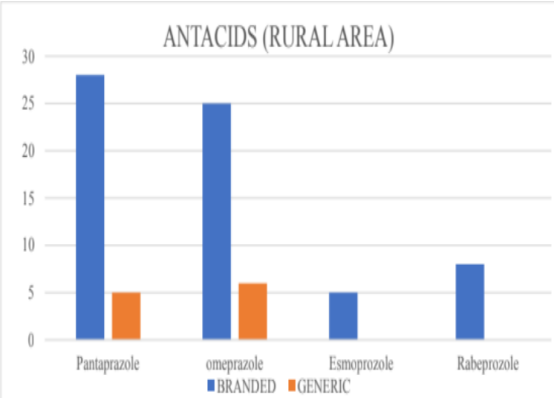


Fig no. 12 Use of Antacids drug in rural area

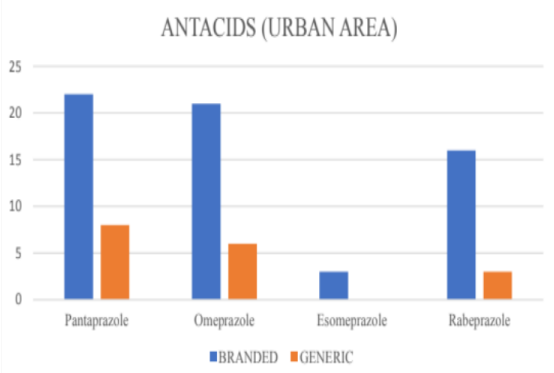


Fig no. 13 Use of Antacids drug in urban area

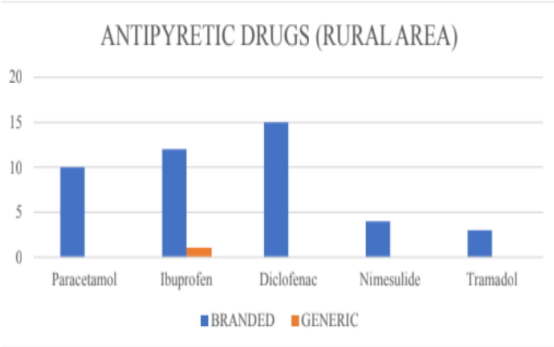


Fig no. 14 Use of Antipyretic drug in rural area

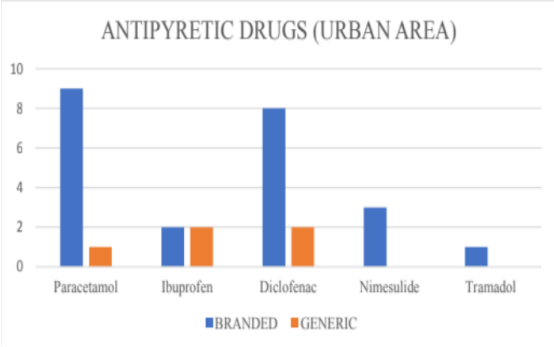


Fig no. 15 Use of Antipyretic drug in urban area

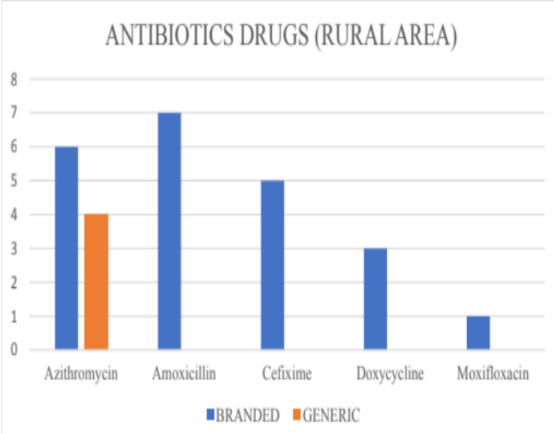


Fig no. 16 Use of Antibiotic drug in rural area

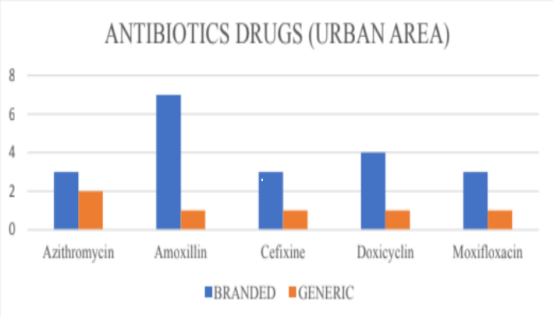


Fig no. 17 Use of Antibiotic drug in urban area

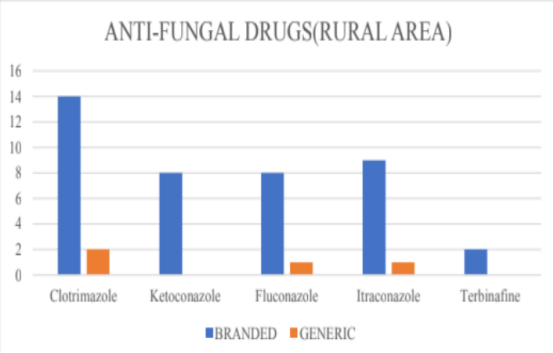


Fig no. 18 Use of Anti-fungal drug in rural area

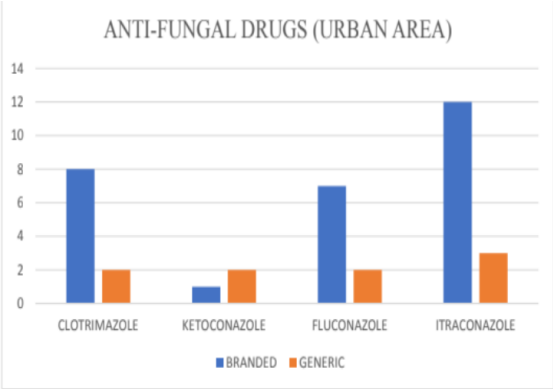


Fig no. 19 Use of Anti-fungal drug in urban area

Mostly used drugs in urban and rural areas of Kolhapur:

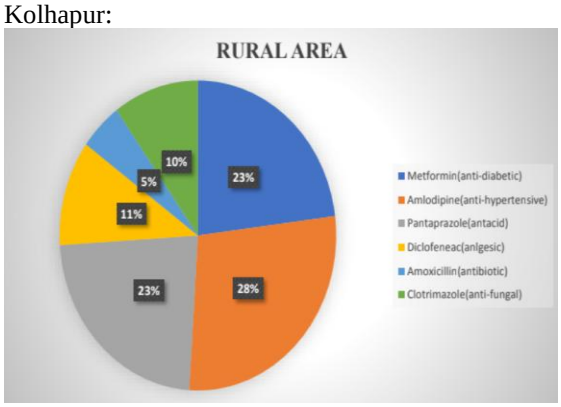


Fig no.20 Mostly used drugs in rural areas of Kolhapur

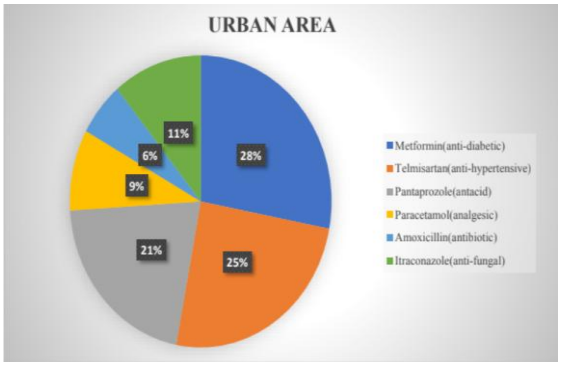


Fig no.21 Mostly used drugs in urban areas of Kolhapur

RESULTS

From the above survey it is found that Branded medicines from each category were widely used in Rural and Urban areas of Kolhapur compare to the Generic medicines. People found less aware about the difference between the Generic and branded medicines in Rural area than the Urban area. Therefore they prefer the medicines which prescribe by the physician. They have idea about the price difference between the both still they prefer the branded medicines. People from urban area knows the quality of branded medicines is higher than the generic medicines therefore they prefer the Branded medicines. Branded medicines were widely used in all categories of a Drugs in Rural and Urban areas of Kolhapur than generic medicines.

DISCUSSION:

Present study states that the use of generic drug is less than branded drugs in both rural and urban areas of Kolhapur. It was observed that large number of people (59%) from rural area were not knowing about difference between generic and branded medicines, whereas from urban area of Kolhapur most of people (66%) were knowing about difference between generic and branded medicines. 57% people from rural area don't know about which type of medicine Indian government promote, while 52% people from Urban area answered Indian government promote generic medicines. Observation was found almost similar that 93% people from Rural area and 85% people from Urban area not aware of government rules regarding generic and branded medicines.

Both Rural and Urban area of people prefer Branded medicine over Generic medicines. 75% people from Rural and 51% from urban area don't know about which type of medicine doctor prescribe. Both Rural and Urban area of people prefer Branded medicine. Maximum people from Rural (68%) and Urban (70%) area already aware about there is price difference in between generic and branded medicine. No one requested their doctor to prescribe generic medicine over branded. There is some

quality difference between generic medicines as compared to branded medicines suggest 52% from Rural and 56% from urban areas of Kolhapur.

Still lots of studies are needed to work on to increase the awareness of people regarding the generic medicines they must know about the quality factor of generic and branded medicines is same. If they got to know about the Indian Regulations regarding the generic medicines it will more beneficial to them considering the cost, quality and availability of medicine.

Comparative study of perception and awareness about Generic vs Branded medicines in Rural and Urban areas of Kolhapur

ACKNOWLEDGEMENT:

We acknowledge to the all persons who had participated in our survey. Authors are acknowledged to Mrs. Neeta U. Atkeere, New College of Pharmacy Kolhapur for their continuous guidance, support and encouragement.

Comparative study of perception and awareness about Generic vs Branded medicines in Rural and Urban areas of Kolhapur

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Review Article

MOUTH DISSOLVING FILM: A REVIEW

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ABSTRACT:

Fast-dissolving films, which bypass hepatic first-pass metabolism and offer quick therapeutic impact, are now more widely accepted and accurate oral dosage forms. The main components of this system are patient compliance and industrial compatibility. Advantages of oral disintegrating dose forms versus solid dosage forms Recently, mouth-dissolving films have entered the market because they are more convenient and simple to use than other dosage forms, such as orally disintegrating pills. The type of drug delivery method known as a mouth dissolving film dissolves or disintegrates when placed in the oral cavity in a matter of seconds without the need for water. This technique is mostly employed in specific populations like children, the elderly, patients who are bedridden, patients who are mentally ill, and the general public. The present review provides various formulation considerations, methods of preparation, and evaluations of film.

INTRODUCTION

Oral administration is the most popular route due to ease of ingestion, pain avoidance, versatility (to accommodate various types of drug candidates), and most importantly, patient compliance also, solid oral delivery systems do not require sterile conditions and are, therefore, less expensive to manufacture. Patients with geriatric, pediatric, nauseated, bedridden, and noncompliance issues typically have trouble swallowing the traditional oral dose form and do not take their medications as directed. This problem is thought to have affected 50% of the population, which ultimately increases the likelihood of noncompliance and unsuccessful therapy. Due mostly to longer life expectancies, the elderly makes up a significant segment of the population nowadays. The biggest issue with tablets is their size and potential choking hazards. Patients with geriatric and pediatric conditions, as well as those who are travelling and may not have easy access to water, are more likely to have trouble swallowing medicines. To get around this Oral fast disintegrating drug delivery system were created as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who have trouble swallowing conventional oral solid dosage forms.
These systems were first created in the late 1970s. These dose forms either dissolve or disintegrate in the mouth without water in around three minutes. Due to improved patient compliance, oral fast disintegrating dose forms are starting to gain favor as an innovative drug delivery technology. An oral fast-dispersing dosage form is, by definition, a solid that quickly dissolves or disintegrates in the mouth to generate solution or suspension without the need for water to be administered. Dysphagia, or trouble swallowing, affects people of all ages, but it's more prevalent among the elderly. It can also make it difficult to take regular tablets and capsules. Various medical diseases, including as stroke, Parkinson's, AIDS, thyroidectomy, head and neck thyroid treatment, and other neurological conditions, such as cerebral palsy, are linked to dysphagia. rapid dissolving films and mouth-dissolving tablets make up the oral rapid disintegrating dosage form. Tablets that dissolve in the mouth are linked to a few issues, including residues that produce a grittiness in the mouth, a fear of choking, and difficulties swallowing tablets. A new drug delivery method for the oral distribution of the pharmaceuticals, called as Fast dissolving films/oral dispersible film/mouth dissolving films/oral disintegration film/oral dissolving film, was investigated to overcome the problems with mouth dissolving tablets. [1,2]

History of Fast Dissolving Oral Films:

In 1970, fast-dissolving oral films were introduced to North America. Oral films were first launched at that time as staff care products and mouth fresheners. Fast-dissolving films, also known as Listerine® pocket packs TM and used as breath fresheners, were invented by Pfizer. However, the United States and European markets quickly framed rapid dissolving films. There are currently 15 businesses creating oral fast-dissolving films using a constantly evolving tablet dose form. According to the article, Labtech GmbH, APR, established a novel method for the creation of oral fast-dissolving films. Oral strips have gained popularity in the past few years for their ability to quickly dissolve and release a minty flavor while also refreshing the

breath. Pharmaceutical companies are now making these oral strips as over the counter and prescription pharmaceuticals.

The more recent technology used in the production of oral disintegrating dose forms are oral films. They are attractive thin films made of ingestible, water-soluble polymers in a range of dimensions, such as square, rectangle, and disc. The stripes could be clear or opaque, flexible, or brittle. They are created to break down quickly on the tongue without the aid of water. The specific surface area for disintegration in fast disintegrating films (FDFs) is considerable. The films overcome the shortfalls of oral rapid dissolving pills by reducing the risk or worry of choking, making them simple to handle and administer and easy to make. These dosage forms' low medication loading capacity and limited flavor masking possibilities are significant drawbacks. [3,4]

Salient feature of fast dissolving drug delivery system: -

- Convenience in administering to mentally sick, disabled, and recalcitrant patients.
- Don't need water.
- Gets through the medicines' unpleasant taste.
- May be created to leave little to no aftertaste in the mouth and to provide the user a satisfying mouthfeel.
- The ability to offer liquid medicinal benefits in the form of a solid formulation.
- Cost effective.
-

Advantage of Fast Dissolving Oral Films: -

- Convenient dosing.
- No water needed.
- No risk of chocking
- Taste masking.
- Enhanced stability.
- Improved patient compliance.
- The drug enters the systemic circulation with reduced hepatic first pass effect.
- Site specific and local action.
- Availability of large surface area that leads to rapid disintegration and dissolution within oral cavity.
- Dose accuracy in comparison to syrup.

Disadvantages: -

- High doses cannot be incorporated.
- Excessive bitter drugs are not feasible.
- Dose uniformity is a technical challenge.
- They require special packaging for the products stability and safety.
- Drugs which irritate the oral mucosa cannot be administered by this route.

Overview of the oral cavity: -

The outermost layer of stratified squamous epithelium makes up the oral mucosa. A basement membrane, a lamina propria, and the submucosa—the deepest layer—are located beneath this. In terms of permeability, the oral mucosa falls somewhere between the intestinal mucosa and the epidermis. The buccal mucosa's permeability is thought to be 4–4000 times larger than the skins. Because oral mucosa has various shapes and functions, there are significant variances in permeability between different areas of the oral cavity.[3,5]

Mechanism of Absorption through Oral Mucosa:-

For passive drug transference, the oral mucosa has two transcellular (intracellular, passing into the cell) and paracellular penetration passageways (intercellular, passing around the cell). Drug fragments can be used simultaneously on different tracks, but depending on the physicochemical properties of the drug, one track is preferred over the other. Due to its lipophilic nature and low partition coefficient, the cell membrane has difficulty allowing hydrophilic solutes to pass through. Due to the intercellular spaces acting as a barrier to permeation, the lipophilic substances have low solubility in passive transport systems. In the meantime, the fusion of these two itineraries stratifies the oral epithelium and convokes solute permeation. The pathway that has the fewest barriers to passage is therefore preferred over the other for penetration through the oral mucosa.

Factors affecting absorption: -

- Biphasic solubility of the medicine is required for absorption in addition to high lipid solubility when determining the drug's ability to dissolve in salivary secretions.
- Binding to the oral mucosa: Drugs that bind to the oral mucosa are not widely available in the system.
- Saliva's typical pH is 6.2-7.6, which favors the absorption of medicines that are still unionized. Saliva's pH and pKa. If the pKa for an acid is greater than 2 and for a base is less than 10, the medications are also absorbed via the oral mucosa.
- Lipophilicity of the drug.
- Passive permeation requires a medicine to have a little higher lipid solubility than that needed for GI absorption for it to be entirely absorbed through the sublingual route.
- Oral epithelium thickness: As contrast to buccal thickness, the sublingual epithelium is thinner at 100–200 m. As a result of the

thinner epithelium and the drug's immersion in a smaller volume of saliva, the absorption of medicines is accelerated. [11,15]

SR. No.	Oral Disintegrating Tablets	Orally Dissolving Films
1	It is a tablet	It is a film
2	Lesser dissolution due to less surface area	Greater dissolution due to larger surface area
3	Less durable as compared with oral films	Better durable than oral disintegrating tablets
4	Less patient compliance than films	More patient compliance
5	High dose can be Incorporated	Low dose can only be Incorporated
6	It has a fear of chocking	No risk of chocking

Table no.01: - Comparison between Fast Dissolving oral Films and Tablets.

FORMULATION CONSIDERATION: -

- Active pharmaceutical ingredient
- Film forming polymer
- Plasticizer
- Sweetening agent
- Saliva stimulating agent
- Surfactant
- Super disintegrants
- Flavoring agent
- Coloring agent

Ingredients	Amount (w/w)
Drug	5-30 %
Water Soluble Polymer	45 %
Plasticizer	0-20 %
Saliva Stimulating Agent	2-6 %
Surfactant	q.s
Sweeting Agent	3-6 %
Flavor, Color, Filler	q.s

Tables no.02: - Ingredients and amount in percent

Active Pharmaceutical Ingredient: - The amount of the active pharmaceutical ingredient in the film formulation ranges from 1-30% w/w. Always use minimal doses of the active pharmaceutical ingredients because it is challenging to combine big doses of the medicine into a film that dissolves quickly. Several drugs, such as antihistamines, anti-diarrheal, anti depressants, vasodilators, anti-asthmatics, and antiemetics, can be utilized as fast-dissolving oral films. Fast-dissolving films can deliver a variety of APIs.

Choice of drug: -

- Drug should pleasant teste.
- Drug dose quantity are less up to 40 mg.
- Drug should be smaller molecular size and low molecular weight.
- Drug should be good stability and solubility in water as well as saliva.
- Drug should be partially unionized at the pH of oral cavity.
- It should have the ability to permeate oral mucosal tissue.
- Drug Lipophilicity.

Film forming polymer: - All thin film oral dose forms depend mainly on the disintegration in the oral cavity's saliva, hence the final film utilized must unavoidably be water soluble. Excipients or polymers must be water soluble, have a low molecular weight, and have an excellent ability for film formation to create a thin film formulation that is water soluble.

Examples of polymers are,

- Pullulan
- Polyvinyl alcohol
- Hydroxy propyl methyl cellulose
- Starch
- Polyethylene oxide
- Hydroxy propyl cellulose
- Sodium carboxy methyl cellulose
- Maltodextrins [1,3]

Ideal properties of the polymers used in the oral film

- Polymers should be made of nontoxic, bland, and painless materials.
- It should not have any flavor.
- There shouldn't be any drainable poisons in it.
- It needs to be simple to obtain and tiny.
- It shouldn't be an overwhelming obstacle during the deterioration interaction.
- It needs to have outstanding wetting and spreading abilities.
- It needs to be ductile, shear, and strippable enough.
- It should be long-lasting and realistically usable, and it shouldn't spread oral illness.

Plasticizer: - It is an important factor of oral films. The choice of plasticizer is affected by the polymer's compatibility as well as the different type of solvent used in the film casting process. It lessens the brittleness of the film and increases its flexibility. Reducing the polymer's glass transition temperature considerably enhances the strip characteristics of the

plasticizer. They are used in concentrations between 1 - 20% weight per weight of dry polymer.
Examples of plasticizer,

- Glycerol
- Propylene glycol (PG)
- Polyethylene glycol (PEG)
- Diethyl phthalate
- Triethyl citrate

Sweetening agent: - Sweeteners now have an important function in pharmaceutical products which are intended to dissolve or disintegrate in the mouth. Sucrose, dextrose, fructose, glucose, liquid glucose, and isomaltose are the traditional sources of sweetness. When compared to sucrose and dextrose, fructose's sweetness is more quickly tasted in the mouth. Because fructose is sweeter than sorbitol and mannitol, it is a common sweetener. The most popular sweeteners include sucrose and low molecular weight carbohydrates. Sucrose has a high solubility in water and doesn't give the final formulation any unfavorable color because it is colorless. Over the pH range of 4 to 8, it is stable.[8,10]

Saliva stimulating agent: -
The objective of using saliva stimulating agents is to enhance saliva production, which will help the formulations for rapid dissolving film dissolve more quickly. Broadly speaking, salivary stimulants can be made from acids that are used in meal preparation. These agents are used along are in combination between 2-6 % w/w of the film.
Examples are,

- Citric acid
- Malic acid
- Tartaric acid
- Ascorbic acid
- Lactic acid

Surfactant: - Surfactants are used as solubilizers, wetting agents, and dispersants, causing the film to quickly degrade and enabling the delivery of the active treatment. In quickly dissolving buccal films, surfactants also aid in the decomposition of ineffectively solvent drugs. Poloxamer 407, sodium lauryl sulphate, benzalkonium chloride, benzethonium chloride, tweens, and spans etc.

Super disintegrants: - When super disintegrants are added to OTF formulations, the combined effects of swelling and water absorption result in fast disintegration. Due to their high-water absorption, super disintegrants provide absorption and swelling, which speeds up disintegration. Strong saliva interaction is essential for disintegration.[1,2]

Flavoring agent: -In the OFDF formulations, flavors are added up to 10%w/w preferably. The initial flavor quality, which is noticed in the first few seconds after the product has been consumed, and the after taste of the formulation, which lasts for at least about 10 minutes, are the two main factors that determine whether an individual will accept an oral disintegrating or dissolving formulation. The sort of medicine to be included in the formulation will determine what fragrance is used.

Coloring agent: - FD&C approved coloring agents are used (not exceeding con centration levels of 1 percent; w/w) in the manufacturing of orally fast dissolving films. e.g., titanium dioxide.[11,13]

METHOD OF PREPARATION: -

Different methods for achieving fast dissolving film formulation by the following,
1. Solvent casting
2. Semisolid casting
3. Hot melt extrusion
4. Solid dispersion extrusion
5. Rolling

1.Solvent Casting: -
The most popular method for creating ODFs that uses de-ionized water as a solvent is called solvent casting. High shear pressures produced by a shear processor are then applied to the mixture to make it homogeneous. Fast-dissolving buccal films are typically created using the solvent casting method, in which the water-soluble ingredients are combined to create a clear, viscous solution, and the drug and other excipients are dissolved in a suitable solvent. After the two solutions have been combined and stirred, the mixture is then cast into a Petri dish and allowed to dry. In the solvent casting method, a film-forming polymer is typically immersed in a suitable solvent for the duration of the night.

Procedure: -Water soluble polymers are dissolved in water when using the solvent casting method, while the drug and other excipients are dissolved in a suitable solvent. The two solutions are then combined and mixed before being cast into a Petri dish, dried, and then cut into the required size pieces.

Advantages: -

- Simplicity.
- Room temperature operation.
- Suitable for heat sensitive drugs.
- Better uniformity of thickness and better clarity than extrusion.
- This method is suitable for films containing heat sensitive drug/API as the temperature needed to remove the volatile solvents is comparatively low than hot melt extrusion method.

Disadvantages: -

- Water or a volatile liquid must be soluble in the polymer.
- It is important to create a stable solution with a suitable minimum solid content and viscosity.
- Depending on the fluid rheology, the intended applied mass, and the necessary dosage uniformity, a variety of casting techniques may be chosen.[1,2]

2. Semisolid Casting: -

A water-soluble film-forming polymer solution is made. To Prepare the solution of water-soluble film forming polymer. The resulting solution is mixed with an acid- insoluble polymer solution (e.g., cellulose acetate phthalate, cellulose acetate butyrate). The right quantity of plasticizer is applied to produce a mass of gels. Then, using heat-controlled drums, the gel mass is cast into the films or ribbons. The film should be between 0.015 and 0.05 inches thick. The ratio of film-forming polymer to acid- insoluble polymer should be 1:4.

3. Hot melt extrusion: -

This method is solvent free process. Granules, sustained release tablets, transdermal drug delivery systems, and transmucosal drug delivery systems are all frequently created through hot metal extrusion. Since 1971, the pharmaceutical sector has employed melt extrusion as a manufacturing method. With this technique, polymer is heated and formed into a thin layer. The drug and polymer combination are first poured into a hopper and then transported, mixed, and melted by an extruder. A die molds the liquid into the desired shape. This technique calls for a low temperature and a short (2 minute) residence time for the drug polymer mixture. This technique doesn't use organic solvents and it can run continuously with little product waste. This technique effectively controls operating factors. solvent free process due to processing of thermolabile substance is a major drawback of this process due to the use of high temperature during extrusion.

4. Solid dispersion extrusion: -

Dispersion of one or more active materials in an inert carrier in a solid state in presence of amorphous,

- hydrophilic polymer is said to be solid dispersion.
- Drug is dissolved in a liquid solvent. The solution is incorporated in to melt of Polyethylene Glycol obtained below 70°C.
- The solid dispersion is shaped into the film by means of dies.

5. Rolling Method:

The water or a water and alcohol combination is used as the solvent. Film-forming polymer, a polar solvent, and an additional ingredient should be prepared as a premix. Fill the master batch input tank with premix. It was fed to one or both first and second mixers using a first measuring pump and control valve. To create a consistent matrix, combine the drug with the master batch premix. The pan is then fed with a predetermined quantity of uniform matrix using second metering pumps. Finally, the film is pressed firmly against the base before being removed by the support roller. Then, using controlled bottom drying, the wet sheet is dried. [11,13]

Various Technology used in Oral Film Formulation: -

- **XGel: -** Xgel film technology allows for the incorporation of active pharmaceutical components and can be taste-masked, colored, and layered. Any oral dosage form can be made to encapsulate it, and it can be made to dissolve in either cold or hot water. The first powder fill version of its Xgel Film System was marketed by Bio Progress Technology International, a UK-based company that developed it.
- **Sol leaves: -** This is applied to goods that release flavor, like vitamins, candy, and mouth fresheners. Utilizing SOLULEAVES technology, active ingredients can be effectively, pleasantly, and conveniently transported to the oral region.
- **Foam burst: -** The FOAMBURST drug delivery device uses foamed film formed from capsules. During manufacture, gas is blown into the film, creating a honeycombed structure. The void in the film may be filled with gas, left empty, or filled with another substance to provide a particular taste and texture or to deliver an active drug. The quick dissolution of capsules with a light honeycomb structure that melt in the tongue.
- **WaferTab:** - A trying to cut quick oral administration device called WAFERTAB produces drug-loaded thin films that can be applied orally using a special method. After casting, the active ingredient is integrated. This technology is one of the patent technologies in which the drug is been incorporated with a suitable film for oral or topical application.
- **MiCap: -** Micro encapsulation technology is combined by Micap and Bio Progress to create water-soluble films. New delivery methods for the $1.4 billion global market for smoking cessation medications will be provided by the advances (SCPs). Micap

signed an agreement in 2004 to get the expertise in the microencapsulation technology with the bio progress water soluble films.

EVALUATION OF FAST DISSOLVING FILM: -

- Organoleptic evaluation
- Weight variation/ Weight of film
- Thickness
- Folding endurance
- Surface pH
- Swelling index
- Moisture loss
- Moisture uptake
- In vitro disintegration test
- Drug content uniformity
- Dissolution Test

- **Organoleptic evaluation: -**

Color, odor, and taste were assessed as an organoleptic property.

- **Weight variation/ Weight of film: -**

Weight variation is studied by individually weighing 10 randomly selected films and by calculating the average weight.

- **Thickness: -**

The thickness of the film was measured using a Digital vernier caliper at five distinct locations, and an average of three readings was derived. The precision of the dose in the film is closely related to the uniformity of film thickness, hence this is crucial for measuring.

- **Folding endurance: -**

Repeated folding of the strip at the same location until the strip breaks is used to measure folding endurance. The folding endurance value is calculated as the number of folds the film can endure without breaking.

- **Surface pH: -**

The test film was put in a Petri dish, wet with 2 ml of distilled water, and allowed to stand for 30 seconds. After bringing the electrode of the pH meter into contact with the formulation's surface and giving it a minute to equilibrate, the pH was recorded. For each formulation, an average of three determinations were performed.

- **Swelling index: -**

The swelling studies of films are examined using simulated saliva. A stainless-steel wire mesh with a predetermined initial weight for the film is then used. The film containing the mesh is then submerged in a simulated saliva solution. Until there is no more an increase in weight, the weight of the film continues to increase at constant pre-determined time intervals. Several factors determine the swelling's degree,

Degree of swelling = final weight (wt.) – Initial weight (w0)/ Initial weight (w0)

Wt = weight of film at time interval t, w0 =weight of film at time 0.

- **Moisture uptake: -**

A film's ability to absorb moisture is evaluated by first cutting it to a 2x2 cm2 size. These strips are later placed for 7 days at 40°C temperature to an atmosphere with a relative humidity of 75%. The percentage weight increase of the strips is used to calculate moisture absorption.

Percentage moisture uptake = final weight(w2) – Initial weight(w1) / Initial weight(w1)

- **Moisture loss: -**

It is determined by first finding the initial weight of the film, afterward, putting this film in desiccators for three days. Desiccators possess calcium carbonate. After three days, strips are taken out and weighed again. Moisture loss is determined by applying the following formula,

Percentage moisture loss = Initial weight(w1) - final weight(w2) / Initial weight(w1) *100

- **In vitro disintegration test: -**

The disintegration time of a film is calculated using disintegration equipment that is listed in authorized pharmacopoeias. The disintegration time often varies depending on the formulation and generally occurs between 5 and 30 seconds. For this test, the USP disintegration apparatus is typically used. For calculating the disintegration time of orally fast disintegrating films, there are no official guidelines available. Disintegration time is the time when an oral film starts breaking when brought in contact with water or saliva.

- **Drug content uniformity: -**

A standard assay procedure that is prescribed for each specific drug according to different pharmacopoeia is used to determine a film's contents. 20 samples are used in this test, which is carried out utilizing analytical methods. According to the Japanese Pharmacopoeia, the test's acceptance value is less than 15%. USP27 states that the contents should range between 85% and 115%, with a standard deviation of no more than 6%. For determining the number of drugs in each individual film, content uniformity is calculated.

- **Dissolution Test: -**

Any of the pharmacopoeia's standard basket or paddle apparatus can be used for dissolution testing. The sink conditions and API dose will primarily be taken into consideration while selecting the

dissolving medium. The tendency of the strip to float onto the dissolving media when the paddle equipment is used frequently makes the dissolution test challenging.

CONCLUSION:

The current review demonstrates that mouth dissolving films are one of the innovative pharmaceutical sciences formulations. In comparison to other conventional dose forms, they have superior acceptance and patient compliance, no risk of choking, and better safety and efficacy. The usual oral dose form is typically difficult for patients with geriatric, paediatric, sick, bedridden and noncompliance challenges to swallow, and they frequently do not take their prescriptions as prescribed. A solid that quickly dissolves or disintegrates in the mouth to produce a solution or suspension without the requirement for water to be delivered is by definition an oral fast-dispersing dose form. Dysphagia, or difficulty swallowing, affects people of all ages, but the elderly are more likely to have it. Fast dissolving films, also known as oral dispersible films, mouth dissolving films, oral disintegration films, or oral dissolving films, are a new drug delivery technique for the oral distribution of drugs that was researched to address the drawbacks of mouth dissolving tablets.

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Review Article

REVIEW ON CORONAVIRUS DISEASE 2019 TRANSMISSION, DIAGNOSIS AND TREATMENT.

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ABSTRACT:

COVID-19 is caused by SARS-CoV-2, which first appeared in Wuhan, Hubei Prvince, Central China, in December 2019 and has spread rapidly since then. Coronavirus Disease 2019 (COVID-19) is caused by an infection with the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and has caused one of the largest global outbreaks in recent years, posing a serious threat to global public health. World Health Organization (WHO) declared a global health emergency on January 30, 2020. Despite global efforts to prevent SARS-CoV-2 transmission by quarantining infected people and their family members, social distancing, and school closures, the spread of infection could not be stopped. The case fatality rate is estimated to range from 2 to 3%. Diagnosis is by demonstration of the virus in respiratory secretions by special molecular tests. Common laboratory findings include normal/ low white cell counts with elevated C-reactive protein (CRP). The computerized tomographic chest scan is usually abnormal even in those with no symptoms or mild disease. Treatment is essentially supportive; role of antiviral agents is yet to be established'

Key Words: SARS-CoV-2, COVID-19.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has caused a sudden significant increase in hospitalizations for pneumonia with multiorgan disease. COVID-19 is caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 infection may be asymptomatic or it may cause a wide spectrum of symptoms, such as mild symptoms of upper respiratory tract infection and life-threatening sepsis. COVID-19 first emerged in December 2019, when a cluster of patients with pneumonia of unknown cause was recognized in Wuhan, China. As of July 1, 2020, SARS-CoV-2 has affected more than 200 countries, resulting in more than 10 million identified cases with 508 000 confirmed deaths. This review summarizes current evidence regarding pathophysiology, transmission, diagnosis, and management of COVID-19.

PATHOPHYSIOLOGY

Coronaviruses are single-stranded RNA viruses that are large, enveloped, and found in humans and other mammals such as dogs, cats, chickens, cattle, pigs, and bSARS-CoV-2 virions have a diameter of 60 nm to 140 nm and distinct spikes ranging from 9 nm to 12 nm, giving the virions the appearance of a solar corona. Through the process of genetic recombination Coronaviruses can adapt to and infect new environments due to their diversity.hosts. Bats are thought to be a natural reservoir for SARS-CoV-2, but this is not proven. It's possible that humans became infected with SARSCoV.2 through an intermediary host, such as a pangolin.

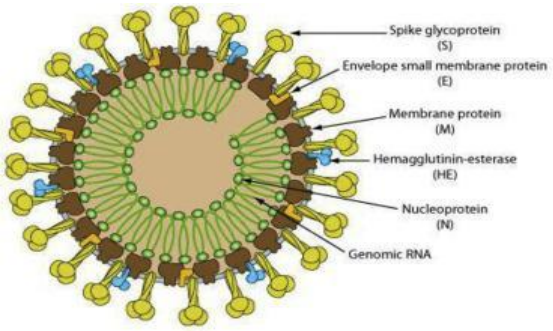

Figure 1 structure of covid 19

SARS-genomic CoV-2's component encodes four major structural proteins: spike (S), membrane (M), envelope (E), and nucleocapsid (N). It also encodes a slew of non-structural and accessory proteins. The pathogenicity of this virus is primarily determined by the virus-host interaction between the virus S protein and the host membrane receptor angiotensin-converting enzyme 2. (ACE2) The binding affinity of SARS-CoV-2 with ACE2 is greater than that of other CoV species, resulting in a higher rate of transmission,

MECHANISM OF SARS-COV-2 INVASION INTO HOST CELLS

SARS-CoV-2 is classified within the genus Betacoronavirus (subgenus Sarbecovirus) of the family Coronaviridae. Coronaviruses are 30 kb enveloped, positive-sense, single-stranded RNA viruses. They infect a wide range of hosts. Based on their genomic structure, they are classified into four genera α, β, γ, and δ. coronaviruses only infect mammals. Human coronaviruses such as 229E and NL63, which cause the common cold and croup, are coronaviruses. SARS-CoV, Middle East respiratory syndrome coronavirus (MERS-CoV), and SARS-CoV-2, on the other hand, are coronaviruses. The virus is transmitted via respiratory droplets and aerosols from person to person. Once inside the body, the virus binds to host receptors and enters host cells through endocytosis or membrane fusion. The virus's life cycle with the host consists of five steps: attachment, penetration, biosynthesis, maturation, and release. When viruses bind to host receptors (attachment) they enter host cells through endocytosis or membrane fusion (penetration). Once viral contents are released inside the host cells, viral RNA enters the nucleus for replication. Viral mRNA is used to make viral proteins (biosynthesis). Then, new viral particles are made (maturation) and released. Spike is a transmembrane trimetric glycoprotein that protrudes from the viral surface and determines coronavirus diversity and host tropism.

Spike is made up of two functional subunits: the S1 subunit is in charge of binding to the host cell receptor, and the S2 subunit is in charge of the viral and cellular membranes.

Angiotensin converting enzyme 2 (ACE2) was discovered to be a functioning SARS-CoV receptor. The spike for SARS-CoV-2 linked to ACE2 according to structural and functional analyses. The lung, heart, ileum, kidney, and bladder all had significant levels of ACE2 expression. On lung epithelial cells, ACE2 was strongly expressed. Further research is needed to see if SARS-CoV-2 attaches to another target.

The spike protein is cleaved by proteases after SARS-CoV-2 binds to the host protein. A two-step sequential protease cleavage model for activating SARS-CoV and MERS-CoV spike protein was proposed as a model, consisting of priming cleavage at the S1/S2 cleavage site and activation cleavage at the S′2 location, which is proximal to a fusion peptide .S1 and S2 subunits remain non-covalently linked after cleavage at the S1/S2 cleavage site, and the distal S1 subunit assists in the prefusion stabilisation of the membrane-anchored S2 subunit. The spike is apparently activated for membrane fusion by irreversible conformational changes caused by subsequent cleavage at the S′2 location. Because it may be cleaved and activated by a variety of proteases, the coronavirus spike is uncommon among viruses. The presence of a furin cleavage site (the "RPPA" sequence) at the S1/S2 site distinguishes SARS-CoV-2 from other coronaviruses. During biosynthesis, the S1/S2 site of SARS-CoV-2 was completely cleaved the S2 subunit. Patients infected with SARS-CoV-2 have symptoms that vary from mild to severe respiratory failure with multiple organ failure. Even in asymptomatic patients, the typical pulmonary ground glass opacification can be visible on a computerised tomography (CT) scan. Because ACE2 is strongly expressed on the apical side of lung epithelial cells in the alveolar area, this virus has a good chance of infecting and killing them. This is consistent with the fact that early lung injury frequently manifested in the distal airway.

HOST RESPONSE TO SARS-COV-2

1. **Cytokine response**

COVID-19 produces cytokines in one of two ways: directly through pattern-recognition receptors, particularly virus-specific Toll-like receptors (TLR3, TLR7, TLR8, and TLR9), and indirectly through the mediation of damage-associated Non-cytokine inflammatory mediators have been understudied in COVID-19

2. Non-cytokine mediators

Non-cytokine inflammatory mediators have been understudied in COVID-19, with the exception of ferritin and C-reactive protein (CRP; both acute-phase proteins). In critically unwell individuals, circulating ferritin is a detectable indication of secondary haemophagocytic lymphohistiocytosis (HLH) and macrophage activation syndrome (MAS-HLH)

Hormones and endocrine factors

COVID-19 problems and mortality are linked to comorbidities such hypertension, type 2 diabetes, and obesity. Circulating hyperglycaemia and diabetes were found to be independent predictors of morbidity and mortality in SARS patients. The thyroid, endocrine pancreas, testes, ovaries, and adrenal and pituitary glands, among other metabolic organs, express ACE2. Infection of pancreatic cells with SARS-CoV-2 resulted in glycaemic dysregulation, implying that coronavirus-dependent -cell dysfunction can occur in people who do not have diabetes. COVID-19 severity and mortality were found to be linked to glucose control in a retrospective analysis of 952 individuals with type 2 diabetes. Patients with well-controlled glycaemia (variability between 3•9–10•0 mmol/L) had lower mortality than those with high glycaemic variability (>10•0 mmol/L). A higher frequency of cardiovascular illness, increased ACE2 expression, lower viral clearance, and metabolic derangements may all contribute to increased COVID-19 severity in diabetic patients

In patients with severe COVID-19 the renin–angiotensin–aldosterone system (RAAS) is significantly active. Although the effect of therapeutic RAAS blocking (ACE inhibitors and angiotensin receptor blockers) is unknown, existing research does not justify stopping the medications. Through the type 1 angiotensin II receptor (AT1), angiotensin II may cause hyper inflammation by inducing IL-6 in endothelial and vascular smooth muscle cells. Furthermore, angiotensin II causes vasoconstriction and water reabsorption by increasing aldosterone levels

Cellular immune response Mild neutrophilia and T-cell lymphopenia are common in COVID-19 patients, leading in an elevated neutrophil-to-lymphocyte ratio, which is a helpful predictive marker for COVID-19 severity. Other leukocyte subsets exhibit similar fluctuations and trajectories, however they are more diverse Granulocytes.

Despite inconsistent findings on eosinophil count, the majority of investigations have found mild peripheral neutrophilia in individuals with COVID-19, regardless of disease severity. Highly active CD38+, CD11b+, and HLA-DR+ neutrophils, as well as myeloid-derived suppressor cells, make up peripheral neutrophils (MDSCs). The increase in MDSCs is suggestive of an inflammation-related, emergency haematopoiesis.

1) Monocytes and macrophages
COVID-19, studies on monocyte–macrophage composition differ, despite the fact that monocyte numbers are not significantly altered. Some research has found a shift from CD16+ monocytes to conventional CD14+ monocytes, while others have found very minor changes. . In severe COVID-19, circulating monocytes display indications of activation, such as enhanced CD and increased IL-1 and IL-6 production. Activated monocytes have been shown to migrate to the lungs in patients with COVID-19 and in mouse models of SARS-CoV-2 infection.

2) Dendritic cells
Patients with COVID-19 have a decrease of myeloid and plasmacytoid dendritic cells in their blood, according to limited data. In one study, patients with severe COVID-19 had lower dendritic cell numbers in their lungs. The key function of dendritic cells in pathogen sensing and adaptive immune responses, dendritic cell depletion might compromise the development of a protective anti-viral T-cell response.

3) T cells
For virus eradication, the cytotoxic T-cell response, a complicated process involving antigen-activated CD4+ helper T cells, is critical. Excessive T-cell activation can cause host cell death, whereas insufficient activation can aid viral propagation. The development of perivascular T lymphocytes has been linked to the deterioration of the lungs' epithelium and endothelium in severe COVID-19. Notably, in children with mild-to-moderate COVID-19, lymphopenia is rare and mild, whereas in severe paediatric cases with multisystem inflammatory syndrome, Evidence suggests that a higher proportion of T cells from patients with COVID-19 express markers characteristic of activation and exhaustion than do those from healthy participants. Lung infection by respiratory viruses typically results in recruitment and local accumulation of distinct T-cell populations mediated by various chemoattractants.

4) Natural killer cells
Natural killer cells are commonly enriched in the lungs and respond rapidly to a broad collection of viral infections. Consequently, patients with moderate-to-severe COVID-19 feature an accumulation of natural killer cells in the infected lungs, whereas natural killer cells counts in the periphery decline

TRANSMISSION OF COVID 19 BETWEEN PEOPLE

The SARS-CoV-2 virus, which can travel between humans in a variety of ways, is known to be the cause of the disease.
Coughing, sneezing, speaking, singing, and breathing can spread the virus from an infected person's mouth or nose in microscopic liquid particles. • Current data suggests that the virus transmits mostly amongst people who are in close proximity to one another, often within 1 metre (short-range). When the virus is breathed or comes into direct contact with the eyes, nose, or mouth, a person might become infected

- According to current evidence, the virus transmits primarily amongst people who are in close proximity to one another, often within 1 metre (short-range). When virus-containing aerosols or droplets are breathed or come into direct contact with the eyes, nose, or mouth, a person can get infected.
- The virus can also spread in cramped and/or poorly ventilated interior environments, where people tend to spend longer periods of time. This is due to the fact that aerosols remain suspended in the air or reach a distance of more than one metre (long-range).

SYMPTOMS OF COVID-19

The most common symptoms of COVID-19 are

- Fever, Dry cough, Fatigue

Other symptoms that are less common and may affect some patients include:

- Loss of taste or smell, Nasal congestion, Conjunctivitis (also known as red eyes), Sore throat, Headache, Muscle or joint pain, Different types of skin rash, Nausea or vomiting, Diarrhoea, Chills or dizziness.

Symptoms of severe COVID-19 disease include:

- Shortness of breath, Loss of appetite, Confusion, Persistent pain or pressure in the chest, High Temperature

Other less common symptoms are

- Irritability, Confusion, Reduced consciousness (sometimes associated with seizures),

Anxiety, Depression, Sleep disorders,

CORONAVIRUS DISEASE 2019 (COVID-19) TREATMENT & MANAGEMENT

COVID-19 is usually treated with supportive care, depending on the organ systems that are involved. Considering the high mortality rate among hospitalised patients and the facilities available for infection control, the setting of patient treatment, i.e., intensive care unit or high dependency unit versus general wards, should be selected early in the course of the disease. Patients that required hospitalisation were treated with broad-spectrum antibacterial antibiotics and glucocorticoids, according to published evidence from preliminary therapeutic experiences Non-invasive ventilation, mechanical ventilation, and extracorporeal ventilation may be used to treat respiratory failure depending on the treatment plan.

1.Antiviral drugs

Remdesivir (CIPREMI/COVIFOR)

Remdesivir has in vitro efficacy against several RNA viruses (including Ebola) and may be useful for both prophylactic and therapy of coronavirus infections, according to some preclinical investigations. Remdesivir is a broad-spectrum antiviral drug that works by inhibiting viralRNA. Although Remdesivir was found to be superior to placebo in reducing lower respiratory tract infection rates and shortening hospital stays in two different studies, there was no meaningful difference between a 5-day and a 10-day course of remdesivir. In comparison, therapeutic doses of lopinavir (LPV)/ritonavir (RTV) improved pulmonary function, albeit only marginally.

Lopinavir/ritonavir (KALETRA)

In vitro and in animal tests, LPV has been demonstrated to suppress coronavirus protease activity and to reduce mortality rates, as seen in a cohort study. The effective dose of LPV is 400 mg orally every 12 hours, and it was first thought to be a treatment option for COVID-19 based on its efficacy during prior SARS and Middle East respiratory syndrome virus epidemics. A recent randomised controlled trial, however, found no conclusive benefit of LPV/RTV therapy when compared to standard management.

Favipiravir

Favipiravir is active against RNA viruses because it is converted into the ribofuranosyl triphosphate derivative by host enzymes and then inhibits the viral RNA-dependent RNA polymerase selectively. Toyama Chemical Company in Japan was the first to discover it for use as a treatment for resistant influenza infections. The medicine has also been demonstrated to be successful in the treatment of avian influenza and could be used to treat illnesses caused by viruses such as the Ebola virus and COVID-19. Glenmark Pharmaceuticals has launched Favipiravir under the brand name ‘FabiFlu' in June 2020 for patients with mild-to-moderate COVID-19, making it the first drug of its kind. In vitro, Favipiravir has shown to be effective against the SARS CoV2 virus, and COVID-19 demonstrates a considerable improvement in mild to moderate cases. It's linked to a rapid drop in viral load and early symptom relief.

2.Immunomodulatory drugs (tocilizumab, chloroquine and hydroxychloroquine)

Tocilizumab

Tocilizumab is a humanised IgG1 monoclonal antibody that targets the IL-6 receptor and is used to treat rheumatoid arthritis, juvenile arthritis, and giant cell arteritis. It may be considered in patients with mild disease who have elevated inflammatory markers (IL-6) and a gradually higher oxygen demand, as well as mechanically ventilated patients who are recalcitrant to therapy. In patients with severe COVID-19 pneumonia, tocilizumab treatment, whether given intravenously or subcutaneously, may reduce the need for invasive mechanical ventilation or death.

Chloroquine and hydroxychloroquine

Chloroquine is a frequently used antimalarial medication with antiviral action throughout a broad spectrum.76 Chloroquine (500 mg every 12 hours) prevents SARS-CoV receptor glycosylation and so limits virus infection by raising the endosomal pH necessary for virus/cell fusion. Its demonstrated Efficacy in reducing COVID-19 pneumonia exacerbations as well as accelerating viral and symptomatic clearance. The chloroquine analogue HCQS (200 mg every 12 hours) has a better safety profile and anti-SARS-CoV efficacy in vitro. In

SARSCoV-2-infected Vero cells, HCQS was found to be more effective than chloroquine. Both chloroquine and HCQS have been observed to have Immunomodulatory effects and have the capacity to suppress the massive immune response in COVID-19 (cytokine storm) induced by mediators such as IL-1, IL-6 and IL-10.

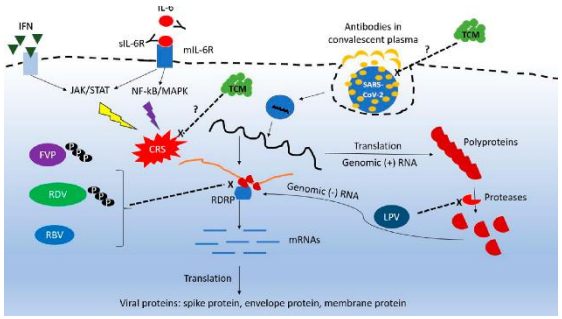

Figure 2 Conceptual diagram of mechanism of repurposing antiviral agents against SARS-CoV-2

3. Antibiotics

Although an optimal and effective antibiotic regimen is not always indicated in viral pneumonia, it can help avoid or treat subsequent bacterial infections and sepsis. Azithromycin and other macrolides are very successful at preventing pulmonary infections in patients with viral pneumonias, as well as having a considerable anti-inflammatory effect on the airways.

Corticosteroids

In patients who demonstrate progressive deterioration of oxygen saturation, increased activation of the pro-inflammatory response, and rapid worsening of characteristics on chest imaging, steroids can be given for a short period of time, 3–5 days. Methylprednisolone was the first and only steroid recommended at first, with doses ranging from 0.5–1 mg/kg/day for moderate instances to 12 mg/kg/day for severe cases. Due to the delay in virus clearance caused by steroid-mediated immunosuppression, higher doses were not indicated.

Dexamethasone has recently been discovered to be useful in reducing mortality in severe and critically ill patients.

Convalescent plasma

Convalescent plasma could confer SARSCoV2 coronavirus humoral protection in the short to medium term. The vast majority of people who recover are able to return to work.COVID19 infection leads to the development of circulating neutralising antibodies. Antibodies to the proteins of the SARS CoV2 virus 2 to 3 weeks detectable by ELISA or other methods after infection tests that are quantitative Plasma transfer from these patients should kill the virus to prevent it from spreading further .replication as well as stopping the progression of tissue damage. This In patient, this method is expected to function best.

Covid 19 vaccines available in India

Name	Manufacturer	Type of vaccine	Efficacy rate
Covishield **	Serum Institute of India	Viral vector	81.3%
Sputnik V	Gamaleya	Viral vector	91.6%
Covaxin	Bharat Biotech	Inactivated	80.6%

Covaxin is an inactivated vaccine that is developed by Hyderabad based Bharat Biotech International limited in collaboration with ICMR (Indian Council of Medical Research) and National institute of Virology, Pune. It is based on a tried and tested platform of dead viruses. The vaccine is developed using a whole-virion Inactivated Vero cell divide platform technology. Inactivated vaccines do not replicate and are likely to revert and cause pathological side effects. They contain dead viruses that is incapable of infecting people but still able to instruct the immune system to mount a defensive reaction against an infection

Covishield is based on a viral vector platform, a chimpanzee adenovirus called ChAdOx1 (the vector), that has been modified to carry the corona virus pipe protein into human cells. While the injected cold virus is harmless it serves as an instruction manual for the body on how to fight against similar viruses. This virus is used for infections like Ebola.

The **Sputnik V** vaccine is based on a proven and well-studied platform of human adenoviral vectors, which cause the common cold and have been around for thousands of years. Sputnik V uses two different vectors for the two shots in a course of vaccination, providing immunity with a longer duration than vaccines using the same delivery mechanism for both shots. There are no strong allergies caused by Sputnik V.

EFFICACY

The efficacy data of Covaxin is about 81.6%. For Covishield the efficacy varies between 70-90% depending on the gap between the two doses given to patients. Both the vaccines are authorized for market use, and emergency permission is given by the government as well that prevent Covid 19 disease individuals above the age of 18. According to Gamaleya National Research Centre of Epidemiology and Microbiology of the Ministry of Health of the Russian Federation and the Russian

Direct Investment Fund, Sputnik V vaccine demonstrated efficacy of 97.6%, based on the analysis of data on the infection rate of coronavirus among those in Russia vaccinated with both components of Sputnik V. it is one of only three vaccines in the world with efficacy of over 90%; Sputnik V provides full protection against severe cases of COVID-19.

COMMON SIDE EFFECTS

Vaccines allow the body to build immunity by activating T and B lymphocytes, cells that, respectively, recognize the targeted virus and produce antibodies to combat it.A vaccine cannot cause COVID-19. No vaccine contains a complete form of the virus responsible for this illness.
the World Health Organization (WHO)Trusted Source, common side effects of a COVID-19 vaccine include:
a fever, fatigue, headaches, body aches, chills, A person might also experience side effects around the injection site, which is usually the upper arm. These might include swelling, pain, redness, an itchy rash, and other mild forms of irritation.

Allergic reactions and anaphylaxis

Rarely, a person experiences an allergic reaction to one or more of the ingredients in a vaccine. They might develop hives or another type of skin rash, swelling, and respiratory symptoms. A severe allergic reaction can lead to anaphylaxis, and it involves low blood pressure, nausea, and difficulty breathing, among other symptoms. Anaphylaxis is an extremely rare side effect of vaccination. According to the CDC, around 2–5 people per million Trusted Source, or fewer than 0.001% of people vaccinated in the U.S. have experienced anaphylaxis afterward. Allergic reactions to mRNA vaccines have been of particular concern, as they contain a chemical, called polyethylene glycol (PEG) that has never been used in an approved vaccine before. PEG is in many drugs have occasionally triggered anaphylaxis. In these vaccines, it coats the mRNA molecule and supports penetration into cell.

TYPES OF POST-COVID CONDITIONS

Long COVID

Long COVID is a range of symptoms that can last weeks or months after first being infected with the virus that causes COVID-19 or can appear weeks after infection. Long COVID can happen to anyone who has had COVID-19, even if the illness was mild, or they had no symptoms. People with long COVID report experiencing different combinations of the following symptoms:

Tiredness or fatigue, Difficulty thinking or concentrating (sometimes referred to as “brain fog”), Headache, Loss of smell or taste, Dizziness on standing, Fast-beating or pounding heart (also known as heart palpitations), Chest pain, Difficulty breathing or shortness of breath, Cough, Joint or muscle pain, Depression or anxiety, Fever Symptoms that get worse after physical or mental activities.

DIAGNOSIS AND IMAGING

Molecular tests (RT-PCR)

The upper respiratory tract is sampled using nasopharyngeal and oropharyngeal swabs, whereas the lower respiratory tract is sampled using expectorated sputum and bronchoalveolar lavage (only for mechanically ventilated patients). After being stored at 4°C, the samples are transported to the laboratory for reverse-transcription amplification of the viral genetic material. Finally, the conserved sections of the SARS-CoV-2 genetic code are detected on the amplified genetic material.

How the RT-PCR test works

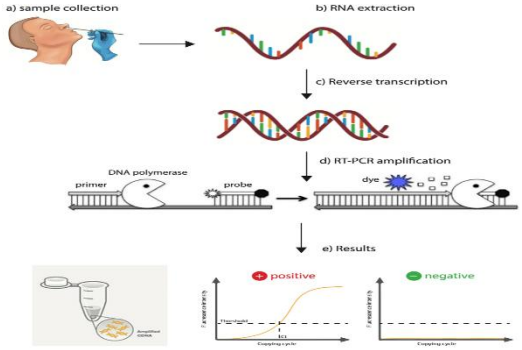

Figure 3 Process of RT PCR Test

Steps in the RT-PCR test:

a) Specimen is taken from the nose or throat of individual
b) RNA is extracted.
c) RNA transcribed into complementary DNA (cDNA).
d) Once the primers have bound to the DNA, they provide a starting point for the DNA polymerase to help copy it. DNA polymerase then degrades the bound probe which results in an increased fluorescence signal
e) The fluorescence increases as copies of the virus DNA are made. If the fluorescence level crosses certain threshold, the test is positive(Figure 2a).If the virus was not present in the sample, the PCR test would not have made copies, so the fluorescence threshold is not reached — the test is then negative (Figure 2b).
In situations of a positive test, the test should be repeated for verification, as well as to confirm viral

clearance in COVID-19 positive cases. The sensitivity of these tests is low; roughly 53.3 per cent of COVID-19-confirmed patients had positive oropharyngeal swabs, and around 71 per cent of COVID-19-confirmed patients had RT-PCR positive sputum samples. After 2–8 days, the RT-PCR results frequently reveal positive.

Rapid tests (antigenic and serological) these tests are less reliable than RT-PCR tests but can be performed at the point-of-care, or in community settings without the need of expensive equipment. The concept of the test is a bit similar to how pregnancy tests work. They make use of antibody-antigen recognition, using monoclonal antibodies to detect viral antigens. Test strips are coated with antibodies that bind to a viral protein (there are prototypes that use aptamers instead). If the patient's sample contains such proteins, they will bind to the antibodies, forming a coloured indicator on the strip. Colloidal gold nanoparticles are the most commonly used material to induce a change in colour in the presence of the analyte. This represents one of the wonderful uses of nanoplasmonics

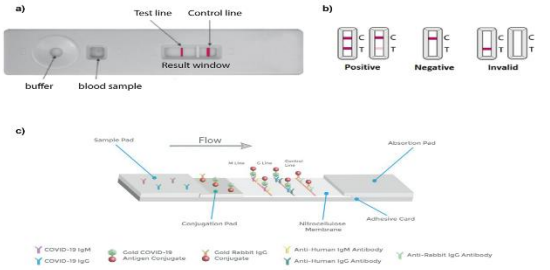

Figure 4 Rapid Antigen Test

Typical lateral flow assay for a serological test

a. Inside the cassette is a strip made of filter paper and nitrocellulose. Typically, a drop of blood is added to the cassette through one hole (sample well), and then a number of drops of buffer usually through another hole (buffer well). Buffer carries the sample along the length of the cassette to the results window.

b. Interpretation of results.

c. A schematic of the COVID-19 lateral flow test from the antibody first binds to an antigen conjugated to colloidal gold in the conjugation pad, and the resultant complex is captured on the strip by a band of bound antibody, forming a visible line (T - test line) in the results window. A control line (C-control line) gives information on the integrity of the antibody-gold conjugate.

These tests can be done in 10-30 min and far away from big laboratories, but in order for them to give reliable measurements, the concentration of the analyte needs to be higher than 10 copies/ul. This means that most of these tests may only work in symptomatic individuals.

Chest X-ray

In the early stages of the disease, a chest X-ray is frequently inconclusive and may not reveal any major alterations. Bilateral multifocal alveolar opacities appear as the infection proceeds, which may be coupled with pleural effusion. The high rate of false negatives in chest X-rays, as in PCR, is a drawback. The prematurity of the imaging test and the absence of pulmonary disease at the time of presentation; the limitations of the X-ray technique, especially in portable X-ray systems; and the fact that COVID-19's ground-glass opacities and reticular pattern can be difficult to detect on chest X-rays are all possible causes

CT

Even in the early stages of COVID-19 pneumonia, high-resolution CT (HRCT) is the method of choice for diagnosing the virus. Multifocal bilateral ‘ground-glass' areas associated with consolidation and a patchy peripheral dispersion are the most typical features, with lower lobe involvement being more common. A ‘reversed halo sign,' defined as a central area of patchy opacities surrounded by a peripheral ring with consolidation, can also be detected in some cases. Pleural effusion, cavitation, calcification, and lymphadenopathy are some of the other things that can be found.

OTHER METHODS

CRISPR/Cas tests

The CRISPR/Cas system is a bacterial immune mechanism that fights foreign DNA or RNA invasion. Bacteria use CRISPR RNA (crRNA) and Cas proteins to detect target DNA/RNA and cut invading foreign nucleic acids. CRISPR is a potent gene editing tool that can trim, cut, replace, or add to organisms' DNA sequences. CRISPR/Cas is therefore known as "molecular scissors." In recent years, it has been demonstrated that CRISPR and related proteins, primarily Cas12a and Cas13, may be utilised to recognise specific nucleic acids in samples. Cas12a and Cas13 bind to RNA or DNA targets, as determined by guide RNA (gRNA) s. Cas12a or Cas13 were used to detect the COVID-19 predicted sequence, and the virus was then validated by cleavage of the reporter molecule. Multiple detection methods have recently developed into diagnostic tools for the quick detection of SARS-CoV-2 RNA, integrating various isothermal amplification techniques (such as LAMP and RPA) and CRISPR

Cas12 is a protein that cuts double-stranded DNA. Cas12a also provides extracurricular activities. Cas12a not only cleaves the target sequence but also

any single-stranded DNA (ssDNA) in the system once crRNA binds to it specifically. CRISPR-FDS methods, includes 3 steps, the RNA extraction, target amplification, and fluorescent signal detection. Detection by this method requires that a sample contains at least 2 copies of the target RNA sequence; no detectable target signal is produced if the DNA target amplified by qPCR has less than 5 copies.

ELISA-based tests

Siddhartha Tripathi and Amit Agrawal proposed a microfluidic sandwich ELISA system to detect SARS-CoV-2 antibodies. On the microfluidic chip, a T-shaped microchannel is used to separate plasma from whole blood .The plasma is then used for a SARS-CoV-2 ELISA. Approximately 10 μL of plasma can be isolated from 1 mL of whole human blood in approximately 3 min. Xudong Fan's group invented a microfluidic ELISA method to quantitatively and sensitively detect SARS-CoV-2. IgG and viral antigen-S protein in serum was used as targets. The ELISA took 15–20 min to complete

Biosensor-based identification

Apart from the aforementioned methods, there is still an urgent need for rapid and sensitive SARS-CoV-2 identification techniques .Recently; miniature biosensors have exhibited potential as analytical platforms because of their unique characteristics, such as sensitivity, reliable specificity and rapid diagnosis, etc. biosensor, typically composed of a functional receptor, transducer, and signal detector/analyser, can sense the intruded target and directly provide sufficient feedback to the end-user with optical signals, electrical signals, etc.
Biosensor-based diagnosis is considered an alternative solution for relieving the heavy pressure on PCR-based testing, which has been proved as a promising platform during the pandemic.
Two types of biosensors are -

- Plasmonic biosensors
- Electrochemical biosensors

RT-LAMP Technology

Loop-mediated isothermal amplification, or LAMP, is an assay that can be used for viral RNA detection. Reverse-transcription LAMP (RT-LAMP) allows for quicker analysis of genetic material than traditional PCR and has been successfully used in the detection of the COVID-19 virus The methodology for RT-LAMP was based on the mechanism behind auto cycling strand displacement DNA synthesis. A polymerase carries out the reaction, and the polymerase has high strand displacement activity. There are also two pairs of primers used; one pair of inner and one of outer primers. These primers are specially designed for the reaction.
RT-LAMP can achieve high specificity due to the target sequences. Unlike other technologies, RT-LAMP recognizes the target sequence using six independent sequences at the start and by four independent sequences towards the latter stages.
RT-LAMP is the perfect technology for use in the COVID-19 pandemic due to its accuracy and relatively simple equipment. These means tests can be carried out in non-standard institutions, such as airports or rural hospitals or medical centres.

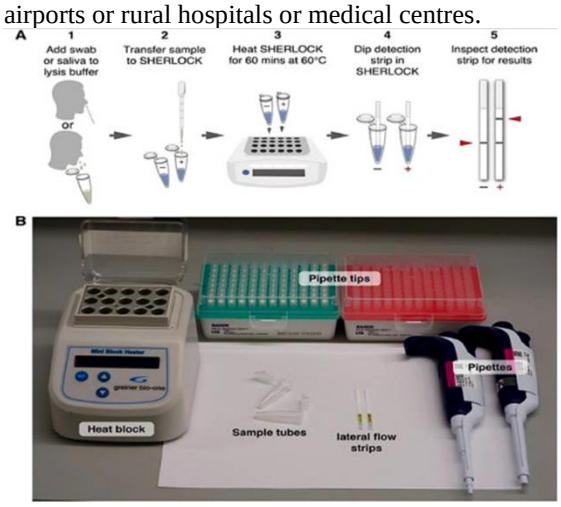

Figure 5 Process of RT LAMP Technology

CONCLUSION

The COVID-19 pandemic is still severe, and most of the drugs currently available for COVID-19 are not designed specifically against SARS-CoV-2. The search for effective antiviral agents specific to SARS-CoV-2 is still on-going. The current battle againstCOVID-19 pandemic also emphasizes the need for policies for being better equipped for any future pandemic, which includes increased funding to drugs and vaccines development, kits development, testing facilities, and fast-track FDA approval policies. Clinical evidence suggests that remdesivir can shorten the recovery time of advanced COVID-19 pneumonia. However, The clinical efficacy and safety of other agents for emergency use is controversial owing to the limitations of study designs. IL-6 inhibitors, which alleviate severe inflammation induced by cytokine release after viral infection, may improve clinical outcome of critical cases of COVID-19. Several clinical trials of IL-6 inhibitors for severe COVID-19 patients are conducted. It is still too early to draw conclusions until more evidences from well-designed clinical trials are available. COVID-19 vaccine is the most promising strategy to end the current pandemic in addition to anti-viral agents. Design of novel anti-viral agents which are specific for SARS-CoV-2 will provide more effective

therapy for COVID-19 patients. Development of effective vaccines and anti-viral drugs both needs multidisciplinary cooperation. Before effective vaccines and antiviral drugs are available, therapy with repurposing drugs are still the mainstreams. Drugs which suppress virus may benefit patients in the early phase of COVID-19.

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Research Article

STUDY ON DRUG UTILIZATION IN GENERAL SURGERY AND ALLIED SURGERY DEPARTMENTS UNDER NATIONAL HEALTH SCHEME OF AYUSHMAN BHARATH AROGYA KARNATAKA IN TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Objectives: Assess drug use patterns, effectiveness, patient awareness, and adherence to the WHO Essential Drug List and NLEM under the ABARK health scheme in General Surgery and allied departments. Materials and Methods: prospective cross-sectional study was conducted in general surgery and allied surgery departments of Krishna Rajendra Hospital Mysore, Karnataka. A total of 871 cases were observed over a period of 6 months.

Results: Among 461 patients in general Surgery department the most frequently prescribed drug type is Analgesics 15.39%, 63% and 77% of drugs are prescribed from WHO EML and NLEM respectively. Electrolyte Replenisher 11.8%, analgesics 18.9%, antibiotic 35.7%, analgesics 13.8%, are most frequently prescribed drug type in Neurosurgery, Urology, Ophthalmology, ENT departments respectively. 62%, 67.40%, 32%, 59% of drugs are prescribed from WHO EML Neurosurgery, Urology, Ophthalmology, ENT departments respectively. Among 552 patients, 415 patients responded to the ABARK questionnaire where the majority of the patients were moderately aware about the ABARK scheme that is 60% and 33% of the patients were poorly aware and 7% of the patients were highly aware about the ABARK scheme. Conclusion: After comparing Drug utilization with WHO EML and NLEM. It is understood that there is scope of improving prescribing drugs from WHO EML and NLEM especially in Ophthalmology. From The responses of ABARK questionnaire. It is understood that Prior awareness about the ABARK scheme to people will help them to utilize the scheme to greater extent.

Key words: ABARK, Drug utilization pattern, General surgery, Allied surgery, WHO EML, NLEM.

INTRODUCTION

According to World Health Organization (WHO), Drug utilization research is the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequence and the pattern of use covers the extent and profiles of drug use and the trends in drug use and costs over time. The basic goal of drug utilization research is to make it easier for people to use medications rationally.[1]
Government of Karnataka introduced Arogya Karnataka on 2nd March 2018 with the objective of providing universal health coverage to all the house holders of Karnataka state. In 2018 Government of India launched Ayushman Bharath. Since both Arogya Karnataka and Ayushman Bharat scheme have same objective, both schemes were merged under a **co-**branded name "Ayushman Bharat Arogya Karnataka" scheme and is being executed in assurance mode.[2] Essential Drug List (EML) is a core list presents a list of minimum medicine needs for a basic health-care system, listing the most efficacious, safe and cost–effective medicines for priority conditions. The aim of comparing drug utilisation pattern with WHO Essential drug list is to provide high-priority pharmaceuticals to everyone at all times as part of a functioning health system, guiding physicians to evidence-based and rational prescribing.[3] As ABARK health scheme provides financial protection, a large number of patients are utilizing it. Therefore, it is significant to analyse the

awareness and effectiveness of ABARK, required improvements in the scheme and to conduct drug utilization pattern research under the ABARK health scheme. Hence it is significant to conduct drug utilization research on the rationality and effectiveness of the drugs administered under the ABARK health scheme.

MATERIALS AND METHODS

Study site: The study was conducted in General surgery and allied surgery departments of Krishna Rajendra Hospital Mysore, Karnataka. It is a tertiary care teaching hospital attached to Mysore Medical College and Research Institute Mysore, Karnataka, India.

Study Design: The study was a Prospective Cross-Sectional Study.

Study Population: We observed 871 cases in three months.

Departments Selected for The Study: General Surgery, Neurosurgery, Ophthalmology, Urology and ENT departments.

Ethical Approval: Ethical clearance was obtained from the Institutional ethical committee, Mysore Medical College and Research Institute (Ref no: CR/366/06/2021) and the same will be submitted to RGUHS University after obtaining the clearance.

Source of Data: All the relevant and necessary data were collected from Case profile of ABARK registered patients from medical record section, Patient interview, Surgery notes, Discharge summary.

Study Procedure: This Prospective Cross-Sectional Study was conducted in General surgery and allied surgery departments of Krishna Rajendra Hospital Mysore, Karnataka. A total of 871 cases were observed over a period of 3 months. Ethical approval was obtained from the Institutional ethical committee of the institute. A data collection form was suitably designed that included all the required fills and a questionnaire form which meant to evaluate awareness and knowledge of ABARK SCHEME was prepared, containing 10 multiple choice questions and the questionnaire was validated by 5 experts. An informed consent form was designed and the consent was obtained from the patients. Data was collected from case profiles of patients from General Surgery, Neurosurgery, Ophthalmology, Urology and ENT departments. Patients of both gender and all age category, who were registered under ABARK health Scheme were included. Data was collected, entered and assembled in Microsoft Excel 2010. The entered data was analysed with the help of Microsoft excel using Descriptive statistical analysis to find out the frequency and percentage of age and gender distribution, surgeries performed, drug utilization patterns and percentage of drugs prescribed from WHO and NLEM essential list. Suitable graphs, tables and charts were added.

RESULTS

Among 871 patients, 56.30% (491) were male and 43.70% (380) were female and the mean age of population was found to be 46.4 years. Out of total study population Maximum 55.22% of patients belonged to the age group 31-60 years followed by 61-90 years (23.30%) and 1-30 years (21.46%).

GENERAL SURGERY DEPARTMENT

Among the study population(n=461) in General surgery department, Hernia repair surgery 23.40% is the most performed and Ileostomy (0.2%), Colectomy (0.2%), Burr hole surgery (0.2%), Nephrectomy (0.2%), Peritonitis (0.2%), Splenectomy (0.2%), Hysterectomy (0.2%), Pericystectomy(0.2%), Rectal polypectomy (0.2%) were least performed surgeries in the department.

Table 1: Details of the Drug Prescribing Pattern of Analgesics in General Surgery Department.

Drug type	Count of drug type	Percentage
ANALGESIC	1231	15.39%
ELECTROLYTE REPLENISHER	975	12.19%
ANTIBIOTIC	923	11.54%
VITAMIN SUPPLEMENT	640	8.00%
GASTROINTESTINAL DRUG	637	7.96%
LOCAL ANAESTHETIC	542	6.78%
ANXIOLYTIC	455	5.69%
ANTIEMETIC	399	4.99%
VACCINE	314	3.93%
GENERAL ANAESTHETIC	216	2.70%
LAXATIVES	168	2.10%
ANTIINFLAMMATORY DRUGS	155	1.94%
IRON SUPPLEMENT	139	1.74%
SKELETAL MUSCLE RELAXANT	135	1.69%
ACH INHIBITOR	133	1.66%
ANTIDIABETIC	132	1.65%

BRONCHODILATOR	119	1.49%
ANTIHYPERTENSIVE	114	1.42%
PROTIEN POWDER	70	0.88%
CHOLINERGICS	69	0.86%
ANAESTHESIA REVERSAL	69	0.86%
COAGULANT	53	0.66%
DRUGS FOR POST OPERATIVE WOUND HEALING	50	0.63%
DRUGS USED FOR ANAL FISSURE TREATMENT	35	0.44%
ANTIHELMINTIC	26	0.32%
CALCIUM SUPPLEMENT	23	0.29%
THYROID HORMONE	22	0.28%
HEPATOPROTECTIVE	18	0.23%
ANTIPLATELET	12	0.15%
ANTIHISTAMINE	11	0.14%
COUGH AND COLD SUPPRRESANTS	11	0.14%
STATINS	9	0.11%
ANTINEOPLASTIC DRUGS	8	0.10%
POTASSIUM SUPPLEMENT	8	0.10%
URINARY ALKALIZER	7	0.09%
ANTICONVULSANT	7	0.09%
VASODILATOR	5	0.06%
ANTISPASMODIC	5	0.06%
ANTIFUNGAL	5	0.06%
PROBIOTICS	5	0.06%
DRUGS FOR BPH	4	0.05%
ANTICOAGULANT	4	0.05%
ANTIDEPRESSANT	4	0.05%
ANTIVIRALS	4	0.05%
ANTIEPILEPTIC	4	0.05%
MISCELLANEOUS TOPICAL	4	0.05%
DIGESTIVE ENZYME	3	0.04%
MAGNESIUM SULFATE	3	0.04%
ANTIANGINAL	3	0.04%
ANTIPARKINSON DRUGS	3	0.04%
SEDATIVE	2	0.03%
ANTICHOLINERGIC	2	0.03%
MUCOLYTIC	1	0.01%
DECONGESTANT	1	0.01%
ANTIDIARRHEAL	1	0.01%

In general surgery department the most frequently prescribed drug type is Analgesics, in analgesics the most prescribed drugs are Paracetamol 28.30% (n=348) followed by Diclofenac 23.50% (n=289) and the least prescribed are Etoricoxib + Paracetamol 0.1% (n=1), Thiocolchicoside + Aceclofenac 0.1% (n=1), Drotaverine + Aceclofenac.

In electrolyte Replenisher, the most frequently prescribed one is Ringer Lactate 34.60%(n=337) least prescribed Electrolyte Replenishers are 25% Dextrose injection 1(0.1%), Oral Rehydration salt 1(0.1%).

In antibiotics, the most frequently prescribed class are 3rd Generation Cephalosporin 41.70%(n=385) In 3rd generation cephalosporin(n=385) Ceftriaxone was the most prescribed drug 93.8% (n=361). The least prescribed antibiotic was class tetracycline 0.1%(n=1), Fluroquinolones + β lactamase inhibitor 0.1%(n=1).

In vitamin supplement(n=640), the most frequently prescribed vitamin supplements are vitamin B complex 48.90(n=313). The least prescribed are, folic acid + cyanocobalamine + nicotinamide, Vitamin D.

In gastrointestinal drugs(n=637), the most frequently drug class are PPI 68.90%(n=439). In PPI(n=439) Pantoprazole 96.4%(n=425) is the most prescribed drug and the least prescribed class was dopamine receptor antagonist + PPI 1.25%(n=8).

In Anaesthetics(n=758), the most frequently prescribed anaesthetics was Local anaesthetics 71.50%(n=542) followed by general anaesthetics 28.50%(n-216). In local anaesthetics the most commonly prescribed Local anaesthetic was Lidocaine(n=322) and in general anaesthetic the most prescribed anaesthetic was propofol(n=111).

NEUROSURGERY DEPARTMENT

Among study population (n=20) in neurosurgery department, Laminectomy + discectomy 30% was most performed surgery in this department. Meningocele repair with detethering of cord 5%, laminectomy 5% least performed surgeries in the department.

DRUG UTILIZATION PATTERN

Table 2: Details of the Drug Prescribing Pattern in Neurosurgery Department.

Drug type (n=372)	**Count of drug type**	**Percentage**
ELECTROLYTE REPLENISHER	44	11.8%
ANXIOLYTIC	38	10.2%
ANALGESICS	37	9.9%
GENERAL ANAESTHETIC	23	6.2%

GASTROINSTESTINAL DRUG	21	5.6%
ANTIBIOTIC	21	5.6%
ACH INHIBITOR	19	5.1%
LOCAL ANAESTHETIC	19	5.1%
VACCINE	19	5.1%
ANALGESIC+SKELETAL MUSCLE RELAXANT	18	4.8%
ANTIINFLAMMATYORY DRUGS	18	4.8%
SKELETAL MUSCLE RELAXANT	17	4.6%
ANTIDEPRESSANT+ANTI CONVULSANT	17	4.6%
ANTIEMETIC	16	4.3%
CHOLINERGICS	10	2.7%
ANTIDEPRESSANT+ANXI OLYTIC	7	1.9%
ANAESTHESIA REVERSAL	6	1.6%
BRONCHIODILATOR	5	1.3%
ANTICONVULSANT	4	1.1%
ANTIDIABETIC	3	0.8%
ANTIHYPERTENSIVE	3	0.8%
LAXATIVE	1	0.3%
DRUGS FOR NEUROPATHIC PAIN	1	0.3%
ANTICOAGULANT	1	0.3%
THYROID HORMONE	1	0.3%
LTRAS	1	0.3%
ANTIHISTAMINE	1	0.3%
LIPID LOWERING DRUG	1	0.3%

In electrolyte replenisher, the most frequently prescribed one is Ringer Lactate 34%(n=15) and Normal saline 34%(n=15) and least prescribed electrolyte replenishers are 32% Dextrose Normal saline.

UROLOGY DEPARTMENT

Among study population (n=41) in Urology department, TURP 27% was most performed surgery in this department. Pyelolithotomy 2%(n=1), URS 25%(n=1), Ureterolithotomy2%(n=1), Incision and drainage 2%(n=1), Varicocelectomy2%(n=1), Nephrostomy 2%(n=1), Nephrectomy 2%(n=1), Penectomy+Urethrostomy 2%(n=1) were least performed surgeries in the department.

Table 3: Details of the Drug Prescribing Urology Department.

Drug type	Count of drug type	Percentage
ANALGESIC	106	18.9%
ANTIBIOTIC	73	13.0%
ELECTROLYTE REPLENISHER	68	12.1%
LOCAL ANAESTHETIC	63	11.2%
GASTROINTESTINAL DRUGS	60	10.7%
ANXIOLYTIC	39	7.0%
ANTIEMETIC	33	5.9%
VACCINE	30	5.3%
VITAMIN SUPPLEMENT	16	2.9%
GENERAL ANAESTHETIC	12	2.1%
ANTIDIABETIC	11	2.0%
SKELETAL MUSCLE RELAXANT	7	1.2%
BRONCHIODIALATOR	7	1.2%
ANTIINFLAMMATORY	6	1.1%
ACHINHIBITOR	6	1.1%
ANTIHYPERTENSIVE	4	0.7%
CHOLINERGIC	4	0.7%
DRUGS FOR PAIN AND SWELLING REDUCTION	3	0.5%
THYROID HORMONE	2	0.4%
URINARY ALKALIZER	2	0.4%
ANAESTHESIA REVERSAL	2	0.4%
LAXATIVE	2	0.4%
ANTIHYPOTENSIVE DRUG	1	0.2%
ANTIHELMINTIC	1	0.2%
DRUGS FOR BLEEDING PREVENTION	1	0.2%
ANTISPASMODIC	1	0.2%
DRUGS FOR BPH	1	0.2%

In analgesics the most prescribed drugs are Tramadol 30.20% (n=32), followed by Buprenorphine 25.50% (n=11) and the least prescribed are Mefenamic acid 0.90%(n=1).

OPTHALMOLOGY DEPARTMENT

SICS WITH PCIOL surgery is the most performed surgery in this department 64.4% and Excision Biopsy 0.9%, DCR 0.9%, SICS With Planned

Aphakia 0.5%, Central Tear Repair 0.5% were least performed surgeries in the department.

Table 4: Details of the Drug Prescribing Pattern in Ophthalmology Department.

Drug type(n=1124)	Count of drug type	Percentage
ANTIBIOTIC	401	35.7%
ANALGESIC	304	27.0%
ANTIBIOTIC + ANTIINFLAMMATORY	201	17.9%
GASTRO INSTESTINAL DRUG	160	14.2%
ANTIINFLAMMATORY DRUGS	14	1.2%
ANTIHYPERTENSIVE	10	0.9%
MISCELLANEOUS TOPICAL	4	0.4%
ANTIDIABETIC	4	0.4%
ANXIOLYTIC	4	0.4%
ANTIALLERGIC	3	0.3%
LOCAL ANAESTHETIC	2	0.2%
DRUGS FOR INTRAOCULAR PRESSURE TREATMENT	2	0.2%
VITAMIN SUPPLIMENT	2	0.2%
ANTIFUNGAL	2	0.2%
ACH INHIBITOR	2	0.2%
ANTIASTHMATIC	2	0.2%
DRUGS FOR GLAUCOMA TREATMENT	1	0.1%
DRUGS FOR OPTIC NEURITIS PREVENTION	1	0.1%
STATIN	1	0.1%
IRON SUPPLIMENT	1	0.1%
ELECTROLYTE REPLENISHER	1	0.1%
CALCIUM SUPPLIMENT	1	0.1%
ANTIMETABOLITE	1	0.1%

In antibiotics, the most frequently prescribed class are Fluoroquinolones 57.1%(n=229) followed by Chloramphenicol Antibiotic 32.7% (n=131). In Fluoroquinolones (n=229), ciprofloxacin was the most prescribed drug 168(73.4%). The least prescribed class was Nitroimidazole 0.2% (1), Carbapenem Antibiotic 0.2% (1).

ENT DEPARTMENT

Details of the surgery performed for study population in ENT department are given in following Table Adenotonsillectomy was the most performed surgery in this department 17% and Myringoplasty(1%), Incision and drainage(1%), Local excision(1%), Conservative management(1%) were least performed surgeries in the department.

Table 5: Details of the Drug Prescribing Pattern in ENT Department.

Drug type(n=1852)	Count of drug type	Percentage
ANALGESIC	256	13.8%
ANXIOLYTIC	206	11.1%
GENERAL ANAESTHETIC	192	10.4%
ANTIBIOTIC	178	9.6%
GASTRO INSTESTINAL DRUG	130	7.0%
LOCAL ANAESTHETIC	119	6.4%
VACCINE	117	6.3%
SKELETAL MUSCLE RELAXANT	98	5.3%
ANTIHISTAMINE	96	5.2%
ANTIINFLAMMATORY DRUGS	96	5.2%
ACH INHIBITOR	94	5.1%
ANTIEMETIC	85	4.6%
CHOLINERGICS	57	3.1%
ANAESTHESIA REVERSAL	39	2.1%
ELECTROLYTE REPLENISHER	27	1.5%
VITAMIN SUPPLEMENT	22	1.2%
BRONCHIODIALATOR	12	0.6%
ANTIHYPERTENSIVE	7	0.4%
DECONGESTANT	5	0.3%
DRUGS FOR POST OPERATIVE WOUND HEALING	4	0.2%
ANTIPSYCHOTIC	2	0.1%

In analgesics the most prescribed drugs are Diclofenac 41.0%(n=105) followed by Fentanyl 23.8%(n=61) and the least prescribed are Diclofenac + Serratiopeptidase 0.4%(n=1), Mefenamic Acid + Paracetamol 0.4%(n=1).

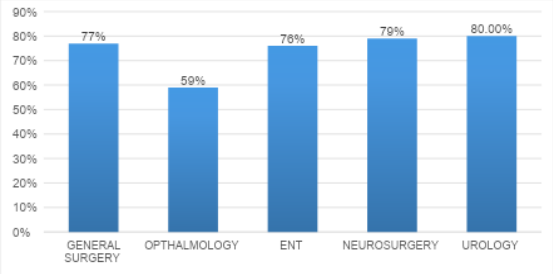

Figure 1: Percentage Wise Distribution of Drugs Prescribed for Study Subjects in Allied Surgery Departments in WHO EML.

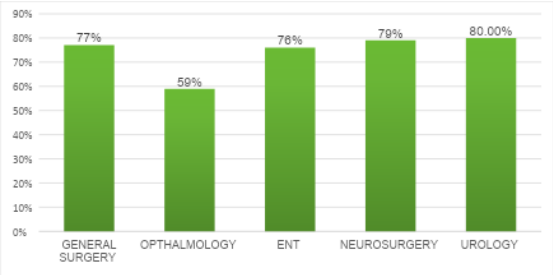

Figure 2: Percentage Wise Distribution of Drugs Prescribed for Study Subjects in Allied Surgery Departments in NLEM.

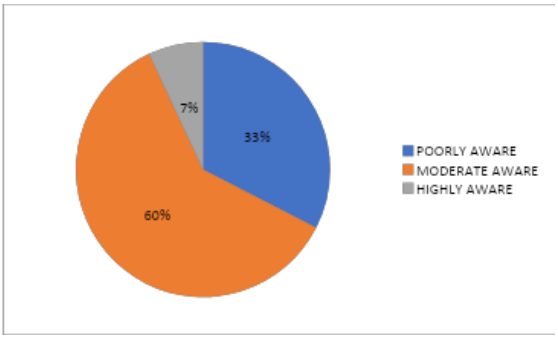

Figure 3: Representation of Results of Awareness Based Questionnaires.

RESULTS OF KNOWLEDGE BASED QUESTIONNAIRES

Here 66% patients got the awareness from the healthcare workers 19% of the patients got awareness from the other patients, 10% of the patients got the awareness from family/friends and 6% of the patients got awareness from the advertisements.

46% of the patients claim got approved within 1 week, 36% of the patients claim got approved within 3 days, 11% of the patients got the claim to approved on admission, it took more than a week for 6% of the patients for the claim to be approved.

36% of the patients were not much benefited by the scheme due to availability of required laboratory services outside the hospital, 46% of the patients were not benefited due to availability of the required drugs outside the hospital, 11% of the patients were not benefited due to delay in registration, 6% of the patients were not benefited due to other reasons.

DISCUSSION

In general surgery department the most prescribed class was analgesics and In analgesics the most prescribed drug was Paracetamol and Ringer lactate was the most prescribed electrolyte Replenisher, But In a study conducted by Khyati M Patel, Shilpa D Jadav et al.., Tramadol was most prescribed analgesic, Paracetamol had lower value than our study and Dextrose normal saline is most prescribed electrolyte Replenisher.[4] In our study Antibiotics was the third most prescribed drug in our general surgery department. In antibiotics, the most frequently prescribed class are third Generation Cephalosporin and in third generation cephalosporin Ceftriaxone was the most prescribed. Whereas Ciprofloxacin antibiotics was most prescribed in Khade, MSM Bashir et al.., study.[5] In General Surgery department 63% and 77% of drugs are prescribed from WHO EML and NLEM respectively. In N.B Bhansali, T.R Gosai study 45.71% of drugs was prescribed from NLEM Which is lower than our study.[6] In Salman M T, Akram MF et al.., study 61.4% of drugs are prescribed from WHO EML, which is lower than our study.[7] In Neurosurgery department Electrolyte Replenisher are most commonly prescribed followed by Anxiolytics and in general anaesthetics the propofol was commonly used general anaesthetics. Whereas thiopentone + propofol combination general anaesthetic was administered most in a study conducted by Dr Rejanigandha, Dr Resmi Douglas et al..,.[8]

In urology department the most frequently prescribed drug type is analgesics followed by antibiotic. In our study Ceftriaxone was the most prescribed 3rd generation cephalosporin antibiotic which differs from R Uppal et al.., study where gentamycin was the most used antibiotic in urology department.[9]

Antibiotics takes fourth place in drug prescribing pattern list in ENT Department. In Antibiotics third generation cephalosporin was most prescribed class and in third generation cefotaxime was most prescribed. In Dr. Deependra Prasad sarraf, Bajarang Prasad Sah study ceftriaxone was the most prescribed antibiotic drug.[10]

In ophthalmology department the most frequently prescribed drug type is antibiotic. which is similar to Pooja Prajwal, Mohandas Rai et al.., study.[11]

The responses for ABARK questionnaire say that more than half of the patients are moderately aware of the scheme and most of the patient's got awareness about ABARK scheme from healthcare workers. Nearly half of the patients claim got approval by 1 week and 46% of patients were not

benefitted by ABARK scheme due to availability of drugs outside the hospital.

CONCLUSION

As ABARK scheme is utilised by large number of people this study focuses on drug utilisation pattern under ABARK health scheme, ABARK scheme awareness and effectiveness in surgery and allied surgery department. it also focuses on utilisation of drugs from WHO EML and NLEM.

Analgesic is most prescribed in ENT, General surgery, Urology, in Ophthalmology antibiotic was prescribed and electrolyte replenisher was most prescribed in neurosurgery.

After comparing drug utilisation with WHO EML and NLEM. It is understood that there is scope of improving prescribing drugs from WHO EML AND NLEM especially in Ophthalmology.

From The responses of ABARK questionnaire which was asked to study population, it is understood that more than half of the patients are moderately aware of the scheme and only few were highly aware of the scheme and nearly half of the patients claims got approval by 1 week. So Prior awareness about the ABARK scheme to people will help them to utilise the scheme to greater extent and awareness should be given to people in all the possible ways for maximum utilisation scheme.

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Research Article

A STUDY ON DRUG UTILIZATION EVALUATION OF ANTICANCER DRUGS USED IN ONCOLOGY DEPARTMENT UNDER NATIONAL HEALTH SCHEME OF AYUSHMAN BHARATH AROGYA KARNATAKA IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

DUE is an ongoing systematic process that promotes rational use of drugs, it is an integral part of patient care and could also be used to assess the quality of services delivered for patients in different medicare system, including oncology. The study's major goal is to improve patient knowledge in all areas, which will help to improve current health care as well as find the various forms of cancer, most frequently prescribed drugs, rational use of cytotoxic medication and prescription indicator(s) in a tertiary care teaching hospital.

Materials and Methods: A prospective observational study was conducted in oncology department of Krishna Rajendra Hospital, Mysuru. The study comprised of patient(s) diagnosed with cancer, of either gender who required treatment with chemotherapy and were analyzed for prescribing indicators.

Results: A total of 255 patients were included. Breast cancer was the prevalent cancer, with more predominance among females. The average number of anti-cancer drug per prescription was 2.15. Commonly used cytotoxic medication was Paclitaxel and 5 Fluorouracil. Multivitamins, Anti-emetics and Antacids were the most regularly used adjuvant drugs. The percentage of anti-cancer medications prescribed from WHO and NLEM was 85.94% and 84.74% respectively. Among 255 patients, 95% of people respond to AB-ARK questioner 50% of patients were moderately, 38% were substantially and only 7% were poorly aware about scheme.

Conclusion: Monitoring DUE can help hospital to manage inventory and use health-care resources more efficiently. The prescribing practices are appropriate and incompliance with NCCN guidelines. AB-ARK scheme did not benefit the patients as much as it should have because the supportive medications were paid from out-of-pocket cost.

Keywords: DUE, AB-ARK, NLEM, WHO-EML, Cancer, Chemotherapeutic agents.

Introduction

Cancer remains as a major public health problem and second most common cause of death in worldwide.

Drug Utilization evaluation, evaluate aspects linked to how medications are marketed, prescribed, dispensed, administered, as well as, with a focus on the medical, social and economic implications.

Health insurance is one of the important approaches that can help in boosting universal health coverage (UHC) through improved health care utilization and financial protection. In 2018, the Ministry of Health and Family Welfare's Ayushman Bharath Mission was launched. The scheme's scope is to provide patient with best quality health care at a free or reasonable cost(s). The National Comprehensive Cancer Network (NCCN), a non-Profit Organization of Cancer Centers Founded in 1995 by the National

Cancer Institute Purpose of describing cancer treatment guidelines Guidelines integrate real-time changes in order to stay up with rapid advances in cancer research and management American Society of Clinical Oncology (ASCO) Professional association created in 1964 Primary resource for best practice in Clinical Oncology Research, Academic and Community Practice **WHO Essential Medicines List (EML)** List of pharmaceuticals that every health-care system should have Significant resource for all countries in determining which medicines have a favorable risk/benefit ratio Categorized by medical category and identified by generic names Over 460 medications are currently on the list **National List of Essential Drugs of India** Compiled and published in 1996 by the Ministry of Health and Family Welfare Included 279 medicines The current NLEM was published in 2015 with 376 medicines

MATERIALS AND METHODS

Study Site

The study was conducted in the Oncology department of Krishna Rajendra Hospital Mysore, Karnataka. It is a tertiary referral Centre and teaching hospital (with the total of 1330 beds, 37 beds in oncology department) attached to Mysore Medical College and Research Institute Mysore, Karnataka, India.

Study Design

The study was a Prospective Cross-sectional study.

Study Period

The study was carried out for a period of six months.

Ethical Approval

Ethical Clearance for this study was obtained from the Institutional Ethics Committee, Mysore Medical college and Research Institute (Ref no CR/366/04/2021). The same will be submitted to RGUHS University after obtaining the clearance.

Source for Data

All relevant and imperative data were collected from patient case records, Patient or patient's care taker(s) interview, Prescription charts, Discharge Summaries.

Study Procedure

This Prospective Cross-sectional study was conducted in oncology department of Krishna Rajendra Hospital Mysore, Karnataka. Ethical approval obtained from the ethical committee of Mysore Medical College and Research Institute. Total 255 people were enrolled in the study over a period of 6 month. An Informed consent form was suitably designed in English as well as in Kannada to obtain consent form patients who volunteered for the study and fulfilled the study criteria. Data collection form with all the necessary fields was suitably designed. A multiple-choice questionnaire was created to assess awareness and knowledge of ABARK scheme and the questionnaire was validated by 5 experts. Data was gathered from patient case profile and documented electronically in specially designed database using Microsoft excel 2010. Patient of all age group and both gender who have registered in AB-ARK receiving chemotherapy either with/without radiation included in the study. Descriptive statistical analysis was used to analyze the data entered in the data collection form to determine the prevalence of various cancer types, system, age and gender and wise distribution of cancer and prescription pattern of drugs used in department of oncology.

RESULTS AND DISCUSSION

Out of 255 patients, 166 (61.1%) were women and 89 (34.9%) were men (Figure 1). The patient data only revealed Women's predominance over Men in the overall sample population. The reason could be unclear or variable as mentioned by Dave et.al suggesting causes due to hormonal fluctuations during menopause, use of birth control pills, hormonal replacement therapy and life style. Age is a major risk factor for cancer. The age of the study participants was ranged from 21 to 90 years. The age group of 51 to 60 years old had the highest incidence of cancer (31%) summarized in Figure 1. Cancer prevalence is enforced by age due to reduced immune, hormonal, physiological and functional alterations in the body that may cause pro- oncogene activation.

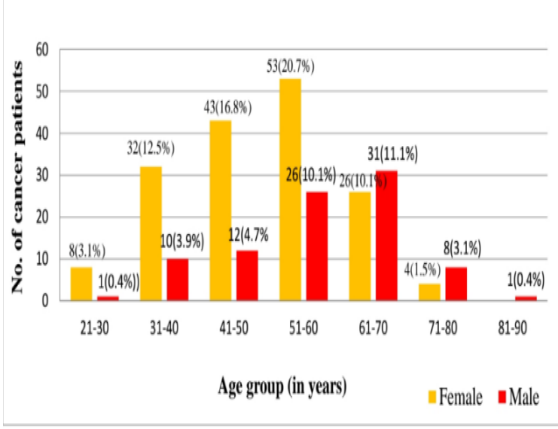


Figure 1: Age and Gender wise distribution of Cancer.

In males, Lung cancer 14(5.49%) were more predominant, followed by Stomach cancer 10(3.92%). Whereas, Sarcoma 1(0.39%), Breast cancer 3(1.17%) was found to be least predominant. This statement corresponds to Gupta et al explanations of the predominance of these cancers

in males as a result of unhealthy food habits based on an India-wide survey." In females, Breast cancer 71(27.84%) were more predominant followed by Ovarian cancer 27(10,58%). Cancers of Oral 1(0.39%) and Skin 1(0.39%) was found to be least predominant (Figure 2). This assertion is consistent with the findings of survey done in several Indian states, which reveal that the majority of female persist breast and ovarian cancer. Colon cancer 12(4.7%) was common in both male and female.

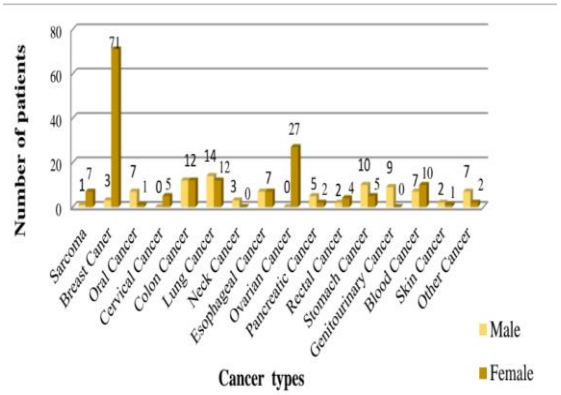


Figure 2: Prevalence of Cancer Types.

The most commonly used class of anticancer agents were the alkylating agents 39.59% followed by Plant derivatives and similar compounds 21.71%, Antimetabolites 18.79%, least prescribed drug class was Miscellaneous 0.55% followed by Immunomodulators 0.36%. The most commonly used drugs were Paclitaxel 83(15.14%) followed by 5-FU 75(13.68%), Cyclophosphamide 60(10.94%). Various modalities have been available for the treatment of cancer and these include immunotherapy, surgery, hormonal therapy, and chemotherapy. In our study cytotoxic drugs were majorly prescribed (n=527) summarized in Table 1. All cytotoxic drugs were given in injectable form (100%) this is matching exactly with study of Khan GM et al. Even though, lower injectable prescription is recommended and should be as minimal as possible to limit the possibility of infection spreading via the parental route and to reduce therapeutic costs, it is not applicable in the case of cancer treatment and the use of cytotoxic medications because most cytotoxic medication should be administered by parenteral route at a constant infusion rate. This explained the cent percentage of cytotoxic injectable. Platinum compounds were found to be the most common type of chemotherapeutic drug in the study. Carboplatin, rather than Cisplatin, was the most often utilized platinum analogue due to its mild neurotoxic profile. The plant derivatives were the next commonly prescribed anticancer drugs. Amongst the taxanes, the commonest was paclitaxel followed by docetaxel. In our study. the generally given double therapy was paclitaxel and carboplatin. Carboplatin protects nerves against the neuropathy caused by paclitaxel

Table 1: Distribution patterns of chemotherapeutic agents.

Sl. No	Chemotherapeutic agents	Class	Drug	Number of patients	Percentage (%)
1	Alkylating Agents	Nitrogen mustard	Cyclophosphamide	60	10.94
			Ifosfamide	2	0.36
			Bendamustin	2	0.36
		Platinum Coordination Complex	Oxaliplatin	39	7.11
			Carboplatin	57	10.4
			Cisplatin	50	9.12
		Triazine	Dacarbazine	7	1.28
2	Cytotoxic antibiotics	Anthracyclines	Doxorubicin	33	6.02
			Epirubicin	50	9.12
		Other	Bleomycin	5	0.91
3	Antimetabolites	Folate antagonist	Pemetrexed	4	0.73
		Pyrimidine antagonist	5 FU	75	13.68
			Gemcitabine	18	3.28
			Capecitabine	6	1.09
4	Plant derivatives and similar compounds	Campothecins	Irinotecan	2	0.36
		Podophyllotoxin	Etoposide	4	0.73
		Taxanes	Paclitaxel	83	15.14
			Docetaxel	18	3.28
			Vincristine	10	1.82
		Vinca Alkaloids	Vinblastine	2	0.36
5	Immunomodulators	Angiogenesis Inhibitor	Lenalidomide	2	0.36
6	Miscellaneous	Proteasome Inhibitor	Bortezomib	3	0.55
7	Monoclonal Antibody	Anti CD20/CD30/CD52	Rituximab	12	2.2
		Anti VEGF	Bevacizumab	4	0.73

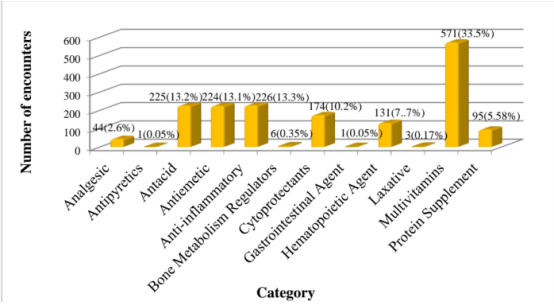
The majority of anti-cancer medications came with their own variety of adverse effects, such as nausea, vomiting, and allergic reactions were most commonly treated with intravenous administration of Antacid, Antiemetic, Anti-inflammatory and Antihistamines before starting the chemotherapy. Table 2 displays the prescription pattern of pre-medication among the Cancer Patients. Dexamethasone were the most commonly prescribed pre-medication (31.5%) followed by Ondansetron (29.28%), Pantoprazole (23.82%), Ranitidine (7.81%), Pheniramine Maleate (4.96%), Granisetron (2.35%) and Hydrocortisone (0.12%).

Table 2: Prescription pattern of pre-medication.

Drug	Number of prescription (n=806)	Percentage (%)
Dexamethasone	255	31.5
Granisetron	19	2.35
Hydrocortisone	1	0.12
Ondansetron	236	29.28
Pantoprazole	192	23.82
Pheniramine Maleate	40	4.96
Ranitidine	63	7.81

Figure 3, shows the prescription pattern of discharge medication among the cancer patients. Out of 1606 discharge medications, Multivitamins (571) stands out to be the most prescribed one followed by Antiemetic (224), Anti-inflammatory (223), Antacid (221), and Cytoprotectants (174). The mitigation and management of anticancer therapy related side effects and toxicities are vital. 12 One of the key purposes of supportive care is to achieve this.

The study shows that antiemetics, cytoprotectants, gastro-intestinal drugs, nutritional supplements, analgesics, iron supplements were the most common supportive care drugs given, which is similar the study conducted by S Ramalakshmi et al. 13
Pain is a common subjective symptom in cancer patients, which is manageable. In our study. 44 patients prescribed with analgesics among these 42 patients with tramadol and 2 patients with tramadol-acetaminophen combination were prescribed. G-CSF is the most commonly prescribed cytoprotectants. Fibril neutropenia can impair the efficacy of cancer treatment which is one of the most serious dose-limiting toxicity seen. 15 Thus; Clinical practice guidelines (S3 Guideline for supportive therapy) proposed the use of G-CSF to lower the risk of neutropenic consequence. Cancer could make it very difficult to absorb nutrients from diet. Malnutrition in cancer patients necessitates the use of a nutritional supplement and thus intake of these supplements routinely is in need."



The prescription indicator shows that the average number of anti-cancer drug per prescription was 2.15, which was consistent with the finding of other Indian studies (2.7). In our research, we discovered that the average number of medications per prescription was significantly greater. This is because, in addition to cytotoxic medication, antiemetic drugs, PPI, antihistamines, antacid, vitamin and other drugs used in the treatment of cancer (supportive care), increased the number of prescriptions prescribed per prescription. The percentage of anti- cancer medications prescribed from WHO and NLEM was 85.94% and 84.74% respectively.

All drugs (cytotoxic drugs) are prescribed in generic name which indicates rational use of drugs, which is similar the study conducted by A Bepari et al. 16

Table 3: WHO Prescribing Indicators.

Sl. No	Prescribing indicators	In Patients
1	Average number of cytotoxic drugs per prescription	2.15
2	Average number of other drugs per prescription	9.45
3	Average number of drugs per prescription	11.6
4	Percentage of drugs prescribed from EDL	85.94%
5	Percentage of drugs prescribed from NLEM	84.74%

The Figure 4 shows that, 52% of patients were moderately aware about the scheme, 40% were substantially and only 8% were poorly aware about scheme. Patients were made aware of the AB-ARK scheme's benefits and received information about it from healthcare workers. The approval claim was completed within one week. The scheme did not benefit the patients as much as it should have because of the drugs that were purchased from out-of-pocket cost.

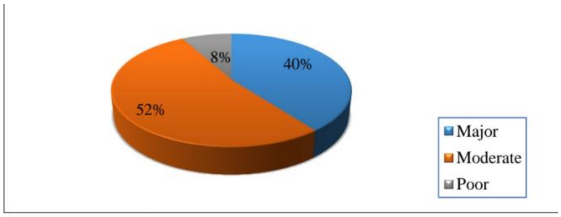


Figure 4: AB-ARK Awareness Survey.

CONCLUSION

We come to the conclusion that using cytotoxic medication was virtually found to be rational. In this hospital 24 different chemotherapeutic drugs were prescribed out of which 20 are from WHO essential list and 18 are from NLEM. The prescribing practice are appropriate and in compliance with NCCN guidelines. The most predominant form of cancer observed in our study was female breast and ovarian cancer along with lung, stomach cancer in males. In our study, women were more likely than men to develop cancer. Paclitaxel was the most commonly used cytotoxic drug followed by 5-FU and Cyclophosphamide. Cytoprotective medicines were also prescribed with anticancer treatment, Peg filgrastim being the most commonly prescribed and Mesna being prescribed less frequently. Among the adjuvant drugs Multivitamin, Dexamethasone, Pantoprazole, Ondansetron, and Iron supplement are the most commonly prescribed drug. Patients were made aware of the AB-ARK scheme's benefits and received information about it from healthcare workers. The approval claim was completed within one week. The scheme did not benefit the patients as much as it should have because the supportive drugs that been purchased outside the hospital. The government should take steps to execute the scheme and add additional feature, and patients should be

made aware of the scheme. Further drug utilization studies, accordance to the WHO, are needed in every health care setting to assess and ensure rational drug use.

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