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Prescribing Practices in Pediatrics and Drug Utilization Studies Promoting Pediatric Health

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Abstract: Knowledge of drug administration in children and infants lags behind that of adults for many reasons. These include developmental differences that affect the pharmacodynamic and pharmacokinetic profiles of drugs, ethical and financial reasons, research capabilities, and regulatory guidelines and constraints. Most of the drugs prescribed for children have not been tested in the pediatric population due to the difficulties in carrying out clinical studies in children and ethical issues due to children not being able to make their own decisions to participate in a clinical trial. Epidemiological evaluation of medicine use in elderly is now a highly visible topic, but drug prescribing studies in pediatric patients have been limited. The higher incidence of infections in pediatric population as compared to adults leads to higher prescription of Antimicrobial Drugs (AMDs), at times more than two in single prescription. The use of antibiotics in children has been a major area of concern. . Periodic prescriptions analysis and effective feedback to clinician should be done based on results to ensure rational prescribing and effective health care management, which will ultimately lead to a better child health. In this review article, we will to analyze prescribing practices in pediatrics and drug utilization studies promoting pediatric health.

Keywords: Pediatrics, Rationale Prescribing, Antibiotics, Drug Utilization.

1. INTRODUCTION

Knowledge of drug administration in children and infants lags behind that of adults for many reasons. These include developmental differences that affect the pharmacodynamic and pharmacokinetic profiles of drugs, ethical and financial reasons, research capabilities, and regulatory guidelines and constraints. Irrational drug use, especially antimicrobials in a pediatric population, has become a commonly noted practice. A study in the USA and Canada has shown that 50% and 85% of antibiotics, respectively, were prescribed

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inappropriately to children. Evidence suggests that medication errors have a higher incidence in children and infants than in adults [1]. The irrational use of drugs is known to an increase in the cost of treatment, incidence of adverse drug reactions. Markets for children's medicines tend to be small and the range of doses used may be wide for any drug formulation because many drugs prescribed widely for infants and children are not available in suitable dosage forms, leading to a lack of attention to pediatric medicines. Most of the drugs prescribed for children have not been tested in the pediatric population due to the difficulties in carrying out clinical studies in children and ethical issues due to children not being able to make their own decisions to participate in a clinical trial. Therefore, many medications have not been approved by the Food and Drug Administration for children. Epidemiological evaluation of medicine use in elderly is now a highly visible topic, but drug prescribing studies in pediatric patients have been limited. The need for the safe and effective drugs for use in sick neonates, infants, children and adolescents requires the establishment of thoughtful drug therapy strategies [2].

Drugs play a key role in protecting, maintaining and restoring health. Prescription writing is a science and an art, as it conveys the message from the prescriber to the patient. It is an order for a scientific medication for a person at a particular time. It brings into focus the diagnostic acumen and therapeutic proficiency of the physician with instructions for palliation or restoration of the patient's health. Now-a-days the prescribing pattern is changing and it has become just an indication of medicine with some instructions of doses without considering its rationality [3]. It has been frequently observed that doctors are adopting polypharmacy, promoting unnecessary use of tonics and other drugs under the sales influence of drug companies. Infants and children are among the most vulnerable population groups to contract illnesses. The use of antimicrobial agents, especially antibiotics has become a routine practice for the treatment of pediatric illnesses. There has been an unexplained world-wide increase in antibiotic use the last decades. Overuse and misuse of antibiotics lead to unnecessary side effects, costs and emergence of antibiotic resistant bacteria [4]. Although the antimicrobial agents are effective and play an important role in the management of infectious diseases, they have serious consequences. The worldwide multi-drug resistant microorganisms were identified and were associated with the widespread use of antimicrobial agents in both inpatients and outpatients. For example, many studies have shown that there is an emergence of resistant strains of Streptococcus pneumoniae to antimicrobial agents and these strains are rapidly increasing. The emergence of multi-drug resistant microorganisms is expected to lead to more serious infections than what we have initially encountered. Another serious problem associated with the irrational use of antimicrobials, especially among pediatrics, is the ability of strong antibiotics to disturb the colonization of gastro-intestinal micro flora which may induce serious clinical symptoms like pseudo membranous colitis and toxic megacolon [5]. In order to have the concept of essential drug program to promote rational drug use, WHO published its report on selection of essential drugs in 1977. Further to promote the rational use of drugs, the concept of drug utilization came into picture. Drug utilization review is the process by which the quality of drug prescribing is measured by organizing important predetermined criteria. DURs form part of the quality assurance (QA) programmes within hospitals and are designed to monitor the use of prescription medicines [6].

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2. RELATED WORK

Research on prescribing practices in pediatrics and drug utilization studies is paramount for enhancing pediatric healthcare outcomes. This field delves into how medications are prescribed, utilized, and monitored in children, aiming to optimize treatment efficacy while minimizing potential risks.

Prescribing practices in pediatrics encompass a spectrum of investigations:

- 1. **Adherence to Guidelines**: Studies assess the extent to which healthcare providers comply with established clinical guidelines when prescribing medications for children. This includes adherence to dosage recommendations, preferred first-line treatments, and antibiotic stewardship guidelines.
- 2. **Off-label and Unlicensed Use**: Understanding the prevalence and reasons for off-label or unlicensed medication use in pediatrics is critical. Off-label use refers to prescribing medications for indications, doses, or age groups not approved by regulatory agencies.
- 3. **Medication Errors**: Research explores the incidence and types of medication errors in pediatric prescribing. This encompasses errors related to dosage calculation, inappropriate drug selection, and administration errors.
- 4. **Safety and Adverse Events**: Studies investigate the safety profiles of medications used in pediatrics, including the incidence of adverse drug reactions and drug interactions specific to children.
- 5. **Behavioral Factors**: Some research examines the behavioral aspects influencing prescribing practices, such as physician preferences, patient expectations, and perceived barriers to guideline adherence.
 - Drug utilization studies promoting pediatric health encompass several key areas:
- 6. **Epidemiological Studies**: These studies analyze the prevalence and trends of medication use among pediatric populations. They provide insights into the most commonly prescribed medications, therapeutic classes, and changes in prescribing patterns over time.
- 7. **Pharmacoeconomics**: Research evaluates the cost-effectiveness of different treatment options in pediatrics. This includes analyzing the economic burden of pediatric medication use and assessing interventions to optimize healthcare resource allocation.
- 8. **Longitudinal Studies**: Some investigations track children over time to evaluate the impact of medication use on health outcomes, including disease progression, hospitalization rates, and quality of life measures.
- 9. **Health Services Research**: This area explores how healthcare delivery models influence pediatric drug utilization and subsequent health outcomes. It includes assessing the impact of primary care versus specialty care on medication prescribing and health outcomes.
- 10. **Interventions to Improve Drug Use**: Research focuses on interventions aimed at optimizing pediatric drug use. This may include educational programs for healthcare providers, implementation of electronic prescribing systems, or development of clinical decision support tools.

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Understanding prescribing practices and drug utilization patterns in pediatrics is essential for evidence-based decision-making in clinical practice. By optimizing medication use in children, healthcare providers can improve treatment outcomes, enhance patient safety, and promote pediatric health globally. Continued research in this field is crucial for developing and refining guidelines, interventions, and healthcare policies tailored to the unique needs of pediatric populations.

3. METHODOLOGY

This review article aims to systematically analyze prescribing practices in pediatrics and drug utilization studies promoting pediatric health. The methodology adopted for this review involves a comprehensive literature search, data extraction, synthesis, analysis, and interpretation. Firstly, a systematic search strategy was implemented across key databases including PubMed, MEDLINE, Scopus, and Web of Science. The search utilized relevant keywords such as "pediatric prescribing," "drug utilization," and "pediatric health," along with appropriate Medical Subject Headings (MeSH) terms. Articles published in peerreviewed journals from the inception of databases to the present were included, while non-English articles, editorials, letters, and conference abstracts were excluded. Following the literature search, retrieved articles underwent screening based on titles and abstracts to identify studies relevant to the review's objectives. Full-text articles meeting the inclusion criteria were retrieved and thoroughly reviewed for data extraction. Data extraction encompassed various study characteristics including design, population demographics, healthcare settings, prescribing patterns, drug utilization metrics, and key findings. The extracted data was synthesized to identify common themes and patterns across the reviewed studies. Comparative analysis was conducted to explore variations in prescribing practices among different populations, regions, and healthcare settings. Additionally, critical appraisal of the literature will be performed to assess the quality of evidence and potential biases, ensuring the reliability of the review findings. Subsequently, the synthesized data was analyzed to draw meaningful insights into prescribing practices in pediatrics and their impact on pediatric health outcomes,

Drug Utilization Studies in Pediatric Settings

One of the important objectives of a drug utilization study is to find out rationality in drug use. Drug use indicators developed by WHO are highly standardized and are being field tested from time to time. One such initial study was done by international network for the rational use of drugs in collaboration with the WHO action program on essential drugs to develop and field test a set of basic drug use indicators. The study was carried out in 12 developing countries. The results showed that average number of drugs per encounter was high in Indonesia and Nigeria (3.3 & 3.8); prescription of antibiotics were high in Uganda and Sudan (56% & 63%); 94% of drugs were prescribed by generic name in Zimbabwe, whereas only 375 in Ecuador. Similar studies using WHO recommended indicator has been carried out in different countries like Spain, Sweden, Italy, Tanzania, Nigeria etc. to understand drug use pattern in pediatric out patients [7].

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In India also drug utilization studies have been carried out in order to provide insight into the drug use patterns and prescribing practices. While there are several studies in adults [8], few studies has been carried out in pediatric setting. Such studies on pediatric population are compared in table.

Comparison of DUR studies in INDIA [9-11]

	Mirza et al (2000)	Mathur et al (2004)		Karande et al (2005)	Dimri et al(2006)
Indicators	Ped.OPD	Ped. Govt.*	Ped. Sat.#	Ped. OPD	Ped. OPD
Number of prescriptions	606	63	56	500	254
Average no of drugs/ prescription	3.72	4.02	4.57	2.9	2.31
% encounter with an antibiotic prescribed		33.3%	39.2%	39.6%	29.1%
% encounter with an injection prescribed		-	-	0.2%	1.18%
% drug prescribed with generic names	30.7%	-	-	73.4%	5.8%
% drugs prescribed from EDL	77.61%	-	-	90.3%	45%

^{*} Ped. Govt = Pediatrics, Government Hospital; # Ped. Sat. = Pediatrics, Satellite Hospital

4. RESULTS AND DISCUSSION

The higher incidence of infections in pediatric population as compared to adults leads to higher prescription of Antimicrobial Drugs (AMDs), at times more than two in single prescription. The use of antibiotics in children has been a major area of concern. In a prospective study involving 2171 pediatric Bangladeshi in patients, it was found that the most commonly prescribed antimicrobials in children for infections (like bronchopneumonia and diarrhea) were ampicillin, gentamicin, amoxicillin, cloxacillin and ceftriaxone. The results of this study showed that 56.1% of the admitted children received two or more antimicrobials in combinations for treatment [12]. The same study also revealed that there was a high level of inappropriate antimicrobial treatment for the most common infectious disease and suggested the need for intervention to improve antimicrobial use in hospitals. Results of various studies have shown that antibiotics were prescribed to 30 - 70% of the pediatric patients with upper respiratory tract infection, to 30 - 76% patients with bronchitis, 44.1% with tonsillitis, 10 -44% with common cold and 76% patients with acute pharyngitis. Though decreased use of antibiotic for respiratory tract infection has been reported in many studies but use of inappropriate antibiotic is still common and use has not been reduced for all antibiotics and all children [13]. For example a study done by Arch et al showed that there was decline in use of antibiotics for URI and bronchitis but there was also proportional increase in prescribing of

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broad spectrum antibiotics. In another two studies also it was reported that there was increased use of broad spectrum macrolides among preschool children. The results of a study carried out in Madagascar on evaluation of the antibiotics' usage in pediatric in-patients showed that three antibiotic families' co-trimoxazole, penicillins derivatives and amino glycosides were frequently used. The result showed that antibiotic prescriptions were irrational; and, the probable reason was insufficiency of biological labs and expensive costs of laboratory tests [14]. In yet another retrospective study on antimicrobial prescribing patterns in Trinidad involving a total of 527 cases, it was found that 44% of patients had received one or more antibiotics and pediatric patients received 70.8% of antibiotics. The most frequently prescribed antibiotics to children were ampicillin, chloramphenicol and gentamicin. The reason for overuse of antibiotics was poor communication and lack of confidence in laboratory technician expertise. In a study on use of antimicrobial agents for treating community acquired lower respiratory tract infections, the prescriptions of a total of 613 children (age 2-14 years) hospitalized for acute bronchitis or pneumonia were analyzed, it was found that 92.1% children received AMD [15]. Likewise, another study done in Italy on clinical and economic outcomes of pneumonia in children, 99 inpatients of pediatric hospital receiving antibiotic treatment were enrolled. A parenteral antibiotic therapy was administered in 64.6% of cases whereas 35.4% received oral antibiotic therapy; the most frequently prescribed parenteral antibiotic was ceftriaxone and for oral antibiotic therapy cefprozil. The study concluded that hospital management of pediatric pneumonia was influenced by the early discharge policy than by clinical variables without under-cure [16].

In a prospective survey of antibiotic utilization in pediatric hospitalized patients in Switzerland it was found that in total 125 out of 349 patients were prescribed with 246 antibiotics out of which medical ward pediatric patients received 42% of antibiotics compared with surgical ward pediatric patients (31%). It was found in this study that empirical prescription was more frequent than therapeutic or prophylactic prescription. The rate of inappropriate prescription was similar in both wards in which higher inappropriate prescription rates were noted for macrolides, co-trimaxozole and betalactams [17]. A study done in Ethiopia on prescribing pattern of AMDs on 407 patients found that 82% antibiotics were prescribed in pediatric ward and the most frequently prescribed antibiotic was penicillin, chloramphenicol and ampicillin. It was concluded that there was inappropriate use of antibacterial and a need to develop a policy on hospital antibacterial use was felt [18]. Prescribing by generic name has been declining and should be encouraged. This was reported by a study carried out in the pediatric patients at Nepal which aimed to assess the drug prescribing patterns and average cost of the drugs. In a sample of 356 patients, the average number of drugs prescribed per admission was 4.5; and 48.9% drugs were administered by the parenteral route. Antibiotics were prescribed in 69.9% cases and Staphylococcus aureus, Escherichia coli, and Acinetobacter species were the common microorganisms isolated. The average (±SD) cost of drugs per admission was 5.4 (±1.6) US dollars [19]. The results from a pediatric hospital in Kathmandu on prescribing patterns of antibiotics revealed that a high percentage of patients (93%) were prescribed at least one among the 121 pediatric patients analyzed. Benzyl penicillin gentamicin/cefotaxim were found to be mostly used combination antibiotics in case of

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pneumonia which was the most prevalent disease. In this study, 75% of antibiotics were given by injection. The average number of antibiotic per patient was 2.41±1.02 [20].

A study conducted on antibiotic utilization for hospitalized pediatric patients in Netherlands revealed that antibiotics were prescribed at least once for 36% of hospitalized children although only 12.3% of the patients receiving antibiotics had proven bacterial infection. It was also concluded that a high percentage of all hospitalized children receive antibiotics whereas in most cases they are started on an empirical basis, without proof of a bacterial infection [21-23].

Discussion

Education and experience of physician, parental expectations and economic pressure has been suggested as possible reasons for over prescribing of antibiotics in children. In a questionnaire study it was reported that patients presenting with acute lower respiratory tract infections symptoms often believe that infection is the problem and antibiotic is the answer and patient pressure most commonly influenced the decision to prescribe even when doctor thought antibiotic were not indicated [23-26]. Further it was demonstrated in a study that children with physician -parents were least likely to receive potentially inappropriate antibiotic preparations suggesting the role of parental education. However parental education alone is not sufficient to effect change; factors like ready access to care on an urgent basis, better communication between treating physician and physician - patient relationships when the patient is a physician, may play a role in reducing inappropriate use of antibiotics [27-29].

5. CONCLUSION

Infant health is as important as elderly health. A wide gap is found about the literature related to pediatric health. There is still scope of improvement in various areas like dosage calculation, proper documentation, prescribing drugs by generic name and from WHO-EML for children as far as possible. Development and implementation of Standard Treatment Guidelines (STGs) based on essential drug concept and promoting rational drug therapy will lead to more and more rational prescribing in pediatrics. Periodic prescriptions analysis and effective feedback to clinician should be done based on results to ensure rational prescribing and effective health care management, which will ultimately lead to a better child health.

6. REFERENCES

- 1. Zehravi M, Maqbool M, Ara I. Polycystic ovary syndrome and infertility: an update. International journal of adolescent medicine and health. 2021 Jul 22; 34(2):1-9.
- 2. Lihite RJ, Lahkar M, Das S, Hazarika D, Kotni M, Maqbool M, Phukan S. A study on adverse drug reactions in a tertiary care hospital of Northeast India. Alexandria journal of medicine. 2017 Jul 11; 53(2):151-6.
- 3. Zehravi M, Maqbool M, Ara I. Correlation between obesity, gestational diabetes mellitus, and pregnancy outcomes: an overview. International Journal of Adolescent Medicine and Health. 2021 Jun 18; 33(6):339-45.

Vol: 04, No. 04, June-July 2024

http://journal.hmjournals.com/index.php/JCPP **DOI:** https://doi.org/10.55529/jcpp.44.35.43



- 4. Maqbool M, Bekele F, Fekadu G. Treatment strategies against triple-negative breast cancer: an updated review. Breast Cancer: Targets and Therapy. 2022 Jan 11:15-24
- 5. Rasool S, Maqbool M. An overview about Hedychium spicatum: a review. Journal of Drug Delivery and Therapeutics. 2019 Feb 15; 9(1-s):476-80.
- 6. Zehravi M, Maqbool M, Ara I. Depression and anxiety in women with polycystic ovarian syndrome: a literature survey. International Journal of Adolescent Medicine and Health. 2021 Aug 23; 33(6):367-73.
- 7. Maqbool M, Gani I, Dar MA. Anti-diabetic effects of some medicinal plants in experimental animals: a review. Asian Journal of Pharmaceutical Research and Development. 2019 Feb 15; 7(1):66-9.
- 8. Zehravi M, Maqbool M, Ara I. Polycystic ovary syndrome and reproductive health of women: a curious association. International journal of adolescent medicine and health. 2021 Apr 21; 33(6):333-7.
- 9. Mohd M, Maqbool M, Dar MA, Mushtaq I. Polycystic ovary syndrome, a modern epidemic: an overview. Journal of Drug Delivery and Therapeutics. 2019 May 15; 9(3):641-4.
- 10. Maqbool M, Fekadu G, Jiang X, Bekele F, Tolossa T, Turi E, Fetensa G, Fanta K. An up to date on clinical prospects and management of osteoarthritis. Annals of Medicine and Surgery. 2021 Dec 1; 72:103077.
- 11. Majeed A, Bashir R, Farooq S, Maqbool M. Preparation, characterization and applications of nanoemulsions: An insight. Journal of Drug Delivery and Therapeutics. 2019 Mar 15; 9(2):520-7.
- 12. Zehravi M, Maqbool M, Ara I. Healthy lifestyle and dietary approaches to treating polycystic ovary syndrome: a review. Open Health. 2022 May 2;3(1):60-5.
- 13. Maqbool R, Maqbool M, Zehravi M, Ara I. Menstrual distress in females of reproductive age: a literature review. International journal of adolescent medicine and health. 2021 Jul 22; 34(2):11-7.
- 14. Ara I, Maqbool M, Fekadu G, Hajam TA, Dar MA. Pharmaceutical significance of Nigella sativa L., a wonder herb. Journal of Applied Pharmaceutical Sciences and Research. 2020;3(4):04-13.
- 15. Maqbool M, Nasir N, Mustafa S. Polycystic in ovarian syndrome and its various treatment strategies. INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES. 2018 Sep 1;5(9):8470-8.
- 16. Maqbool M, Zehravi M, Maqbool R, Ara I. Study of adverse drug reactions in pulmonary medicine department of a Tertiary care hospital, Srinagar, Jammu & Kashmir, India. CELLMED. 2021;11(2):8-1.
- 17. Ara I, Maqbool M, Bukhari B, Ara N, Hajam TA. Present status, standardization and safety issues with herbal drugs. International Journal of Research in Pharmaceutical Sciences and Technology. 2020 May 18;1(3):95-101.
- 18. Ara I, Maqbool M, Gani I. Reproductive Health of Women: implications and attributes. International Journal of Current Research in Physiology and Pharmacology. 2022 Nov 28:8-18.
- 19. Zehravi M, Maqbool R, Maqbool M, Ara I. To Identify Patterns of Drug Usage among Patients Who Seek Care in Psychiatry Outpatient Department of a Tertiary Care

Vol: 04, No. 04, June-July 2024

http://journal.hmjournals.com/index.php/JCPP **DOI:** https://doi.org/10.55529/jcpp.44.35.43



- Hospital in Srinagar, Jammu and Kashmir, India. Journal of Pharmaceutical Research International. 2021 Jun 10;33(31A):135-40.
- 20. Maqbool M, Javed S, Bajwa AA. Assessment OF pain management IN postoperative cases using different scales and questionnaires. INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES. 2019 Jan 1;6(1):983-7.
- 21. Ara I, Maqbool M, Zehravi M. Psychic consequences of infertility on couples: A short commentary. Open Health. 2022 Jan 1;3(1):114-9.
- 22. Bashir R, Maqbool M, Ara I, Zehravi M. An In sight into Novel Drug Delivery System: In Situ Gels. CELLMED. 2021;11(1):6-1.
- 23. Zehravi M, Maqbool M, Ara I. Teenage menstrual dysfunction: an overview. International Journal of Adolescent Medicine and Health. 2022 Sep 19;35(1):15-9.
- 24. Ara I, Zehravi M, Maqbool M, Gani I. A review of recent developments and future challenges in the implementation of universal health coverage policy framework in some countries. Journal of Pharmaceutical Research & Reports. SRC/JPRSR-131. DOI: doi. org/10.47363/JPRSR/2022 (3). 2022;127.
- 25. Maqbool M, Shabbir W, Aamir S. Adverse events of blood transfusion and blood safety in clinical practice. Indo American Journal Of Pharmaceutical Sciences. 2018 Aug 1;5(8):8254-9.
- 26. Maqbool M, Naeem A, Aamer S. Diabetes mellitus and its various management strategies in practice. Indo American Journal of Pharmaceutical Sciences. 2018 Aug 1:5(8):8163-+.
- 27. Maqbool M, Tariq S, Amjad S. Prescribing practices in pediatrics and drug utilization studies promoting pediatric health. Indo American Journal of Pharmaceutical Sciences. 2018 Aug 1;5(8):8070-6.
- 28. Maqbool M, Ikram U, Anwar A. Adverse drug reaction monitoring and occurrence in drugs used in pulmonary disorders. Indo American Journal Of Pharmaceutical Sciences. 2018 Aug 1;5(8):8060-5.
- 29. Maqbool R, Maqbool M, Zehravi M, Ara I. Acute neurological conditions during pregnancy and their management: a review. International Journal of Adolescent Medicine and Health. 2021 Aug 23;33(6):357-66.