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Challenges and Opportunities in Practice of Paediatric Laboratory Medicine

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Abstract

Paediatric laboratory medicine is a huge part of diagnostics posing its own unique challenges and opportunities. This article includes key aspects of paediatric laboratory medicine like preanalytic variables, analytic factors, age-specific reference intervals, clinical impact, and future opportunities. The requirements while providing pediatric laboratory services are different in many aspects as compared to the requirements for adults. The challenges in practicing paediatric laboratory medicine are related to difficulty in sample collection, small sample volume, lesser turn around time and greater need of frequent testing for prognosis. An additional concern in pediatric laboratory medicine is the unavailability of universal reference interval for many biomarkers. Though the challenges are immense, pediatric laboratory testing offers many opportunities for improved patient care, research, and education. The role of newer tools in technology like Artificial Intelligence in paediatric diagnostics will also be highlighted in this article.

Keywords: Paediatrics, Laboratory Medicine, Reference Intervals, Technology, Artificial Intelligence

Full length article **Corresponding Author*, e-mail: minal.pore@bharatividyapeeth.edu

1. Introduction

Considering children as little adults can one of the major blunders in the practice of pediatrics, and laboratory medicine is no exemption to it. The unique challenges of handling paediatric samples are small blood volumes, sample types, and ways of sample collection, test validation and age specific reference intervals. This article will shed light on challenges like sample collection, blood volume requirements, sample stability issues, importance of paediatric reference intervals, ethical considerations and opportunities like advantages of boon in technology in the field of paediatric testing.

2. Challenges in Practice of Paediatric Laboratory Medicine are as follows

2.1. Sample Collection

Collecting samples from paediatric patients can be challenging due to their smaller size, difficulty in obtaining adequate quantities, and the need for specialized techniques. It requires proper training and coordination between healthcare providers and laboratory personnel. Collecting samples from paediatric populations can indeed present unique challenges. Some common challenges are as follows.

2.1.1. Sample Volume

The limited blood volume in children, especially infants, can restrict the amount of sample that can be collected for various tests [1].

2.1.2. Difficult Venipuncture

Veins in young children can be small, fragile, and difficult to access, resulting in frequent venipuncture attempts or the need for alternative sampling methods [2].

2.1.3. Behavioral Factors

Anxiety, fear, and resistance to medical procedures can make sample collection challenging, requiring techniques to reduce distress and increase compliance [3].

2.1.4. Sample Stability

Handling and transporting paediatric samples require extra care to maintain sample integrity, especially for tests that depend on specific sample conditions [4].

2.2. Reference Values

2.2.1. Limited Reference Ranges

The interpretation of test results in paediatric populations can be challenging due to the limited availability of age-specific reference ranges [5]. These references should provide with insights and information on the challenges faced when collecting samples from paediatric populations. Establishing age-specific reference ranges for laboratory tests is essential in paediatric medicine. However, this requires extensive research and data collection to account for the physiological changes that occur during growth and development. Lack of comprehensive reference values can lead to misinterpretation of results. Reference values in paediatric population are important to guide healthcare providers in interpreting laboratory test results in children. Some of the reasons and sources for the importance of reference values in paediatric population are as follows,

2.2.2. Importance of reference values in paediatric population

Paediatric reference values are important because children undergo various physiological changes as they grow, and their laboratory values vary accordingly. The interpretation of test results among children needs to taken into account their age, sex, and developmental stage. These reference values help healthcare providers detect and diagnose pathological processes in paediatric patients, such as infections, anaemias, metabolic disorders, and endocrine diseases. Proper interpretation of test results in children leads to more accurate diagnosis and timely initiation of appropriate treatment.

2.2.3. Sources of reference values in paediatric population

Paediatric reference values are determined using various methods, including statistical analysis of laboratory results from healthy children, longitudinal studies that follow children from birth to adulthood, and physiological models that estimate reference intervals based on age and other relevant parameters. Following are some of the sources of reference values in paediatric population.

2.2.3.1. Clinical and Laboratory Standards Institute (CLSI)

CLSI publishes guidelines and standards for the establishment of reference intervals in laboratory tests. The CLSI C28-A3 guideline provides general recommendations for the definition, establishment, and verification of reference intervals in clinical laboratory tests. This guideline is universally accepted, and its recommendations are followed worldwide [6].

2.2.3.2. National Institutes of Health (NIH)

NIH publishes the National Institutes of Health Clinical Center's laboratory values of normal healthy infants, children, and adolescents. This database provides reference intervals for numerous laboratory analytes used in clinical practice. The database is continually updated to reflect new research findings [7].

2.2.3.3. Pediatric Laboratory Medicine Committee (PLMC)

The PLMC is an international collaborative network of paediatric laboratory medicine experts. PLMC develops and publishes consensus-based reference values for paediatric laboratory tests. The PLMC reference intervals are derived from multiple data sources, including CLSI guidelines and previous studies [8]. These resources are important sources of reference values in paediatric population to guide healthcare providers in interpreting laboratory test results in children and ensuring proper diagnosis and treatment of paediatric patients.

2.3. Limited Paediatric-Specific Testing

There is a lack of comprehensive paediatric-specific laboratory testing options compared to adult medicine. Many tests are adapted from adult methods, which may not accurately reflect paediatric physiology or pathology. This can lead to challenges in diagnosis, treatment, and monitoring in paediatric patients. "Challenges in Conducting Paediatric Clinical Trials: International Perspective" by Turner et al. (2018) [9] review discusses several challenges in conducting paediatric clinical trials, including limited paediatric-specific testing. The authors highlight issues such as the small number of eligible paediatric patients, ethical considerations, and the need for age-appropriate formulations and dosing. They emphasize the importance of collaboration and international cooperation to overcome these challenges. This study conducted a survey among professionals involved in paediatric clinical trials to identify barriers to paediatric drug development. The findings revealed that limited paediatric-specific testing was one of the major challenges, leading to a lack of evidence-based dosing recommendations and safety data for paediatric populations [10]. "Paediatric Drug Development: Challenges and Opportunities" by Roberts et al. (2018) review article discusses the challenges and opportunities in paediatric drug development, including limited paediatric-specific testing. The authors highlight the difficulties in extrapolating data from adult studies to children and emphasize the need for age-appropriate formulations, pharmacokinetic studies, and paediatric-specific safety assessments to ensure optimal drug therapy in children [11]. These studies shed light on the various challenges associated with limited paediatric-specific testing, including issues related to patient enrolment, ethical considerations, and the need for age-appropriate formulations and dosing.

2.4. Ethical Considerations

Paediatric laboratory medicine involves ethical considerations, such as obtaining consent from parents or guardians, ensuring patient confidentiality, and maintaining appropriate data management practices. Balancing the need for information with patient privacy can be challenging. Several ethical considerations need to be taken into account when conducting laboratory testing on paediatric populations. These considerations include.

2.4.1. Informed consent

Obtaining informed consent from the parents or guardians of children is essential. They need to understand the purpose of the testing, its potential risks, benefits, and any potential alternative options.

2.4.2. Privacy and confidentiality

Protecting the privacy and confidentiality of the children involved is crucial. Test results should only be disclosed to authorized individuals, and data should be anonymized whenever possible.

2.4.3. Minimizing harm

Steps should be taken to minimize any potential harm or discomfort to children during the testing process. This may involve using child-friendly equipment, minimizing the amount of blood or other samples collected, and ensuring that the procedure is as comfortable and least invasive as possible.

2.4.4. Justification and necessity

The testing should be justified and necessary for the child's well-being. There should be a clear rationale for why specific tests are being conducted and how the results will benefit the child's health or treatment plan.

2.4.5. Appropriate test selection

The tests selected should be appropriate for the age, development, and conditions of the paediatric population. Paediatric-specific reference ranges and guidelines should be followed.

2.4.6. Competence and expertise

All personnel involved in conducting the laboratory testing should have the necessary competence and expertise in working with children. They should be trained to communicate effectively with children and be knowledgeable about paediatric considerations in laboratory testing.

2.4.7. Cultural and socio-economic considerations

Consideration should be given to the cultural and socio-economic context of the paediatric population being tested. This includes ensuring that the testing is accessible and affordable to all children, regardless of their background or circumstances.

2.4.8. Research ethics

If the laboratory testing is part of a research study, additional ethical considerations apply. This includes obtaining appropriate research ethics committee approval, ensuring the study is designed ethically, and considering the potential risks and benefits for the children involved. Overall, ethical considerations in paediatric population laboratory testing revolve around ensuring the well-being, privacy, and rights of children are protected, while also ensuring the accuracy and validity of the test results.

2.5. Workforce and training challenges

As paediatric challenges are unique, it requires unique training as well. Because of important differences between adults and children, paediatric lab medicine should be a different speciality on its own altogether. The scope of knowledge should cover the paediatric aspects of various disciplines like Clinical Biochemistry, Immunology, Infectious Diseases, Toxicology, Hematology, Molecular biology and Genetics.

3. Opportunities in Practice of Paediatric Laboratory Medicine are as follows

3.1. Advances in Technology

Advances in laboratory technology, such as miniaturization, automation, and molecular techniques, have the potential to improve diagnostic accuracy, speed up results, and enable the development of specialized paediatric tests. Advances in technology have greatly impacted various fields, including paediatric testing and healthcare. Few examples of technological advancements and their impact.

3.1.1. Artificial Intelligence (AI) in Healthcare

AI has shown promise in diagnosing diseases and predicting outcomes. A study published in Nature Medicine [12] highlighted how an AI algorithm outperformed human dermatologists in diagnosing skin cancer. AI is also being used to improve medical imaging, such as in radiology. A study published in the journal Nature demonstrated that an AI algorithm could detect skin cancer from images with a similar accuracy to dermatologists.

3.1.2. Internet of Things (IoT) in Healthcare

IoT allows for the connection and sharing of data between devices. This technology has applications in healthcare, such as remote patient monitoring. A journal article [13] discussed how IoT could improve patient monitoring, disease prevention, and personalized healthcare.

3.1.3. Gene Editing Technologies

CRISPR-Cas9 is a revolutionary gene-editing technology that enables precise modifications of DNA. It has the potential to treat genetic diseases. A study published in

the journal Nature Reviews Genetics [14] provided an overview of CRISPR-Cas9 and its applications in genetic research and therapy.

3.1.4. 5G Technology

5G promises faster data transfer speeds and lower latency, which can have a significant impact on communication, transportation, and remote healthcare. A report by Konstantinos E. Georgiou et al [15] discussed the potential benefits of 5G in healthcare, including telemedicine, remote patient monitoring, and enhanced connectivity for medical devices.

3.1.5. Virtual Reality (VR) in Therapy

VR technology is being utilized in various therapeutic settings, such as treating phobias, post-traumatic stress disorder (PTSD), and chronic pain. A systematic review published in the journal Frontiers in Psychology evaluated the efficacy of VR in treating mental health disorders. These examples highlight the wide-ranging impacts of technological advancements across different sectors. It is important to note that specific advancements can have ethical and societal implications that need to be considered and addressed [16].

3.2. Precision Medicine

Paediatric laboratory medicine can play a crucial role in the emerging field of precision medicine, tailoring treatments based on an individual's genetic, biochemical, and physiological characteristics. This can lead to personalized diagnostics and therapies, improving patient outcomes. Precision medicine, also known as personalized medicine, in the paediatric population is an emerging field that aims to tailor medical treatment and interventions based on an individual child's unique genetic and environmental factors. Here are a few examples of precision medicine in the paediatric population.

3.2.1. Pharmacogenomics in Paediatric Oncology

Pharmacogenomics studies the relationship between an individual's genetic makeup and their response to medications. In paediatric oncology, pharmacogenomics can help determine the most effective and safest treatment options for children with cancer. A study published in JAMA Oncology demonstrated the potential of pharmacogenomics to guide treatment decisions and improve outcomes in paediatric cancer patients.

3.2.2. Precision Medicine in Paediatric Epilepsy

Precision medicine approaches, such as genomic sequencing, are being used to identify the genetic causes of epilepsy in children. This knowledge can inform treatment decisions, including the use of specific antiepileptic drugs. A study published in Nature [17] identified several novel epilepsy-associated genes in paediatric patients, showcasing the potential of precision medicine in managing epilepsy.

3.2.3. Genetic Testing for Inherited Paediatric Disorders

Genetic testing is increasingly being used to diagnose and manage inherited paediatric disorders. This can involve whole genome or targeted gene sequencing to identify specific genetic variants responsible for the disorder. An article demonstrated the successful application of genomic sequencing in diagnosing and treating a child with an undiagnosed neurodevelopmental disorder [18].

3.2.4. Personalized Treatment Approaches for Juvenile Idiopathic Arthritis (JIA)

Juvenile idiopathic arthritis (JIA) is a chronic autoimmune disorder in children. Precision medicine approaches, such as biomarker profiling and genetic testing, are being explored to identify subtypes of JIA and personalize treatment strategies. A study published in the journal of Arthritis Research & Therapy [19] discussed the potential of precision medicine in improving outcomes and guiding treatment decisions in children with JIA. These examples highlight the growing role of precision medicine in paediatric populations and the potential to improve diagnosis and treatment outcomes for children with various conditions. However, it is important to continue research and address ethical considerations to ensure the responsible and equitable implementation of precision medicine approaches in paediatric care.

3.3. Collaboration and Research

Collaboration between paediatricians, laboratory scientists, and researchers can lead to the development of novel tests, reference ranges, and diagnostic algorithms specifically designed for paediatric patients. Research in paediatric laboratory medicine can improve understanding and management of diseases in children. Collaboration and research in the paediatric population are crucial for advancing our understanding of childhood diseases and improving the overall health outcomes of children. Few examples of collaborative research initiatives in paediatric populations.

3.3.1. Paediatric Heart Network

The Paediatric Heart Network (PHN) is a collaboration of clinical centers and core laboratories dedicated to conducting research on congenital and acquired heart diseases in children. The PHN has conducted several multi-centre clinical trials and observational studies to improve the outcomes of children with heart disease. For example, the PHN conducted a multi-centre trial to evaluate the effectiveness of corticosteroids in preventing interstage death or transplantation in infants with hypoplastic left heart syndrome [20].

3.3.2. Children's Oncology Group

The Children's Oncology Group (COG) is a global collaborative research organization dedicated to improving the outcomes for children and adolescents with cancer. COG conducts clinical trials and studies to develop new treatments, improve existing therapies, and address long-term effects of cancer treatment in the paediatric population. For instance, the COG conducted a multi-centre trial to evaluate the cardiac effects of anthracycline chemotherapy in children with solid tumors [21].

3.3.3. Paediatric HIV/AIDS Cohort Study

The Paediatric HIV/AIDS Cohort Study (PHACS) is a collaboration of researchers dedicated to studying the long-term effects of HIV infection and its treatment in children and adolescents. PHACS conducts observational studies and clinical trials to optimize the care and outcomes of children living with HIV. A study conducted by PHACS identified the impact of early antiretroviral therapy on neurodevelopmental outcomes in HIV-infected infants [22].

3.3.4. International Childhood Liver Tumors Strategy Group

The International Childhood Liver Tumors Strategy Group (SIOPEL) is a collaboration of medical specialists and researchers aiming to improve the outcomes of children with liver tumors. SIOPEL conducts clinical trials and studies to develop standardized treatment protocols, improve risk stratification, and develop targeted therapies for pediatric liver tumors. As an example, the SIOPEL group developed a risk stratification system that guides treatment decisions for hepatoblastoma, a common liver tumor in children [23]. These examples highlight the importance of collaboration and research networks in the pediatric population to advance knowledge, improve treatments, and enhance outcomes for children with various diseases. Collaborative efforts allow researchers and clinicians to pool expertise, resources, and data to address complex pediatric health challenges and develop evidence-based interventions.

3.4. Education and Training

Continuous education and training initiatives can enhance the skills and knowledge of laboratory personnel in paediatric-specific techniques, sample collection, and interpretation of results. This can improve the quality and reliability of paediatric laboratory testing. Education and training in the paediatric population are crucial for healthcare professionals to provide high-quality care to children. Here are a few examples of educational programs and training initiatives in paediatric populations, along with relevant references.

3.4.1. Paediatric Residency Programs

Paediatric residency programs provide comprehensive training for medical graduates who wish to specialize in paediatrics. These programs typically include clinical rotations in various paediatric specialties, didactic teaching, research opportunities, and hands-on experiences in managing paediatric patients. The American Academy of Paediatrics (AAP) provides guidelines for paediatric residency education, including core competencies and milestones for paediatric trainees (American Academy of Paediatrics, 2021) [24].

3.4.2. Paediatric Advanced Life Support (PALS) Certification

PALS is a specialized certification course designed for healthcare professionals, such as physicians, nurses, and paramedics, who care for critically ill or injured paediatric patients. The American Heart Association (AHA) offers PALS training programs that focus on advanced life support interventions specific to the paediatric population. PALS courses include both didactic and hands-on training, teaching healthcare providers to recognize and manage paediatric emergencies (American Heart Association, 2021) [25].

3.4.3. Neonatal Resuscitation Program (NRP) Certification

NRP is an educational program specifically designed for healthcare professionals involved in the initial care of newborns, including neonatal intensive care unit (NICU) staff, obstetricians, and midwives. The program, developed jointly by the AAP and the AHA, provides training in neonatal resuscitation techniques. NRP courses focus on knowledge and skills necessary to resuscitate and stabilize newborns in various clinical scenarios (American Academy of Paediatrics & American Heart Association, 2020) [26].

3.4.4. Continuing Medical Education (CME) Programs

CME programs offer ongoing education and training opportunities for healthcare professionals to update their knowledge and skills in paediatric medicine. Organizations like the AAP and various paediatric subspecialty societies offer CME activities, including conferences, webinars, online courses, and journal articles. These programs cover a wide range of paediatric topics, such as emerging treatments, advances in diagnostics, and guidelines for specific paediatric conditions [27].

3.5. Integration of Data

Integrating laboratory test results with electronic health records and clinical data can provide a comprehensive view of a child's health and support clinical decision-making. Analysing large datasets can also facilitate research and enable the identification of patterns and trends in paediatric diseases. Integration of data in the paediatric population refers to the collection, analysis, and utilization of various types of data to improve healthcare outcomes for children. This includes data from electronic health records (EHRs), clinical trials, research studies, public health surveillance, and other sources. Here are a few examples of how data integration is used in the paediatric population.

3.5.1. Electronic Health Records (EHRs)

EHRs contain comprehensive patient information, including medical history, lab results, imaging studies, medications, and immunization records. Integrating EHR data allows healthcare providers to have a holistic view of a child's health, facilitating coordinated and continuous care. Data integration also allows for clinical decision support systems, enabling providers to access evidence-based guidelines and alerts for preventive screenings or potential drug interactions [28].

3.5.2. Clinical Research and Trials

Integration of data from clinical research and trials helps to advance paediatric healthcare by providing insights into the effectiveness and safety of new treatments or interventions. Researchers can combine data from multiple studies to conduct meta-analyses, systematic reviews, and comparative effectiveness research. Furthermore, data integration can facilitate the identification of eligible participants for clinical trials and enhance collaboration between researchers and clinicians [29].

3.5.3. Public Health Surveillance

Data integration in public health surveillance involves combining data from multiple sources to monitor and control diseases and health conditions. This includes not only infectious diseases but also chronic conditions prevalent in the paediatric population, such as asthma or obesity. Integrated data sources may include hospital and clinic data, laboratory reports, immunization registries, and population-based surveys. By integrating these data sources, public health officials can track disease trends, identify outbreaks, and implement timely interventions [30].

3.5.4. Genomics and Precision Medicine

Integration of genomic data in paediatrics can provide valuable information for personalized treatments and interventions. Genomic data, combined with clinical and phenotypic information, can help identify genetic causes of paediatric disorders, predict disease risk, and guide targeted therapies. Data integration in genomics also supports research efforts in understanding disease mechanisms, developing novel treatments, improving diagnostic accuracy Overall, data integration in the paediatric population enables healthcare providers, researchers, and public health officials to make evidence-based decisions, improve healthcare outcomes, and advance the field of paediatric medicine.

4. Conclusions

To conclude it can be emphasized that it is important to consider all the challenges mentioned above to lessen the paediatric patients' discomfort while undergoing laboratory tests and to utilize the various opportunities discussed in this review in order to evolve paediatric laboratory medicine to provide optimal care for paediatric patients.

Disclaimer

AI based tools were utilized and were cited appropriately.

Conflict of interest

None.

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