PEDIATRIC AND MATERNAL-FETAL DIVISION NEWS
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FROM THE MIND OF THE CHAIR

Hello PMF Division members! I'm excited to start of our annual meeting on July 28th. Our division has a number of events for you to check out. The PMF Division is also co-hosting a Mixer with the Health Equity and Access and Informatics Divisions on Sunday night. Join us for food and drinks and networking with your colleagues. Congratulations to our abstract award winners and the Outstanding Contribution to Pediatric and Maternal-Fetal Clinical Chemistry award winner who are announced in this newsletter. They will also be recognized at the mixer.

In this issue Robert Bubar addresses N in The ABC's of Pediatric Laboratory Medicine series, penning an article titled N is for NGAL: A brief review. A listing of PMF-related events at the annual meeting is also provided.

As you may already know, the current division structure is undergoing change to better reflect our profession's role in laboratory medicine, our efforts towards inclusiveness. Leadership changes are in the process of being established and will become effective in the next few months. This is an exciting time for our organization. I urge you to embrace this change and continue to actively participate within our division.

My term as Chair is ending. As I reflect on my time in this role, it is very clear to me that our division is composed of many talented individuals. I am proud to have represented our division and humbled by the skills and effort our current PMF board possesses. The division will transition to the keen eye of Joe Wiencek, and thus the division will be in good hands with his leadership. I look forward to seeing everyone in Chicago!

Sincerely,

Stanley F Lo
Chair, AACC PMF Division

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N THE ABC'S OF PEDIATRIC LABORATORY MEDICINE:

N is for NGAL: A brief review

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Background

Acute kidney injury (AKI) is a term commonly used to describe a state of impaired renal function characterized by reduced waste excretion, electrolyte imbalances, and fluid management disruption. AKI in the pediatric population is most commonly attributable to disturbances in renal blood flow, particularly conditions which result in reduced renal perfusion. These disturbances may be related to iatrogenic causes such as surgery, transplantation, or cardiopulmonary bypass. Systemic conditions such as sepsis, heart failure, and volume depletion can also impair renal function, as can direct damage caused by nephrotoxic agents [1].

Infants and young children are particularly vulnerable to kidney damage compared to older children and adolescents. Nephrons are not fully developed until late in gestation and tubular function does not fully mature until 1 year of age. Additionally, glomerular filtration rate (GFR) does not reach full functionality until 2 years of age.

Epidemiological studies have estimated the incidence of AKI to be 5% amongst all hospitalized pediatric patients and up to 27% in the intensive care setting [1]. Severe AKI is associated with increased mortality, greater hospital length of stay, and increased need for interventional support including mechanical ventilation and continuous renal replacement therapy (CRRT) [1,2]. Hospitalized patients who develop mild AKI early on during admission have increased risk of progressing to more severe stages [2]. This, coupled with the fact that management of AKI depends primarily on prevention and supportive care, makes early detection of AKI critical [1].

Laboratory Testing

The structure of the nephron can be thought of as three distinct regions: the glomerulus, the proximal and distal tubules, and the collecting ducts. Different laboratory tests have been developed to assess the functionality of each of these individual regions. Many gold standard tests involve the collection of urine [3]. This can be both time consuming and challenging, especially in pediatric patients where accurate measurement of urine output may require catheterization or volume estimation [1]. Blood tests are a quicker, easier testing method and multiple blood tests have been developed based on the measurement of endogenous biomarkers used to assess kidney function. Creatinine is the most common endogenous marker of GFR due to the ease of measurement, its nearly constant rate of production, and the fact that it is almost exclusively cleared by the kidney. Because one can assume that creatinine is produced at a constant rate, changes in serum creatinine are mostly dependent on the rate by which it can be filtered via the kidneys. Thus, changes in GFR can be indirectly measured by assessing changes in serum creatinine levels. Additionally, other factors such as total urine output, blood urea nitrogen (BUN) level, and measurement of urine proteins can be used to assess renal function [3].

GFR is just one metric used to assess for AKI, and most currently accepted definitions incorporate multiple metrics for the diagnosis

and staging of AKI in both adults and children. Some commonly used definitions include those outlined in the Pediatric RIFLE (pRIFLE), AKI Network (AKIN), and Kidney Disease Improving Global Outcomes (KDIGO). While the criteria may vary, each method incorporates GFR assessment and/or creatinine measurement into their definition and staging [4].

Even though creatinine is one of the most widely used markers for the assessment of kidney function, it does have limitations, especially in the pediatric population. One of the most limiting issues regarding the reliance on creatinine is that it is a measurement of kidney function, not kidney damage. Reduced GFR can be thought of as a lagging indicator for renal damage that has already occurred. Studies in the pediatric population have shown that creatinine does not elevate until 24-48 hours after renal injury has occurred [1]. Because creatinine is primarily produced by muscles, those individuals with decreased muscle mass, such as children, may have different baseline creatinine levels than the population at-large. Routine chemistry testing is uncommon in children, and establishing a baseline creatinine level for these patients is often not possible [3]. Indeed, studies have shown that up to two-thirds of pediatric patients who meet the urine output criteria for AKI present with normal serum creatinine levels, and that decreased urine output may be a better indicator of increased mortality risk than creatinine abnormalities [2]. Because of these limitations, there has been ongoing research into better endogenous markers for renal function assessment.

Neutrophil Gelatinase Associated Lipocalin (NGAL)

Given the limitations associated with creatinine, additional blood and urine biomarkers are being investigated to better assess renal function. These include markers such as cystatin-C, TGF-β, IL-18, NGAL, and others [5,6]. NGAL is a protein contained within neutrophil granules that interacts with various chemotactic factors and cytokines. Epithelial cells of certain body tissues, including the renal tubules, have also been found to produce NGAL in response to inflammation and ischemia. Animal studies have shown that NGAL levels begin to increase in the proximal renal tubule cells within a few hours following an ischemic insult. These findings drew attention from researchers and encouraged further study into whether NGAL could serve as a useful early indicator of renal damage.
The ease with which new testing can be implemented in the laboratory depends on many factors including ease of sample collection and the ability to measure the analyte in question. Studies in the pediatric population showed that NGAL could be detected in urine using enzyme-linked immunosorbent assay (ELISA). Additionally, this rise in NGAL could be detected as early as 2 hours following an ischemic insult to the kidney, far earlier than could be detected using conventional creatinine analysis [7,8]. NGAL's presence in the urine and the ability to measure it using existing laboratory technology has led it to become one of the more promising new biomarkers currently under investigation.

One of the greatest potential benefits of NGAL analysis is the ability to detect kidney injury early and monitor for both progression or recovery. An analysis of multiple studies by the Acute Dialysis Quality Initiative (ADQI) revealed that improvement in AKI within the first 48 hours of insult is associated with better outcomes while persistence beyond this timeframe is associated with higher risk of injury progression [9]. Given the importance of identifying AKI within this early time window, the benefit of NGAL analysis over conventional creatinine monitoring is clear. Multiple commercially-available urinary NGAL (uNGAL) assays have been developed, including the recently FDA-approved ProNephro AKI™ (BioPorto Diagnostics, Hellerup, DK) [10, 11].

Despite the utility of uNGAL analysis, it is important to keep in mind some of the potential limitations. Because NGAL is produced by multiple different tissues during inflammatory states, it is possible that acute or chronic illnesses outside the kidney may result in NGAL detection in the urine [12]. Additionally, despite numerous studies suggesting how uNGAL may be incorporated into clinical decision making, most of the currently accepted formal definitions

for identifying and classifying AKI remain reliant on metrics such as urine output and GFR [13, 14].

Conclusion

Multiple patient studies have highlighted the importance of identifying new and improved biomarkers for the early detection of kidney injury, particularly in the pediatric population where conventional, creatinine-based analytical methods may be less reliable. NGAL is one emerging biomarker that shows many promising benefits including its early detection in urine, the availability of commercial assays, and increasing evidence showing its utility in clinical decision making. As uNGAL testing becomes more common, the possibility of its integration into formal AKI diagnostic criteria may encourage more laboratories to add uNGAL as part of their test menus. Early detection of AKI can lead to early interventions and better patient outcomes highlighting the critical role that the lab plays in the quest for constant improvement in medicine.

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2024 ADLM ANNUAL SCIENTIFIC MEETING & CLINICAL LAB EXPO: PMF Sessions of Interest and Meeting Highlights

July 28 – August 1, 2024

Sunday July 28th

Opening Plenary:

Patrick Bossuyt, PhD
11001 Why We Need More Strong Clinical Trials of Laboratory Tests

PMF Division Mixer co-hosted with the Divisions of Health Equity & Access, History, and Informatics

8:00-9:30 PM Glessner House AB, Marriott Marquis Chicago.
***Awards will be presented during this time**.

Monday July 29th

Roundtables:

42127/52227 Leaving No One Behind: Management of Hyperbilirubinemia in Preterm Infants Less Than 35 Weeks' Gestation with Clinical Decision Support Tools

42104/52204 Standardization of Testosterone and Estradiol Measurements by the CDC Clinical Standardization Programs: A Comprehensive Approach Going Beyond Calibration

Plenary:

Kojo S.J. Elenitoba-Johnson, MD
12001 Lymphoma Biomarkers and Therapeutic Targets From Mass Spectrometry-driven Proteomics

Scientific Sessions:

32441 Operationalizing Changes to LDT Oversight: Building Roadmaps When the Rubber Hits the Road

32444 Implementation of Equations to Estimate Glomerular Filtration Rate at a Pediatric Institution

32447 Gestational Diabetes Mellitus: Thinking Beyond Current Testing Guidelines

32226 Improving Lead Testing Access: Leaning Into Decision Support Tools and Lead Screening by Dried-Blood Spots

Tuesday July 30th

Roundtables:

43107/53207 Designing Clinical Context-Specific Drug Test Panels

43118/53218 Sweat Testing: Current Practices and Quality Metrics

Plenary:

Ron H.N. van Schaik, PhD
13001Implementation of PGx-based Testing in Precision Health: Do You Have Your DNA-passport?

Poster Walk 12-1pm Poster Hall:
See the artery for meeting spot

1915 Evaluating Emergent POC Technology for Sickle Cell Testing in Resource Limited Settings

545 Rethinking the role of race in prenatal AFP screening for open neural tube defects

246 Establishment of infant free T4 reference interval through indirect methods

1627 Unraveling pathogen dynamics in pediatric meningitis complications during the omicron variant outbreak in Taiwan

2035 One step toward implementation of advanced lipoprotein testing in children: a pilot study on pediatric reference ranges.

Scientific Sessions:

33101 ADLM Healthcare Forum: The Impact of LDT Oversight on the Delivery of Care

33225 Care Continuum: How Hematologists, Laboratorians, and Transfusion Medicine Physicians Partner to Diagnose, Manage, and Support Patients with Sickle Cell Disease

33227 Metabolic Emergencies in the Pediatric Patient: Laboratory Differentiation of Inborn Errors of Metabolism and Acute Drug Exposure

33229 Navigating Constitutional Genomic Disorders Throughout the Exome

Wednesday July 31st

Roundtables:

44117 and 54217 Serology Tests for Celiac Disease Diagnosis in Children

44120 and 54220 Capillary Electrophoresis for Hemoglobin Evaluation: A Case-Based Approach to Learning

44125 and 54225 Recent Developments in Improving Pediatric Reference Intervals

44126 and 54226 Newborn Screening and Follow-up for Metabolic Disorders

Plenary:

Sharon Hillier, PhD
14001 Empowering Choice by Providing More Options in HIV Prevention

Scientific Sessions:

34106 The Changing Landscape for Cystic Fibrosis Testing and Treatment

Thursday August 1st

Plenary:

Diana Foster, PhD
15001 Projected Health and Social Consequences of Ending the Federal Protection for Abortion in the United States

Scientific Sessions:

35102 Preeclampsia in the Unites States: Clinical Details, Best Practices in Laboratory Medicine, and Impact of Foundational Support

PMF Division Awardees

Please help us congratulate the winners of this year's PMF Division Awards!

Best Abstract by a Student or Young Investigator:

William Butler, PhD
Department of Pathology and Laboratory Medicine, University of Pennsylvania
Title: Rethinking the role of race in prenatal AFP screening for open neural tube defects.

Best Abstract:

Irene De Baise MD/PhD
Department of Pathology, University of Utah School of Medicine
Title: Age-specific reference intervals for ethanolamine plasmalogen species in red blood cells using liquid chromatography tandem mass spectrometry.

Outstanding Contributions to Pediatric Maternal-Fetal Laboratory Medicine:

Sharon Geaghan, MD

Professor Emerita, Stanford University School of Medicine, Pathology and Pediatrics

PMF Division Executive Board:

Thank you to our division officers who will be completing their terms this month.

They are:

Newsletter Editor
Sarah Wheeler, PhD

Elections have not yet been completed for new officers.

Our remaining officers are:

Chair
Stanley Lo, PhD

Chair Elect:
Joe Wiencek, PhD

Members At Large
Stephen Roper, PhD
Sydney Webb Strickland, PhD
Amy Pyle-Eilola, PhD
Kara Lynch, PhD

Secretary:
Laura Smy, PhD

Treasurer:
Erin Schuler, PhD

Newsletter Editor
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