Early Diagnostic and Prognostic Value of the Urinary TIMP-2 and IGFBP-7 in Acute Kidney Injury in Critically Ill Children

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ABSTRACT

Background: Acute kidney injury (AKI) is a hidden complication among children within pediatric intensive care units (PICU).

Aim: To evaluate the early predictive and diagnostic value of Urinary [TIMP-2]•[IGFBP7] to detect AKI in PICU patients.

Methods: A case-control study was conducted on 112 children (72 admitted to PICU and 40 healthy controls) Urinary [TIMP-2]•[IGFBP7] was measured within 24 hours of PICU admission.

Results: Acute kidney injury developed in 52 (72.2%) out of 72 critically ill patients. The AKI group had significantly higher serum creatinine, CRP, and pediatric sequential organ failure assessment score (pSOFA) score ($p = 0.001$, 0.01, and 0.001, respectively) and significantly lower estimated creatinine clearance (eCCl) ($p = 0.001$). Urinary [TIMP-2]•[IGFBP7] was significantly higher in the AKI group as compared with the non-AKI group ($p = 0.007$) . The duration of the PICU stay was 1.8-fold higher in the AKI group ($p = 0.004$). At the time of study enrollment, 7 (13.5%) patients had normal initial eCCl. 26 patients (50.0%) fulfilled the "Risk," 18 patients (34.6%) the "Injury," 1 patient (1.9%) the "Failure" and 0 patient (0%) the "Loss" criteria. Nine (17%) patients progressed to the next higher pediatrics risk, injury, failure, loss, end-stage renal disease (pRIFLE) stage. Urinary [TIMP-2]•[IGFBP7] was significantly higher in the "Failure" stage followed by "Injury," stage then the "Risk," stage ($p = 0.001$). Hypovolemia/dehydration had the highest [TIMP-2]•[IGFBP7] values followed by sepsis. Urinary [TIMP-2]•[IGFBP7] was significantly increased in mechanically ventilated and patients who received inotropic medications.

Conclusions: [TIMP-2]·[IGFBP7] was higher in AKI patients compared with non-AKI ones especially cases with hypovolemia and sepsis. It may predict severe morbidity and mortality because its higher levels in mechanically ventilated children and those on positive inotropic support.

Keywords: Acute kidney injury, Critically ill children, Pediatric intensive care unit.

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HIGHLIGHTS

Acute kidney injury (AKI) is often an undetected complication in pediatric intensive care units (PICU) patients. Our study assessed the value of urinary biomarkers TIMP-2 and IGFBP-7 in detecting early AKI based on pediatrics risk, injury, failure, loss, end-stage renal disease (pRIFLE) in PICU patients. The study suggests that TIMP-2 and IGFBP-7 could serve as effective diagnostic tools for early detection of AKI.

INTRODUCTION

In the intensive care unit (ICU), the development of AKI is linked to higher rates of morbidity and mortality. Even with great advancements in treatment, AKI still has a high rate of morbidity and mortality.[1] The primary cause of this is the difficulty in diagnosing renal damage and how much time it takes to do so.[2] The AKI is often identified in high-risk individuals, particularly those who are in the critical care unit. It is a substantial morbid factor linked to extended hospitalizations in the ICU, serious sequalae, and ultimately higher mortality.

Better prognoses for critically unwell children depend on preventing acute renal injury and detecting it in its early stages. The basic tools in normal laboratory exams are serum creatinine and urine output, according to Kidney Disease: Improving Global Outcomes (KDIGO). They are not appropriate, therefore, for the early identification of AKI, since serum creatinine does not accurately reflect the glomerular filtration rate in a patient whose renal function is failing, it is frequently a laborious and imprecise test.[3]

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Furthermore, dialysis eliminates creatinine, therefore, once dialysis starts; it is inappropriate.[4] Meanwhile, a variety of issues, including inaccurate measurement, hydration status, and the use of diuretics and fluids, contribute to the variability in urine production in AKI.[5] Numerous urine biomarkers have been proposed in order to identify

AKI early. Many of these were also thought to be beneficial for use in children.[6] The identification of G1 cell cycle arrest indicators, such as tissue inhibitor of metalloproteinase-2 (TIMP-2) and insulin-like growth factor-binding protein 7 (IGFBP7) in urine, for the early identification of renal injury has been validated by research.[7] Renal tubular cells have a halt in the G1 cell cycle.

After injury, which is meant to prevent cells from proliferating when DNA damage has occurred.[8] Consequently, it is likely to result in apoptosis, cellular senescence, or cellular repair, including the restoration of genomic integrity.[9] Renal tubular cells express the cell-cycle arrest proteins TIMP2 and IGFBP7 in response to cellular stress. The TIMP2 directly promotes cell division or induces G1 cell-cycle arrest to regulate the cell cycle in addition to inhibiting matrix metalloproteinase. A secreted protein, IGFBP7 is a member of the IGFBP superfamily. Moreover, it has been connected to the G1 cell cycle arrest phase that comes after cellular damage.[10]

When it comes to determining the emergence of moderate or severe AKI based on KDIGO criteria in high-risk individuals, urinary [TIMP-2] • [IGFBP7] performed its function more effectively.[11]

Not much study has been done on the benefit of TIMP-2 and IGFBP-7 in pediatrics. Further research is necessary to predict cell-cycle markers of acute renal damage biomarkers in children, despite the promising results.[12] Therefore, our aim is to assess the urine TIMP-2 and IGFBP-7 early predictive value for the development of acute renal injury in pediatric ICU patients as well as the prediction of potential adverse clinical outcomes.

METHODS

A case-control study was conducted involving every patient seen from April 2021 to December 2021 at Cairo University's Pediatric ICU at the Abo El-Elrish Teaching Hospital. Prematurity, inherited nephropathies, chronic dialysis patients, and cyclosporine recipients were the exclusion criteria. During the initial 24 hours following PICU admission, serum creatinine, urine TIMP2, and IGFBP7 were measured. Every child included underwent a comprehensive clinical examination and history taking, with particular attention paid to demographic data, the administration of nephrotoxic drugs, urine output, mean arterial pressure, and the length of the PICU hospitalization.

The severity of illnesses in critically ill children was examined through the pediatric sequential organ failure assessment score (pSOFA). In the initial 24 hours after admission, it was calculated.[13] The six organ systems that are tested by pSOFA are the neurological, hematological, renal, hepatic, respiratory, and cardiovascular. Each component has a subscore ranging from 0 to 4 points; the sum of the six subscores (which have a range of 0–24 points; larger scores denote a poorer outcome) was used to compute the daily pSOFA score.[13,14] The revised Schwartz formula: ($k = 0.413 \times$ height/serum creatinine) was adopted to estimated creatinine clearance (eCCl) in children.[15]

The lowest serum Cr value in the 3 months before the research was extracted from the hospital documents to assess the initial eCCl. If the patient's baseline serum creatinine was unknown and their medical records did not include any prior renal injury, they were deemed to have normal kidney function and were prescribed a baseline eCCl of 120 mL/min per 1.73 m².[16]

The pediatrics risk, injury, failure, loss, end-stage renal disease (pRIFLE) classification is based on the eCCl, where "Loss" is defined as persistent renal failure lasting more than 4 weeks, "Risk" concluded to be when the eCCl decreases by 25% from baseline, "Injury" is concluded to be when the eCCl decreases by 50%, and "Failure" is indicated by a 75% reduction in the eCCl or an absolute value <35 mL/min per 1.73 m².

Every day, follow-ups are conducted to determine which individuals have AKI during their ICU stay. Adverse clinical outcome included: length of PICU stay, inotropic medicine, mechanical ventilation, nephrotoxic drug effects, death or discharge, and multisystem failure (pSOFA).

Biomarker Estimation

Within the first 24 hours following PICU admission, each patient provided fresh urine samples via sterile tubes. The samples were centrifuged at 2000–3000 RPM for about 20 minutes, and the supernatant was subsequently preserved at –80°C. Using a microplate ELISA reader (STAT FAX 2100 Microplate Reader), commercially available sandwich ELISA kits were used to estimate the urinary TIMP-2 (Cat. No. E1218Hu) and IGFBP-7 (Cat. No. E1218Hu). In order to present the values of TIMP-2 and IGFBP-7 in the urine sample in international general units, (ng/mL)²/1,000, in agreement with others, the values of [TIMP-2]*[IGFBP7] were multiplied and then divided by 1,000.[17]

Statistical Analysis

The statistical software SPSS version 15 for Windows (SPSS Inc., Chicago, Illinois, USA) was used to analyze the data. Prior to analysis, the normality of the quantitative variable distribution was evaluated through the application of the Kolmogorov–Smirnov Z test. The mean, standard deviation, and frequencies (number of patients) and relative frequencies (percentages) were used to summarize the data for the normally distributed variables. The means of the variables for the two unrelated groups were compared using the independent t-test. For quantitative variables, on the other hand, the non-normally distributed variables were shown as the median and interquartile range (IQR 25th–75th). The Mann–Whitney test was utilized to compare two non-parametric groups. In contrast, the Kruskal–Wallis test was applied for comparing data from more than two groups.

Receiver-operator characteristic (ROC) curves were created, and the area under the curve (AUC) was computed, in order to quantify the sensitivity and specificity. The AUC values of 0.5 indicate that a biomarker is no better than chance, whereas values of 1.0 indicate an optimal biomarker. The p-values less than 0.05 were considered as significant.

RESULTS

Patient Characteristics

One hundred and twelve participants, comprising forty seemingly healthy control youngsters and 72 patients, took part in the study. Table 1 shows the clinical, laboratory, and demographic data for the patients and controls. In 52 (72.2%) of the 72 critically ill patients, AKI developed.

The comparison among the patients who had AKI and those who did not, is shown in Table 2. It showed that the AKI group had a significantly higher serum creatinine, significantly lower eCCl, significantly higher level for CRP and pSOFA score ($p = 0.001$, $p = 0.001$, $p = 0.01$, and $p = 0.001$), respectively. Urinary [TIMP-2]• [IGFBP7] was significantly higher in the AKI group than those who do not have AKI ($p = 0.007$). Compared with the non-AKI group, the AKI group's PICU hospitalization lasted 1.8 times longer.

When the study first commenced, seven patients had a normal initial eCCl. Twenty six patients (50.0%) fulfilled the "Risk," 18

Table 1: Demographic data of cases and controls

Characteristic	Patients (n = 72)	Healthy controls (n = 40)	p-value
Age (years)	0.6 (0.25–2)	0.75 (0.52–2.2)	0.27
Male	40 (55.6%)	18 (45%)	0.3
Female	32 (44.4%)	22 (55%)	
Weight (kg)	6.5 (4–10)	9 (5–12)	0.4
Height (cm)	66 (57.25–81.25)	74 (48–110)	0.25
BMI (kg/m^2)	14 (12.13–16.38)	14.5 (3–17)	0.5
Urine output (cc/kg/h)	2.4 (1.6–3.2)	2 (1.2–3)	0.2
Initial serum Cr (mg/dL)	0.6 (0.4–0.78)	0. 4 (4–0.58)	0.002*
[TIMP-2]•[IGFBP7] (ng/mL)^2/1000	0.19 (0.14–0.25)	0.05 (0.04–0.08)	0.001*

Data are presented as median and interquartile range

patients (34.6%) the "Injury," 1 (1.9%) the "Failure" and 0 patient (0%) the "Loss" criteria. None of the patients developed end-stage renal disease.

At follow-up, 9 of the patients worsened, reaching the next pRIFLE stage and 22 (42.3%) fulfilled the "Risk," 24 (46.2%) the "Injury," 6 (11.5%) the "Failure" and 0 patient (0%) the "Loss" (Table 2). Etiologies of AKI were post-infectious glomerulonephritis [n = 1 (1.9%)], hemodynamic instability [n = 15 (28.8%)], hypovolemia/dehydration [n = 9 (17.3%)], acute ischemia [n = 7 (13.5%)], and sepsis [n = 20 (38.5%)] (Table 2).

Level of Urinary [TIMP-2]•[IGFBP7] in the Subgroups

The "Failure" stage had a significantly higher urine [TIMP-2]•[IGFBP7] [median 0.48 (IQR 0.42–0.58)] than the "Injury" stage [median 0.22 (IQR 0.19–0.28)], which was followed by the "Risk" stage [median 0.16 (IQR 0.13–0.21)] (p = 0.001) (Fig. 1).

Table 2: Demographic, clinical and laboratory data of patients subgroups according to the occurrence of AKI

Characteristic	Group I (AKI group) (n = 52)	Group II (Non-AKI group) (n = 20)	p-value
Age (years)	0.5 (0.19–1.9)	0.83 (0.5–1.5)	0.17
Male	31 (59.6%)	9 (45%)	0.26
Female	21 (40.4%)	11 (55%)	
Weight (kg)	5.75 (4–10)	7 (5–10)	0.16
Height (cm)	65 (55.25–81.25)	71 (60.75–86.25)	0.34
BMI (kg/m^2)	14.34 (12.13–15.75)	15.2 (12.25–17.09)	0.4
CRP (mg/L)	52.2 (0.1–303)	21 (0.4–119)	0.01*
Urine output (cc/kg/h)	2.7 (1–5.9)	2 (0.7–3.5)	0.08
Initial SCr (mg/dL)	0.6 (0.2–1.8)	0.4 (0.3–0.6)	0.001*
Maximum SCr (mg/dL)	0.7 (0.4–2.8)	0.45 (0.3–0.6)	0.001*
Initial eCCl (mL/min per 1.73 m^2)	43.3 (16–210)	93.25 (38.5–137-5)	0.001*
Maximum eCCl (mL/min per 1.73 m^2)	38.9 (11–84.3)	92.7 (44–137.5)	0.001*
Urinary [TIMP2]•[IGFBP7] (ng/mL)^2/1,000	0.21 (0.15–0.28)	0.15 (0.07–0.2)	0.007*
pSOFA	7.5 (2–18)	3 (2–9)	0.001*
Duration of ICU stay (days)	8 (2–43)	4.5 (2–11)	0.004*
30-day mortality	21 (40.4%)	4 (20 %)	0.001*
Initial pRIFLE stage (n = 45)			
Risk	26 (50%)		
Injury	18 (34.6%)		
Failure	1 (1.9%)		
Loss	0		
Maximum pRIFLE stage (n = 52)			
Risk	22 (42.3%)		
Injury	24 (46.2%)		
Failure	6 (11.5%)		
Loss	0		
AKI etiology			
Severe sepsis/Septic shock	20 (38.5%)		
Hemodynamic instability	15 (28.8%)		
Hypovolemia/dehydration	9 (17.3%)		
Acute ischemia	7 (13.5%)		
Post-infectious glomerulonephritis	1 (1.9%)		

Data are presented as median and interquartile range. AKI, acute kidney injury; CRP, C-reactive protein; eCCl, estimated creatinine clearance; pSOFA, pediatric sequential organ failure assessment score; SCr, serum creatinine
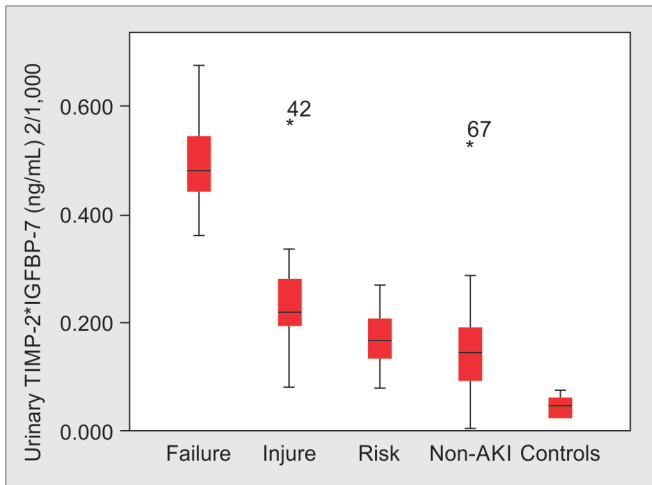
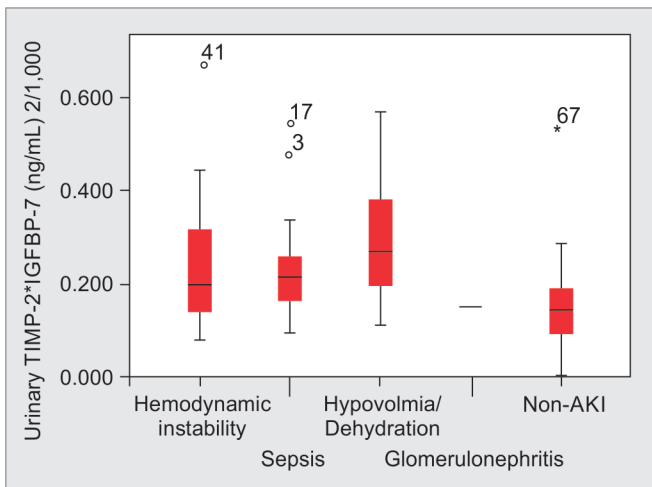**Fig. 1:** Urinary [TIMP-2]•[IGFBP7] in established AKI patients based on pRIFLE classification

Table 3: Comparisons of urinary [TIMP-2] •[IGFBP7] in different subgroups of patients

Patients (n = 72)	Urinary [TIMP-2]•[IGFBP7] (ng/mL)^2/1,000	p-value
Outcome		
Death (n = 25)	0.23 ± 0.14	0.4
Discharge (n = 47)	0.2 ± 0.11	
Nephrotoxic drugs		
Yes (n = 48)	0.23 ± 0.13	0.27
No (n = 24)	0.17 ± 0.10	
Mechanical ventilation		
Yes (n = 32)	0.25 ± 0.15	0.02*
No (n = 40)	0.18 ± 0.09	
Inotropes		
Yes (n = 32)	0.25 ± 0.17	0.001*
No (n = 40)	0.17 ± 0.06	

The data presented as (Mean ± SD)

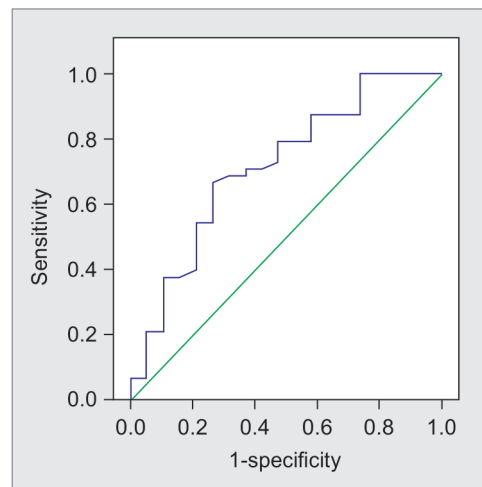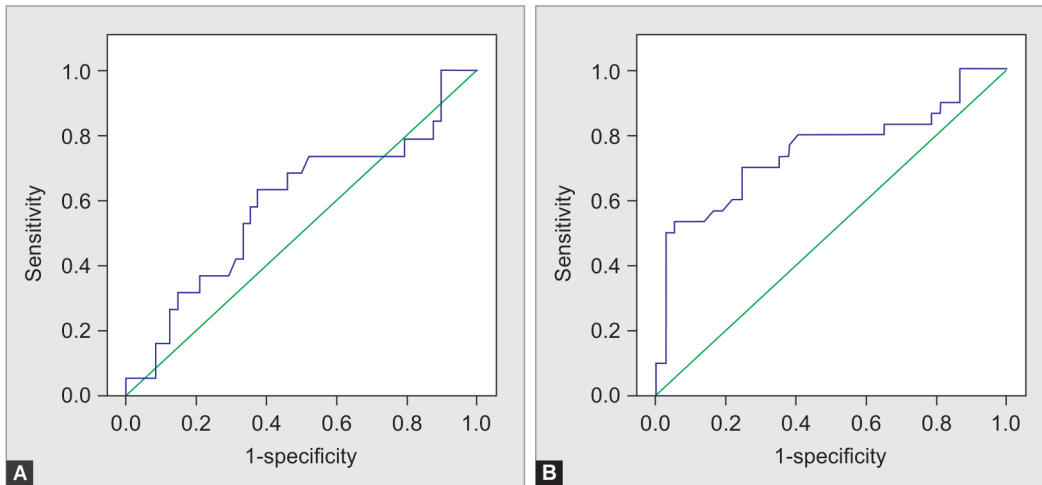**Fig. 2:** Boxplots of urinary [TIMP-2]•[IGFBP7] for varied AKI etiologies

Fig. 3: Receiver operating characteristic (ROC) curve analysis of TIMP-2*IGFBP-7 (ng/mL)^2 for early prediction of AKI in critically ill children at cut-off points of 0.2 (ng/mL)^2/1,000. AUC = 0.71, specificity of 76.4%, sensitivity of 56.25%

According to the underlying AKI etiology, the highest significant [TIMP-2]•[IGFBP7] value was present in patients with hypovolemia/dehydration [median 0.217 (IQR 0.096–0.544)]. Subsequently, a significant increase was found in sepsis [median 0.199 (IQR 0.079–0.675)] compared with non AKI group [median 0.15 (IQR 0.07–0.2)] (p = 0.01) (Fig. 2).

Urinary [TIMP-2]•[IGFBP7] significantly increased in mechanically ventilated and patients who received inotropic medications compared with non AKI (p = 0.0.02 and 0.001, respectively) as shown in Table 3.

Validity of [TIMP-2]•[IGFBP7] to Predict Morbidity and Mortality

When all the cases were analyzed for [TIMP-2]•[IGFBP7] as an early marker of AKI, the AUC was 0.71 (sensitivity 56%, specificity 76.4%) at cut-off point 0.2 (ng/mL)^2/1000 (Fig. 3). Moreover, prognostic accuracy of [TIMP-2]•[IGFBP7] for pSOFA was separately analyzed. The [TIMP-2]•[IGFBP7] attained a sensitivity of 73% and a specificity of 48% for adverse outcomes (AUC = 0.59) while a sensitivity of 80% and a specificity of 60% of pSOFA (AUC = 0.75) (Fig. 4).

DISCUSSION

Acute kidney injury is a frequent adverse event seen in patients admitted to the PICU. It is commonly associated with longer stays in the PICU and hospital as well as increased risks of both short- and long-term mortality.

It was found that the most frequent etiologies of AKI in the critically ill patients are hypovolemia and sepsis followed by nephrotoxic agents.[18] According to the current study, infections accounted for 38.5% of AKI cases, which is in line with previous findings.[19] This can be explained by the substantial degradation of blood flow distribution brought on by sepsis, as well as the reduction of peripheral vascular resistance and disruption of microcirculatory perfusions, such as the renal vasculature. Consequently, abnormal microvascular function and renal inflammation intensify tubular epithelial cells' adaptive response to damage. A reduction in renal function follows as a result.[20]

Figs 4A and B: Receiver operating characteristic (ROC) curve analysis of TIMP-2*IGFBP-7 (ng/mL)^2 for prediction of adverse outcomes (left) and pSOFA score (right)
AUC = 0.59, sensitivity 73%, specificity 48% AUC = 0.75, sensitivity 80%, specificity 60%

The AKI group not only showed significantly higher values for pSOFA ($p = 0.001$) and CRP ($p = 0.01$), but they also spent 1.8 times longer in the PICU than the non-AKI group. Hypovolemia is one of the other etiologies that contribute significantly to the development of AKI. Hypovolemic shock affected nine of our patients (17%). The AKI was more common in critically sick patients who were admitted with hypovolemic shock than others. Shock causes circulatory compromise; hence, renal injury occurs in response to reduced renal blood flow and renal vascular ischemia, and renal function decreases when urine flow declines and excretion is fully knocked out.[21]

Males made up 31 (59.6%) of the patients in the AKI group, which is consistent with their higher vulnerability to renal illness.[22] This is in line with the findings of a study by Halle et al., which discovered that 87 AKI patients (84.5%) out of 103 participants in PICU cases had a median age of 84 months and were primarily male (62%).[23]

Some definitions of AKI that have been used are Acute Kidney Injury Network (AKIN), Kidney Disease: Improving Global Outcomes (KDIGO), and pRIFLE. Each carries its own advantages and limitations for predicting the degree of acute renal injury.

The KDIGO staging and definition system is the more up to date, the preferred definition in pediatric AKI literature. When AKI is detected early rather than AKIN and KDIGO, pRIFLE exhibits higher sensitivity. The three classifications provide excellent inter-stage discrimination and have a strong correlation with the outcome (mortality or length of stay in the PICU).[24] Mild AKI patients, who are frequently missed by the other two techniques, can be quickly and accurately identified by pRIFLE than by serum creatinine alone.

Serum creatinine is influenced by muscle bulk, hydration status, and late elevation after renal insult. Consistent with our results, serum creatinine was proven to be significantly higher in the AKI group at the commencement of the study, compared with the non-AKI group and eCCl noticeably declined in the AKI group compared with the non-AKI one.[25]

The KDIGO recommended diagnosing AKI by urine output and serum creatinine.[26,27] However, a variety of factors, including age, diet, muscle mass, drugs, and the volume of distribution of creatinine, may affect blood creatinine levels. Serum creatinine levels increase gradually, 24–36 hours after renal damage. Serum creatinine measurements are sometimes time-consuming and imprecise, and they do not provide an accurate picture of the glomerular filtration rate in a patient experiencing renal failure. They are, therefore, inappropriate for the initial diagnosis of acute renal damage. Moreover, creatinine is eliminated during dialysis; therefore, it is improper once dialysis begins.[4]

Moreover, blood creatinine levels may be inaccurate in individuals with low muscular mass or fluid overload, which restricts its applicability as a gauge of kidney failure.[28] In addition, a variety of issues, including inaccurate measurement, hydration status, and the administration of diuretics and fluids, contribute to the variability in urine output in AKI.[29] Urine output is significantly less specific and continues until renal function almost completely quits; diuretics can modify this.[30] The G1 cell cycle arrest markers IGFBP7 and TIMP-2 suggest a pre injury condition prior to AKI. They may have an impact on inflammation, oxidative stress, and apoptosis. They can, therefore, indicate early renal damage.[31]

Higher levels of urinary [TIMP-2]•[IGFBP7], have been reported in children with AKI. Our results line up with previous studies conducted among children, indicating that urinary [TIMP-2] *[IGFBP-7] is a valuable AKI marker for the recognition of the deterioration of renal injuries and the mortality in a group of patients with an undetermined time of incidence of renal injuries.[11] Elevations in urine [TIMP-2]*[IGFBP-7] have been linked to necessary renal replacement treatment, longer stays in the ICU, and mortality.[11,32] They are thought to be stress-related indicators of cell cycle arrest that can be found prior to the onset of AKI and have predictive significance, particularly in patients admitted to ICU.[31]

In the present study, the mean urinary level of [TIMP-2]*[IGFBP-7] was significantly higher in the AKI group in comparison to the non-AKI group. In addition, it is also higher in the (failure stage) followed by the (injury) stage then the (risk) one. This is in addition to its higher level in mechanically ventilated children with p value of 0.02 and those on positive inotropic support ($p = 0.001$). This is similar to the findings of Honore et al., who observed higher values of ([TIMP-2]*[IGFBP-7]) in children with AKI in comparison to the non-AKI group, which rose as the severity of the AKI stage increased (stage 3 > stage 2 > stage 1). This illustrates the predictive role of these markers in early diagnosis of AKI.[33]

Sepsis cases who developed AKI showed a higher quantity of [TIMP-2]*[IGFBP-7] as opposed to those who didn't which is consistent with our results where the mean urinary level of ([TIMP-2]*[IGFBP-7]) was significantly higher in cases with hypovolemia and dehydration, sepsis, and hemodynamic instability.[34]

Excellent prediction performance with sensitivity and specificity is a critical first step toward the use of new biomarkers of AKI in clinical practice. Urinary [TIMP-2]*[IGFBP-7] studies were conducted, and the results showed that these tests had better diagnostic performance in predicting moderate to severe AKI (KDIGO stages 2 and 3). One study by Hoste et al. reported an AUC of 0.94, and it was also shown that a cut-off value of 0.3 could predict moderate to severe AKI.[35] With a cut-off point of 0.2 (ng/mL)[2], our results for [TIMP-2]*[IGFBP-7] showed an AUC of 0.71, 56.25% sensitivity, and 76.4% specificity.

In a different study involving ICU patients, Kashani et al. found that TIMP-2 and IGFBP7 had respective AUCs of 0.76 and 0.79.[36]

Numerous studies used 0.3 as the lower cut-off value, however, they involved adult (age > 21 years) patients.[7,32] Another study by Westhoff found that death or dialysis within 3 months in patients with AKI and [TIMP-2] • [IGFBP7] values > 2.0 (high specificity) are at higher risk for adverse outcomes than those with values < 0.3.[11]

Several recent meta-analyses have revealed that the urinary TIMP-2 and IGFBP7 cut-off of 2.0 (ng/mL)[2]/1,000 in the late stages of AKI has the highest overall accuracy.[37]

Since the median in our study was 0.19 (0.14–0.25) for patients and 0.21 (0.15–0.28) for the AKI group, a lower cut-off point of 0.2 was more convenient and sensitive because we were unable to utilize a higher cut off than the median. Because established assays in clinical routine practice have low sensitivity, early identification of patients at high risk of AKI is impeded. In a study comparable to ours, Adler discovered that in high-risk post-cardiac arrest patients, a 0.24 cut-off point accurately predicts AKI.[38]

Furthermore, in our study [TIMP-2]*[IGFBP-7] ROC curve for prediction of adverse outcome and pSOFA score was done with (80 and 73%) sensitivity and (60 and 48%) specificity, respectively, which reflects its role in determining morbidity and mortality in PICU.

Conclusion

Urinary [TIMP-2]*[IGFBP-7] can detect early AKI especially in cases with sepsis and hypovolemia. The [TIMP-2]*[IGFBP-7] can be used to predict severe morbidity and mortality because it's higher levels in mechanically ventilated children and those on positive inotropic support.

Ethical Approval

This study is approved by the Ethics Committee of the NRC in Egypt.

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