

CORRELATION ANALYSIS OF ULTRASONOGRAPHY KIDNEY MORPHOLOGICAL PROFILES AND THE CLASSIFICATION OF PERSISTENT AND TRANSIENT ACUTE KIDNEY INJURY IN CHILDREN DURING THE PANDEMIC PERIOD AT THE DR. SOETOMO GENERAL TEACHING HOSPITAL

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Abstract

Introduction: During the COVID-19 pandemic, especially in 2022, there were 189 cases of Atypical Progressive Acute Kidney Injury (AKI) in children in Indonesia. A phenomenon has been observed where children exposed to COVID-19 accompanied by MIS-C are significantly more at risk of experiencing AKI. The role of Ultrasonography (USG) examination in children is not only to rule out obstructive urinary tract abnormalities but also to provide radiological morphological kidney images consistent with AKI conditions. Morphological features include increased kidney length, echogenicity, volume, and parenchymal thickness. In addition to severity classification (staging), a classification of AKI types in children has been proposed, categorized into Persistent and Transient AKI, referring to recovery time. Recovery is defined as a minimum one-degree decrease in severity according to KDIGO AKI Staging criteria within less than 72 hours. This categorization would facilitate management and etiological evaluation.

Aims: This study aims to determine the correlation between kidney morphology ultrasound and the occurrence of persistent/transient AKI classification in children during this research circumstances.

Methods: This study employed an analytical observational design with a retrospective approach. The study population comprised all medical record data of pediatric patients diagnosed with AKI aged 0-18 years at Dr. Soetomo General Teaching Hospital to assess the relationship between persistent/transient AKI and kidney morphology on USG during the COVID-19 pandemic in 2022. **Result** The study indicates a significant correlation between persistent/transient AKI classification groups and the right kidney ($p=0.007$, correlation coefficient 0.484) and the left kidney ($p=0.002$, correlation coefficient 0.552), total kidney volume ($p=0.008$, correlation coefficient 0.546), right kidney parenchymal thickness ($p=0.025$, correlation coefficient 0.408), left kidney parenchymal thickness ($p=0.004$, correlation coefficient 0.509), and echogenicity classification of kidney parenchyma ($p=0.029$, correlation coefficient 0.398). However, there was no significant relationship between persistent/transient AKI classification groups and the variable of obstructive uropathy features ($p=0.506$). **Conclusion:** There is a significant relationship between Persistent/Transient AKI groups and kidney morphology, specifically in kidney length classification, total kidney volume, kidney parenchymal thickness, and echogenicity classification of kidney parenchyma. However, there is no significant correlation with the variable of obstructive uropathy features.

Keywords: Persistent/Transient AKI; Ultrasound; Children

1. Introduction

COVID-19 infection cases in adults are indeed much higher compared to cases in children, and clinical symptoms in children are relatively milder compared to adults. However, COVID-19 infection can develop

into a condition known as Multisystem Inflammatory Syndrome, a clinical condition that is not commonly encountered but can be quite serious in COVID-19-infected individuals (CDC 2020; Dufort et al. 2020; Lee et al. 2020). Since 2020, the Center for Disease Control and Prevention (CDC) has recorded 9,455 cases of Multisystem Inflammatory Syndrome in Children (MIS-C) during the pandemic, with a total of 78 deaths worldwide (CDC 2022).

In children with acute COVID-19 infection accompanied by clinical manifestations consistent with MIS-C criteria, there is a higher risk of Acute Kidney Injury (AKI). Until October 2022, there were 189 cases of atypical progressive AKI in children in Indonesia, predominantly affecting those aged 1 to 5 years (Ministry of Health 2022).

For AKI patients, ultrasound examinations (USG) typically serve to rule out obstructive abnormalities in the urinary tract (postrenal AKI) (Podoll, Walther, and Finkel 2013). However, modern USG techniques now offer comprehensive radiological imaging of kidney morphology, aiding in the diagnosis of AKI. Recent studies have shown that USG results in AKI cases often reveal increased kidney length, echogenicity, volume, and parenchymal thickness (Liu and Wang 2020).

Children with clinical AKI can be classified into Persistent AKI and Transient AKI categories (Ozlu and Bayhan 2021; Hoste et al. 2018). This classification refers to the recovery time, where recovery is defined as a minimum decrease of one stage according to KDIGO criteria, therefore, it would be more useful to determine the management and etiological evaluation accordingly (Kellum et al. 2021).

The findings from kidney USG can provide information on the morphological profile components and are expected to strengthen their role in Persistent and Transient AKI cases in pediatric patients.

2. Methode

This study utilized an analytical observational design with a retrospective approach. The study population consisted of all medical record data of pediatric patients aged 0-18 years with a diagnosis of AKI (Acute Kidney Injury) based on a minimum increase in creatinine of 1.5 times from baseline and/or urine output <0.5 cc/kgBW/hour within 6 hours, in accordance with KDIGO AKI criteria (Chawla et al. 2017; Kellum 2015), during the period from January 1 to December 31, 2022, at Dr. Soetomo General teaching Hospital in Surabaya.

This research sample consists of the total population that meets the inclusion and exclusion criteria. Inclusion criteria include patients aged 0-18 years with a minimum clinical presentation of two (2) MIS-C criterias according to WHO and patients diagnosed with AKI clinically requested for renal ultrasound examination. Exclusion criteria include the presence of established etiology other than MIS-C (e.g., sepsis, shock, hypovolemic, others) (WHO 2021; Molloy et al. 2023).

The research instrument used in renal ultrasound examination is the Philips Ultrasound ClearVue 550 ultrasound machine with Convex 1.8-3.2 MHz and Linear 5.3 MHz probes. The interpretation of ultrasound images is carried out by a pediatric radiology subspecialist with approximately 20 years of experience, anonymously and randomly, with two observations made at different time intervals.

The data analysis in this study utilized quantitative data analysis to determine the correlation between variables, calculated using IBM® SPSS® Statistics version 26 software. The study employed the Spearman correlation test to ascertain both the direction and strength of the relationship between variables characterizing renal ultrasound morphology and the categories of Persistent and Transient AKI classification. Additionally, a

comparative analysis of Cohen's Kappa was conducted to evaluate the inter-observer reliability between the initial and subsequent observations made by the observer (Akoglu 2018).

In collecting data, the researcher obtained ethical clearance from the Research Ethics Committee, Dr. Soetomo General Teaching Hospital.

3. Result

3.1. Data Distributions

From medical record observations of 35 research samples, 30 patients with AKI were identified. Distribution of observed data is shown in Table 1 below:

Table 1. Distribution of observed data

| Sample with Acute Kidney Injury (n=30) | | Value (n) | Percentage |
|--|-------------------------------------|-----------|------------|
| Gender | | | |
| 1 | Male | 19 | 54% |
| 2 | Female | 16 | 46% |
| Age | | | |
| 3 | Median Population at 3-12 years old | 20 | 66,6% |
| 4 | Youngest age at 1-2 years old | 6 | 17,1% |
| 5 | Oldest age at 14-15 years old | 1 | 3,33% |
| Acute Kidney Injury Staging | | | |
| 6 | Stage 1 | 6 | 20% |
| 7 | Stage 2 | 7 | 23,3% |
| 8 | Stage 3 | 17 | 56,7% |
| Acute Kidney Injury Type | | | |
| 9 | Transient AKI | 9 | 30% |
| 10 | Persistent AKI | 21 | 70% |

From the distribution of the data above, it appears that there is a dominance of stage 3 AKI occurrences amounting to 56.7%, accompanied by Persistent AKI occurrences, which also dominate at 70%.

3.2. Correlation Characteristic of Kidney Length Classification towards Persistent/Transient AKI.

From 30 patients with Persistent/Transient AKI identified, the length of the kidney in the ultrasound image is measured along the longitudinal axis and a comparison of the obtained sizes was made against the normal values of kidney length according to age (Liu and Wang 2020; Obrycki et al. 2023), resulting in the distribution of kidney length classification variables as shown in Table 2 below:

Table 2. Distribution of Kidney Length Classification

| Kidney Lenght | Right | Left |
|------------------|-------|------|
|------------------|-------|------|

| Classification | n | % | n | % |
|----------------|-----------|-------------|-----------|-------------|
| Decreased | 6 | 20% | 5 | 16,7% |
| Normal | 7 | 23,3% | 7 | 23,3% |
| Increased | 17 | 56,7% | 18 | 60% |
| Total | 30 | 100% | 30 | 100% |

Based on the distribution of the classification variable, increase in kidney length was found dominantly in both the right (56,7%) and left kidneys (60%), furthermore a cross-tabulation was performed against the Persistent/Transient AKI classification group, which can be seen in Table 3 below:

Table 3. Contingency Table of Kidney Length Classification towards Persistent/Transient AKI

| Classification | Right Kidney Lenght | | | Left Kidney | | |
|-------------------------------|---------------------|-----------|-----------|-------------|-----------|------------|
| | Decreased | Normal | Increased | Decreased | Normal | Increased |
| Transient AKI (n=9) | 4 (13,3%) | 3 (10%) | 2 (6,7%) | 4 (13,3%) | 3 (10,0%) | 2 (6,7%) |
| Persistent AKI (n= 21) | 2 (6,7%) | 4 (13,3%) | 15(50%) | 1 (3,37%) | 4 (13,3%) | 16 (53,3%) |

In those variables, a Spearman test was conducted to determine the strenght of correlation between the variable of kidney length classification and the classification groups of persistent/transient AKI types. The test yielded significant positive correlation results for both the right kidney ($p=0.007$, correlation coefficient 0.484) and the left kidney ($p=0.002$, correlation coefficient 0.552).

3.3. Correlation in Characteristics of Kidney Volume Classification towards Persistent/Transient AKI.

While the length of the kidney in the ultrasound image is measured along the longitudinal axis, the width and thickness of the kidney are measured along the transverse axis perpendicular to the longitudinal axis (Liu and Wang 2020; Obrycki et al. 2023), The right and left kidney volume was calculated using this formula below:

$$\text{Volume of Kidney} = 0.49 \times \text{kidney length} \times \text{kidney width} \times \text{kidney thickness} \text{ (Liu and Wang 2020).}$$

Subsequently, classification of total kidney volume from 30 samples with AKI was compared with reference values (Leung et al. 2007), yielding the results in Table 4 below:

Table 4. Distribution of Total Kidney Volume Classification

| Total Kidney Volume | n | % |
|---------------------|----|-------|
| Decreased | 7 | 23,3% |
| Normal | 3 | 10,0% |
| Increased | 20 | 66,7% |

| | | |
|--------------|----|------|
| Total | 30 | 100% |
|--------------|----|------|

Based on the distribution of the total kidney volume classification variables, a decreased kidney volume was obtained by (23.3%), a normal kidney volume by (10,0%), and an increased kidney volume by (66.7%). a further cross-tabulation was performed against the Persistent/Transient AKI classification group, which can be seen in Table 5 below:

Table 5. Contingency Table of Total Kidney Volume Classification towards Persistent/Transient AKI

| Classification | Total Kidney Volume | | |
|-------------------------------|---------------------|-----------|-----------|
| | Decreased | Normal | Increased |
| Transient AKI (n=9) | 4 (13,3%) | 3 (10%) | 2 (6,7%) |
| Persistent AKI (n= 21) | 2 (6,7%) | 4 (13,3%) | 15 (50%) |

In those variables, a Spearman test was conducted to determine the strenght of correlation between the total kidney volume classification group towards the Persistent/Transient AKI type classification group, a significant positive correlation test result was obtained ($p=0.002$, correlation coefficient 0.546).

3.4. Correlation Characteristics of Renal Parenchymal Thickness Classification towards Persistent/Transient AKI.

In 30 samples with AKI, ultrasound kidney image measurements were taken for parenchymal thickness parameters, determined as the shortest distance from the renal sinus fat perpendicular to the kidney capsule, measured in the middle quadrant of the kidney (Liu and Wang 2020). The obtained value was compared with reference values (Kadioglu 2010), yielding the results in Table 6 below :

Tabel 6. Distribution of renal parenchymal thickness Classification

| Parenchymal Thickness | Right Kidney | | Left Kidney | |
|-----------------------|--------------|-------|-------------|-------|
| | n | % | n | % |
| Decreased | 0 | 0% | 0 | 0% |
| Normal | 2 | 6,7% | 3 | 10,0% |
| Increased | 28 | 93,3% | 27 | 90% |
| Total | 30 | 100% | 30 | 100% |

In the AKI patient group, no decrease in parenchymal thickness was observed. Moreover, within the normal range of thickness, findings indicated 6.7% in the right kidney and 10% in the left kidney. Notably, a significant increase in kidney parenchymal thickness was predominantly observed in both the right and left kidneys (93.3% and 90% respectively). Subsequent cross-tabulation analysis was conducted towards

Persistent/Transient AKI classification groups, as illustrated in Table 7 below

Table 7. Contingency table of Renal Parenchymal Thickness Classification towards Persistent/Transient AKI

| Classification | Right Kidney Parenchymal Thickness | | Left Kidney Parenchymal Thickness | |
|-------------------------------|------------------------------------|-----------|-----------------------------------|-----------|
| | Normal | Increased | Normal | Increased |
| Transient AKI (n=9) | 2 (6,7%) | 7 (23,3%) | 3 (10%) | 6 (20%) |
| Persistent AKI (n= 21) | 0 (0%) | 21 (70%) | 0 (0%) | 21 (70%) |

Based on Spearman correlation analysis between the groups of kidney parenchyma thickness classification and the groups of Persistent/Transient AKI classification, significant positive correlations were found for both the right kidney ($p=0.025$, correlation coefficient 0.408) and the left kidney ($p=0.004$, correlation coefficient 0.509).

3.5. Correlation Characteristics of Classification Variables of Kidney Parenchymal Echogenicity towards Persistent/Transient AKI.

Based on the kidney ultrasound interpretation, three distinct groups of kidney parenchymal echogenicity were identified: hypoechoic, isoechoic, and hyperechoic, in comparison to the echogenicity of liver and spleen parenchyma (Liu and Wang 2020). The distribution of the echogenicity classification variable of the renal parenchyma can be seen in the table 7 below:

Table 7. Distribution of Renal Parenchymal Echogenicity Classification

| Parenchymal Echogenicity | Right Kidney | | Left Kidney | |
|--------------------------|--------------|-------|-------------|-------|
| | n | % | n | % |
| Hypoechoic | 4 | 13,3% | 4 | 13,3% |
| Isoechoic | 24 | 80,0% | 24 | 80,0% |
| Hyperechoic | 2 | 6,7% | 2 | 6,7% |
| Total | 30 | 100% | 30 | 100% |

According to the distribution outlined above, hypoechoic renal parenchyma was detected in both the right and left kidneys at a frequency of (13.3%), while isoechoic renal parenchyma was observed in both kidneys at a rate of (80%). Similarly, hyperechoic renal parenchyma was found in both the right and left kidneys, each at a rate of (6.7%). Subsequently, these findings were cross-tabulated against the Persistent/Transient AKI classification group, as illustrated in Table 8 below:

Table 8. Contingency Table of Kidney Parenchymal Echogenicity Classification towards Persistent/Transient AKI

| Classification | Right Kidney Echogenicity | | | Left Kidney Echogenicity | | |
|-------------------------------|---------------------------|------------|-------------|--------------------------|------------|-------------|
| | Hypoechoic | Isoechoic | Hyperechoic | Hypoechoic | Isoechoic | Hyperechoic |
| Transient AKI (n=9) | 3 (10,0%) | 6 (20,0%) | 0 (0,0%) | 3 (10,0%) | 6 (20,0%) | 0 (0,0%) |
| Persistent AKI (n= 21) | 1 (3,3%) | 18 (80,0%) | 2 (6,7%) | 1 (3,3%) | 18 (80,0%) | 2 (6,7%) |

In this comparison group, Spearman's test results revealed a positive significant relationship between the Persistent/Transient AKI Classification and the variable of classification kidney parenchyma echogenicity of the both right and left kidney ($p=0.029$, correlation coefficient 0.398).

3.6. Correlation Characteristics of Obstructive Uropathy Features towards Persistent/Transient AKI Cases.

In this study of 30 samples in AKI group, an evaluation of features indicative of Obstructive Uropathy was undertaken, including the dilatation of the renal pelvis and ureter, which may be accompanied by cortical thinning or the presence of obstructive material. The corresponding data is presented in Table 9 below:

Table 9. Distribution of Variables in Obstructive Uropathy Renal Features

| Obstructive Uropathy Features | Right Kidney | | Left Kidney | |
|-------------------------------|--------------|-------|-------------|-------|
| | n | % | n | % |
| Not Present | 29 | 96,7% | 29 | 96,7% |
| Present | 1 | 3,3% | 1 | 3,3% |
| Total | 30 | 100 | 30 | 100 |

According to the table 9, there was only one (3,3%) of sample that showing obstructive uropathy feature that is moderate dilatation of the pelvis dan dilatation of proximal ureter of both kidney.

Furthermore, based on these results, a cross-tabulation was conducted against the Persistent/Transient AKI Classification group, which can be seen in Table 10 below:

Table 10. Contingency Table of Obstructive Uropathy Features towards Persistent/Transient AKI

| Category | Right Kidney Obstructive Uropathy Features | | Left Kidney Obstructive Uropathy Features | |
|-------------------------------|--|----------|---|----------|
| | Not Present | Present | Not Present | Present |
| Transient AKI (n=9) | 9 (30%) | 0 (0%) | 9 (30%) | 0 (0%) |
| Persistent AKI (n= 21) | 20 (66,7%) | 1 (3,3%) | 20 (66,7%) | 1 (3,3%) |

Based on the Spearman correlation analysis, no significant correlation was observed between the

variables representing obstructive uropathy and the classification of Persistent/Transient AKI, for both the right and left kidneys ($p=0.522$, $\alpha=0.05$).

4. Discussion

In this study, observations were made on the morphological profile of kidney ultrasound (USG) in cases classified as Persistent/Transient AKI in pediatric patients, conducted during the surge of COVID pandemic cases in 2022, coinciding with a phenomenon of increased MIS-C cases in children. Although there is still no research found regarding the occurrence of USG findings in Persistent/Transient AKI classification with suspected association to the occurrence of Inflammatory Syndrome in Children (MIS-C), the relationship and influence of the morphological profile of kidney ultrasound examination in AKI cases for Persistent/Transient AKI types can be elucidated in this study.

4.1 Correlation Analysis of Variables of Length Classification, Kidney Volume Classification, and Kidney Parenchymal Thickness towards Persistent AKI/Transient AKI.

The findings of this research indicate a significant correlation between Persistent/Transient AKI types and changes in the classification of length, total volume, and thickness of kidney parenchyma. This is in line with the pathological process that occurs in intra-renal AKI, which involves tubular lumen dilation and inflammatory edema in the interstitial space of the kidney parenchyma. The intercellular tissue structures in the tubules and glomeruli will thicken, and edema in the Injury phase will further progress to fibro-necrotic tissue in the necrosis phase (Gaut and Liapis 2021; Makris and Spanou 2016), Liu et al. stated that this would manifest in an increase in kidney size, including kidney length, kidney volume, and kidney parenchymal thickness (Liu and Wang 2020).

Moses and Fernandes stated that the thickness of the kidney parenchyma can serve as a differentiator between Acute Kidney Injury (AKI) and Chronic Kidney Disease (CKD), where in CKD, the kidney parenchyma gradually narrows with the decrease in glomerular filtration rate (Moses and Fernandez 2022). Conversely, in AKI, an increase in parenchymal thickness is found, especially in cases with intrinsic etiology. However, it is also important to note that tissue damage due to AKI can be irreversible, eventually leading to CKD at a later stage (Chawla et al. 2017; Hsu et al. 2022).

4.2. Correlation Analysis of Persistent/Transient AKI towards Classification Echogenicity of Renal Parenchyma.

The research findings indicate a significant correlation between the Persistent/Transient AKI type and Kidney Parenchymal Echogenicity. According to Kelahan et al. opinion, renal parenchyma begins to show changes towards hypoechoic since the age of 6 months when compared to liver or spleen parenchyma (Kelahan et al. 2019). Therefore, the Isoechoic kidney parenchyma observed in this study's observations (no samples under 1 year old) falls within the classification of renal parenchymal echo that increases alongside kidneys showing hyperechoic parenchyma.

The alterations observed in the renal parenchyma are intricately linked to processes such as Acute Tubular Injury, Acute Tubular Necrosis, and Interstitial Nephritis. These pathological mechanisms underlie changes in renal parenchymal echogenicity observed in AKI conditions stemming from Intrinsic Renal etiologies, a scenario that might manifest in MIS-C (Gaut and Liapis 2021; Moses and Fernandez 2022). While the presence of renal echogenicity doesn't necessarily distinguish between the various causes of renal

disease, it can serve as an indicator of the extent of glomerular sclerosis/crescent formation, tubular atrophy, and interstitial inflammation/fibrosis (Kelahan et al. 2019).

4.3. Correlation Analysis of Corellation of Persistent/Transient AKI with Variables of Obstructive Uropathy Features.

The research findings indicate no significant correlation between Persistent/Transient AKI types and Obstructive Uropathy presentation. When an obstructive uropathy features is found in a case of AKI, it is more intended to detect the presence of post-renal etiology, especially obstructive uropathy, so that appropriate management decisions can be made according to the post-renal AKI etiology (Walther, Podoll, and Finkel 2014; Faubel et al. 2014). Therefore, the findings of this study are still relevant to a condition where AKI with suspected intrinsic renal etiology, such as in cases of AKI associated with MIS-C, requires confirmation by the absence of post-renal etiology.

5. Conclusion

In this study, we investigated the morphological characteristics of kidney ultrasound (USG) in pediatric patients diagnosed with Persistent/Transient AKI during the surge of COVID-19 cases in 2022, coinciding with an increase in MIS-C cases in children. While previous research on the occurrence of USG findings in Persistent/Transient AKI with suspected association to MIS-C is lacking, our study sheds light on the relationship between the morphological profile of kidney ultrasound examination and AKI types in this research circumstances.

Our analysis revealed a significant correlation between Persistent/Transient AKI types and changes in kidney length, volume, and parenchymal thickness. These changes align with the pathological processes occurring in intra-renal AKI, involving tubular lumen dilation and other inflammatory process in the kidney parenchyma structure. Moreover, the thickness of kidney parenchyma serves as a differentiator between AKI and CKD, with AKI typically exhibiting increased parenchymal thickness due to intrinsic etiology.

We also found a notable correlation between Persistent/Transient AKI types and renal parenchymal echogenicity. These alterations are associated with pathological mechanisms such as Acute Tubular Injury, Acute Tubular Necrosis, and Interstitial Nephritis, potentially linked to MIS-C. Renal echogenicity, although not specific to the cause of renal disease, can indicate the extent of tissue damage and inflammation.

However, our study did not find a significant correlation between Persistent/Transient AKI types and obstructive uropathy features. Nevertheless, detecting obstructive uropathy features in AKI cases remains crucial for identifying post-renal etiology and guiding appropriate management decisions.

Overall, our findings contribute to understanding the morphological profile of kidney ultrasound in pediatric AKI cases, particularly those that could be associated with MIS-C, emphasizing the importance of further research in this area to improve diagnosis and management strategies.

Acknowledgements

I would like to extend my heartfelt gratitude to all the mentors and teachers in the Radiology Department of Dr. Soetomo General Teaching Hospital for their invaluable guidance and support throughout the course of my research. Their expertise, wisdom, and unwavering dedication have been instrumental in shaping my understanding of radiology and guiding me through the intricacies of this study.

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