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SERUM ANTI-STREPTOLYSIN O TITERS AMONG PATIENTS WITH ACUTE KIDNEY INJURY: A CROSS-SECTIONAL STUDY

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ABSTRACT:

Background: Renal failure is a major clinical problem with diverse etiologies. Among the possible related conditions, infection-associated renal injury may be accompanied by evidence of previous streptococcal exposure. Anti-streptolysin O (ASO) is a serological marker that can support the diagnosis of recent or previous group A Streptococcus infection, particularly in patients with suspected post-streptococcal disease. **Objective:** The objective was to determine the proportion of patients with acute kidney injury (AKI) who had elevated serum anti-streptolysin O (ASO) titers and to describe the distribution of elevated ASO titers across age groups. **Patients and Methods:** This cross-sectional study conducted at Al-Diwaniyah Teaching Hospital in Al-Diwaniyah Governorate during the period 4 July 2020 to 30 January 2021. All 98 patients enrolled had acute kidney injury (AKI), diagnosed clinically by the treating nephrologist based on standard criteria used at the study hospital. A prospective, direct interviewing and clinical assessment approach was used to gather the data. Blood was drawn under strictly sterile precautions, and serum urea, creatinine and ASO levels were measured. Age specific results of ASO were interpreted with reference to age-specific normal ranges. **Results:** A total of 98 patients aged 1–73 years were included. Males constituted 57 patients (58.2%), while females constituted 41 patients (41.8%). Elevated ASO titers were detected in 5 patients (5.1%), whereas 93 patients (94.9%) had ASO titers within the age-specific reference range. Elevated ASO titers were found in patients aged 2-3.9 years (2 cases), 4-5.9 years (1 case), 40-59.9 years (1 case), and ≥60 years (1 case). **Conclusion:** Elevated ASO titers were uncommon among patients with acute kidney injury, occurring in only 5.1% of participants. Most patients (94.9%) had ASO titers within age-specific reference ranges. These findings indicate that elevated ASO was infrequent in this AKI population. When elevated, ASO titers should be interpreted in the context of age, clinical findings, laboratory data, and the timing of testing. An elevated ASO titer alone does not establish post-streptococcal glomerulonephritis.

Keywords: Renal failure; Anti-streptolysin O; ASO titer; Streptococcal infection; Group A *Streptococcus*.

INTRODUCTION

Infection related glomerulonephritis is a significant cause of acute glomerular disease in children and in populations with a high rate of streptococcal and

other bacterial infections. Acute post-streptococcal glomerulonephritis (APSGN) is an important form of post-infectious glomerulonephritis, which can also manifest with hematuria, proteinuria, edema, hypertension, and acute kidney injury. In recent years, it has become clear that a prerequisite to assessing suspected infection-related glomerulonephritis is evidence of a preceding infection plus appropriate clinical and laboratory data **(Meena et al., 2026)**. Nephritogenic strains of group A Streptococcus (*Streptococcus pyogenes*) are believed to be responsible for the preceding infection associated with APSGN. Renal signs or symptoms typically occur after a latent period following the initial infection, as a result of an immune-mediated inflammatory process that affects the glomeruli. Affecting mainly children, APSGN often leads to complications such as acute kidney injury and, in a small number of cases, kidney failure **(Abugrain et al., 2024)**. Past streptococcal infection can be supported using antibodies against the streptococcal antigens. Serological markers that are commonly used to assess previous (GABHS) infection include anti-streptolysin O (ASO) antibodies. *S. pyogenes* is an extracellular pathogen that produces streptolysin O, which induces antibody production. Therefore, if a history of streptococcal infection is unavailable, an elevated ASO titer may offer helpful information regarding past infection **(Sen and Ramanan, 2014)**. Considering the timing of blood sampling is important when interpreting ASO results, and anti-deoxyribonuclease B (anti-DNase B) may give supportive evidence of a previous streptococcal infection. In children with APSGN, both markers have high rates of positivity with some populations indicating that anti-DNase B antibodies show higher positivity than ASO **(Dhaka et al., 2026)**. In addition, the kinetics of the streptococcal antibody response should be taken into account in evaluating serological data. Among patients with invasive group A streptococcal infections, anti-DNase B showed a significant increase, from 40% to 79%, approximately 9 days after admission, whereas a similar rise was observed for ASO, from 33% to 74%, approximately 2 days after admission. A change in the serum sample collection time may affect antibody titers and findings, suggesting that these antibodies complement each other in instances where evidence of past streptococcal infections is required **(Kailankangas et al., 2026)**.The epidemiology of post-streptococcal glomerulonephritis may differ from region to region and reflect variations in the occurrence of group A streptococcal infections. There has been recently reported rise in the number of cases of APSGN, concurrent with the recent increase in group A streptococcal infections, further underlining the epidemiological significance of streptococcal-associated renal disease **(Sanders et al., 2026)**. The epidemiology of post-infectious glomerulonephritis has also changed during and after the pandemic period. A study by Nooreddeen E and colleagues showed that demographics, clinical severity, and streptococcal serology changed between periods, with a decrease in post-infectious

glomerulonephritis (PIGN) incidence in the early pandemic period, and an increase thereafter **(Nooreddeen et al., 2025)**. Renal failure is a highly variable clinical syndrome and can have a variety of renal and systemic causes. APSGN can result in acute infection-related glomerulonephritis, and is frequently accompanied by serious renal involvement. Evidence of previous streptococcal infection (as suggested by either elevated ASO or anti-DNase B titer) can be helpful in the diagnosis of post-streptococcal glomerulonephritis but must not be relied upon alone **(Atasever et al., 2024)**. There is a known association between streptococcal disease and post-infectious glomerular disease, but limited data are available in the local context on the association of ASO serological markers with patients with acute kidney injury. Knowledge of the prevalence of raised ASO levels in this group may provide descriptive and epidemiological data about previous streptococcal exposure and may help to assessment of patients in whom kidney disease is suspected to be caused by streptococcal infections. Hence the current study was designed to ascertain the prevalence of raised serum ASO levels in patients with AKI and to outline the distribution of raised serum ASO levels across various age groups. The study aimed to describe the serological findings obtained from the ASO testing and not to infer causation between previous streptococcal infection and acute kidney injury.

Patients and Methods:

Study design and setting: This was a cross sectional study carried out at Al-Diwaniyah teaching hospital in Al-Diwaniyah Governorate in Iraq between 4 July 2020 and 30 January 2021.

Study population: A total of 98 patients diagnosed with acute kidney injury (AKI) were included in the study. Patients were recruited from the nephrology consultation clinic and inpatient wards at Al-Diwaniyah Teaching Hospital. AKI was diagnosed clinically by the treating nephrologist based on standard criteria used at the study hospital. Patients with end-stage renal disease on maintenance dialysis or with known chronic kidney disease stage 5 were excluded.

Data collection: Relevant demographic and clinical data were collected through direct interviews and review of available clinical records. The collected information included age, sex, and family history of renal disease. Venous blood samples were obtained aseptically from all participant for laboratory investigations.

Laboratory investigation: Five milliliters of venous blood were collected into serum separator tubes. The blood samples were allowed to clot and were then centrifuged to separate the serum. Serum urea, creatinine were measured using routine laboratory procedures. Anti-streptolysin O (ASO) titers were measured in the hospital laboratory using a standard serological assay, and results were expressed in Todd unit per milliliter (Todd unit/ml). ASO results were interpreted according to the age-specific reference ranges provided by the laboratory.

Ethical considerations: The purpose and procedures of the study were explained to the participants or their parents/guardians prior to participation,

and informed consent was obtained. The study was conducted in accordance with the ethical standards of the responsible institutional committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Ethical approval was obtained from the Ethics Committee of Al-Diwaniyah Teaching Hospital (approval number and date to be inserted if available).

Statistical Analysis: IBM SPSS Statistics version 20 was used for data analysis. Demographic and laboratory characteristics were summarized using descriptive statistics. Categorical variables were presented as frequencies and percentages, while continuous variables were summarized using appropriate measures of central tendency and dispersion.

Results:

Demographic Characteristics:

The total number of patients included in the study with acute kidney injury was 98. The age of participants ranged from 1 to 73 years. Males predominated (57, 58.2%), followed by females (41, 41.8%), giving a male-to-female ratio of 1.39:1 **(Table 1)**.

Table 1: Sex distribution of the study group (patients with acute kidney injury).

Gender	Frequency (n)	Percentage %
Male	**57**	**58.2**
Female	**41**	**41.8**
Total	**98**	**100.0**

As for age distribution, there were 53 patients (54.1%) younger than 20 years, and 26 patients (26.5%) aged 40 years or older. The largest proportion of participants was found in the 40–59.9-year age group (16.3%), followed by the 30-39.9-year age group (10.2%).

ASO Titers According to Age Groups:

The distribution of ASO titers according to age groups is presented in **Table 2**. Because the reference range for ASO varies by age, the results were interpreted using the corresponding age-specific reference ranges.

Elevated ASO titers were detected in 5 of the 98 patients (5.1%). Two of the five patients with elevated ASO titers (40.0%) were in the 2–3.9-year age group, while one patient each was observed in the 4–5.9-year, 40–59.9-year, and ≥60-year age groups.

The highest individual ASO titer was 261 Todd units/ml, recorded in the 4–5.9-year age group. The highest mean ASO titer was observed in the 2–3.9-year age group, with a mean value of 140.5 Todd units/ml. Overall, 93 patients (94.9%) had ASO titers within the age-specific reference range.

Table 2. Distribution of ASO titers among the study participants according to age group.

Cases with elevated ASO titer, n	ASO titer range (Todd units/ml)	Mean ASO titer (Todd units/ml)	%	N	Age group (years)
0	9-22	15.35	4.1	4	<2
2	48-199	140.5	8.2	8	2-3.9
1	57-261	113.44	9.2	9	4-5.9
0	77-159	103.86	7.1	7	6-7.9
0	45-110	77.71	7.1	7	8-10.9
0	29-111	68.67	9.2	9	11-14.9
0	31-77	58.11	9.2	9	15-19.9
0	59-126	91.44	9.2	9	20-29.9
0	22-119	61.70	10.2	10	30-39.9
1	23-167	73.56	16.3	16	40-59.9
1	17-171	62.70	10.2	10	≥60
5 (5.1%)			**100.0**	**98**	**Total**

DISCUSSION:

The present study evaluated anti-streptolysin O (ASO) titers among **98** patients with acute kidney injury (AKI), with an age range from **1 to 73** years. The male-to-female ratio was **1.39:1**, with **58.2%** of the study population being male. The majority of participants were younger than **20** years **(54.1%)**. This age distribution is significant as ASO titers are related to age and population. For these reasons, using age-specific reference ranges, as done in this study, is more appropriate than using a single cutoff for all participants **(Sen and Ramanan, 2014)**.

The results of the present study show that only **five** patients out of **98 (5.1%)** had elevated ASO titers, while **93** patients **(94.9%)** had ASO titers within their age-specific reference ranges. This relatively low percentage needs to be understood within the context of the heterogeneous character of AKI etiologies. Renal failure can be caused by several systemic and renal diseases, whereas in PSGN it is secondary to a preceding streptococcal infection and represents a specific type of post-infectious glomerulonephritis. Recent clinical guidelines focus on the diagnosis of infection, which involves concordant clinical and renal diagnostics plus evidence of a preceding infection, instead of relying on a single serologic marker **(Meena et al., 2026)**. This finding should therefore be interpreted as the proportion of AKI patients with high ASO titers and not as the prevalence of PSGN. This supports the conclusion that Streptococcus pyogenes is still an important pathogen in the school setting among children, as demonstrated by recent Iraqi data. In Baghdad, a study of school children

carried out in 2025 found the rate of GAS detection to be 24% **(Ali and Wadi, 2025)**. This population was very different from the current AKI population, but the results represent up-to-date local evidence of children's exposure to GAS. These data should not be used to assume that GAS carriage is a direct risk factor or to infer rates of renal damage in the current study population.

It is important to note that the presence of GAS exposure in the community does not prove that renal failure among the participants of the present study was contributed to by streptococcal infection. The present study investigated patients with AKI without restricting enrollment to those with clinical criteria for PSGN. Hence, the low proportion of high ASO levels in the current study is consistent with the highly varied population studied.

The results from Iraq can be viewed from a regional perspective as well. A multistate Saudi study investigated pre- and post-COVID-19 aspects of pediatric post-infectious glomerulonephritis and found variations in the epidemiological and clinical parameters between the two eras **(Noureddeen et al., 2025)**. The results suggest that the epidemic course of post-infectious glomerular disease might depend on the time period and infectious environment. The Saudi study resembles our current study in specifically examining glomerulonephritis in children following an infectious cause; however, that study included patients with defined post-infectious glomerulonephritis, whereas the present study included patients with AKI across a wide age range without requiring a history of streptococcal infection. Therefore, disease frequencies could not be directly compared between the two studies.

The proportion of elevated ASO titers in the present study (5.1%) was considerably lower than in international investigations in children with APSGN. In a six-year review from Cape Town, South Africa, elevated ASO titers were detected in 85% of children with APSGN, whereas anti-DNase B was elevated in all tested patients **(Abugrain et al., 2024)**. The higher frequency in that cohort is expected because the study population consisted of children with a specific post-streptococcal renal disease rather than patients with AKI of heterogeneous etiologies.

Likewise, in the study by **Dhakal *et al.* (2023*)*** positive ASO titers were seen in 72.7% of children with APGN, and anti-DNase B was positive in 86.9% **(Dhakal et al., 2023)**. The proportion observed in the present study was considerably lower than the 72.7% reported by **Dhakal *et al.*** This difference is likely due to differences in case definitions and patient selection, since the present study comprised all patients with AKI, while the Nepalese study enrolled patients with a diagnosis of APSGN **(Dhakal et al., 2023)**.

The significance of APSGN in the etiology of acute glomerulonephritis is still recognized in children in recent literature from around the world **(Dhakal et al., 2025)**. The association of APSGN with nephritogenic group A streptococcal infection was stressed, and the role of correct diagnosis and

treatment of infection was emphasized by Dhakal *et al.* (2025).

A recent study in Sri Lanka assessed children with post-streptococcal acute glomerulonephritis and explored the association of proteinuria with renal outcomes **(Ranawaka et al., 2025)**. This provides further evidence that APSGN can have clinically significant renal involvement in children; however, that study population was restricted to patients who had developed post-streptococcal disease, making it not directly comparable with the heterogeneous AKI population in the current study. Similarly, a retrospective study of children diagnosed with APGN, with a five-year follow-up in Nepal, adds to regional evidence regarding the clinical presentation of APGN **(Bajracharya et al., 2024)**. This pediatric form of APSGN tends to have a stronger association with a prior streptococcal infection than an unselected population of patients with AKI **(Bajracharya et al., 2024)**.

ASO is a serological marker indicating past exposure to streptococcal infection and is not a marker of active infection. Hence, in isolation, a raised ASO titer may fail to confirm the presence of a streptococcal infection or be sufficient by itself to verify PSGN **(Sen and Ramanan, 2014)**. It must be taken into consideration along with other blood tests, the patient's age, clinical presentation, and the timing of the blood test.

The maximum individual ASO titer obtained in the present study was 261 Todd units/mL and was found in the 4–5.9-year age group. This is the highest individual value observed, but its clinical relevance should be considered within the age-specific reference range. This finding further highlights the need to avoid using a fixed ASO threshold for all ages, especially among children **(Sen and Ramanan, 2014)**.

The highest mean ASO titer was recorded in the 2–3.9-year age group, with a mean of 140.5 Todd units/ml. The small number of elevated ASO titers and the fact that only two participants in this age group had elevated ASO titers mean that this higher mean should be viewed as a descriptive finding and not as an indicator of a statistically significant age-related association

Conclusion: Elevated ASO titers were uncommon among patients with acute kidney injury, occurring in only 5.1% of participants. Most patients (94.9%) had ASO titers within age-specific reference ranges. These findings indicate that elevated ASO was infrequent in this heterogeneous AKI population. When elevated, ASO titers should be interpreted in the context of age, clinical findings, laboratory data, and the timing of testing. An elevated ASO titer alone does not establish PSGN.

Recommendations:

1. Interpret ASO results using appropriate and age-appropriate reference ranges.

2. Incorporate ASO into clinical assessment and laboratory workup of suspected streptococcal-related renal disease.

3. Conduct larger multicenter studies in Iraq with well-defined renal diagnoses, particularly in patients with AKI and suspected APSGN.

4. Note and evaluate the timing of ASO determination and, if possible, serial measures of antibody levels.

Limitations: The study had a cross-sectional design, a relatively small sample size, and included patients with heterogeneous causes of acute kidney injury. Only ASO was assessed without anti-DNase B, and the timing of preceding streptococcal infection was not systematically documented. The absence of a healthy control group also limited comparison with the general population. Although all participants were diagnosed with AKI according to standard clinical criteria used at the study hospital, the exact KDIGO stage and the underlying etiology of AKI were not systematically recorded for each patient. This limits the ability to correlate ASO titers with specific AKI subtypes or severities.

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