

# Estimation of IL-6 in Acute pyelonephritis in children

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## Abstract

The detection of cytokines in the urine and serum have been used in the diagnosis and monitoring of various urological disease. In this study Interleukine – 6 (IL-6) level in serum and urine have been measured in acute pyelonephritis ( APN) in children patients .

A total of ( 95) urine & blood sample have been collected from children ( 2 month – 12 years) suffering from fever, dysurea, frequency. Twenty –sex patient of APN were include in the present study as well as twenty children of the same age range as control group.

Acute pyelonephritis is suggested by flank pain ,nausea and vomiting, those patients have been diagnosed by the physician and the diagnosis is confirmed by available investigation methods ,laboratory test , ultrasound .

White blood cells (WBCs)& neutrophil count as well as C-reactive protein (CRP) were high significant in APN patients while blood urea & serum creatinine levels were non significant in comparison with control group.

High significant differences were noticed between the sex groups of APN patients (P- value  $\leq 0.01$ ),percentage of male patients was (65.38) larger than that of females (34.62).

Also important differences have been found between APN patients in the age groups ; percentage of disease is the lowest in the age range ( 1-2) years ,and highest in the age range ( more than 2 years).

Urine & Serum IL-6 concentrations were significantly high with means ;109.24 ,28.86 pg/ml respectively compared with control means (12.59,7.93 pg/ml) at (P- value  $\leq 0.05$ ).

**Key words:** Acute pyelonephritis, Cytokines, Interleukin-6.

## **Introduction**

Urinary tract infection is a relatively frequent disease in children, and is the most serious bacterial infection in the childhood. When involving the upper urinary tract, such a disease is called acute pyelonephritis (APN) and it is defined as an acute suppurative bacterial infection of the kidney and renal pelvis, with suppurative necrosis being its hallmark<sup>(1-2)</sup>. If not early and appropriately treated, such a condition may result in permanent renal scarring with sequels of hypertension and chronic renal failure - the most serious long term complications<sup>(3-4)</sup>.

Approximately 6% to 13% of the children with renal scarring will develop arterial hypertension, and in 5% to 10% of cases, renal scarring will cause chronic renal failure<sup>(5)</sup>.

Besides late diagnosis (with associated late therapeutics), age under one year, presence of vesicoureteral reflux (VUR) particularly with high degree, presence of obstructive lesions and occurrence of recurrent APNs, constitute factors associated with the development of permanent renal damage<sup>(2-6)</sup>.

Although clinical symptoms such as fever and common inflammatory markers like erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) can somewhat determine the location of UTI, these symptoms are not always reliable<sup>(7)</sup>. Today, 99m-technetium dimercapto-succinic acid (DMSA) renal scan is used as a valuable imaging method for diagnosis of acute pyelonephritis<sup>(8)</sup>.

Unfortunately, this imaging device is not available in all medical centers and is accompanied with radiations<sup>(9)</sup>. Thus, some studies have stated that rapid diagnostic tests such as cytokines estimation can be used for diagnosis of acute pyelonephritis<sup>(10)</sup>. Interleukin (IL)-1beta and IL-6 are the most prevalent interleukins that are used for differentiation of acute pyelonephritis and lower UTI. Few studies document controversy of mentioned test for differentiating acute pyelonephritis and lower UTI<sup>(11)</sup>. Considering the importance of an early diagnosis and appropriate treatment of acute pyelonephritis, the present study was conducted to determine the diagnostic value of IL-6 in children with acute pyelonephritis in children

## **Materials and Methods**

This study was have been carried out between December. 2013 and April. 2014.( 95 ) Urine and blood samples were obtained from children (2 month – 12 years ) of both genders who were out patients and inpatients in

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Ibn albaldy hospital, A total of ( 95 ) mid-stream urine samples were taken from children. 5 ml of venous blood were obtained from each children .

White blood cells (WBCs) count, neutrophil (Neutl) count, , CRP, Blood urea and serum creatinine were measured as soon as possible. For measuring serum and urine IL-6, 5 ml of venous blood and urine were obtained from each children , the serum and urine was obtained by centrifugation at 3,000 rpm for 5 minutes at 4° until IL-6 assay. The serum IL-6 were measured using an enzyme-linked immunosorbent assay and commercially available kits ( CUSABIO), then standard curves were made to estimate the concentrations of the immune parameters. The Statistical Analysis System<sup>(12)</sup> was used to show the effect of different factors in study parameters. Chi-square test was used to significant compare between percentage & Least significant difference –LSD test was used to significant compare between means in this study.

### Results and Discussion

Twenty -six patients of APN were included in the present study as well as twenty children of the same age range as controls. All were of both genders., High significant importance was noticed between the APN and six groups (p-value was  $\leq 0.01$ ). The Number of male patients in this study was larger than that of females ,Percentage for male was (65.38 %) while for female was (34.62 %)as in table ( 1 ).

**Table ( 1 ). Distribution of study group according to gender**

Sex	No.	Percentage (%)
Male	17	65.38
Female	9	34.62
Total	26	100 %
Chi-square value	---	9.056 **
** (P $\leq$ 0.01).		

our results are compatible with Özçakar et al<sup>(13)</sup> the refer to that male patients and acute pyelonephritis (APN) episodes were more frequent at small ages, The rate of female patients and cystitis episodes predominated with increasing age.

The prevalence rate of UTI in boys depends on many factors including congenital malformations and uncircumcised genitalia which often contaminated<sup>(14)</sup>.

Patients in this study were also grouped into three age groups, Data from table ( 2 ) indicate that the number and percentage of patients are the

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lowest in the age range (1-2) years ,While highest in the age range (more than 2 years) ,High significant important was noticed between the APN and age group in Table (2 ).

Our results have been agreed with the study of Robert et al<sup>(15)</sup> Which Noticed that children older than 5 years have a 4.5-fold greater risk of acute pyelonephritis when evaluated for febrile UTI compared with infants, as Well as agree with <sup>(16)</sup> those remembered that children 5 years of age had a higher risk of APN than did a children <12 months of age.

**Table ( 2 ). Distribution of study group according to patients age**

Age group	No.	Percentage (%)
Less than 1 year	7	26.92
1-2 year	5	19.23
2-12 years	14	53.85
Total	26	100 %
Chi-square value	---	10.174 **

\*\* (P≤0.01).

According to Hichrom medium and Vitek 2 diagnostic system bacterial isolates were Identified as following that; *E.coli*(50.0 %) was the main pathogen in patients with APN , *this compatable with* <sup>(17-18-19-20)</sup> *these studies have documented that ;Escherichia coli is the most common pathogen in acute pyelonephritis with percentage (85.5%, 80 % ,70% ,88.1 %) respectively,* followed by , *Enterococcus fecalis* . (3.6%), and *Psedomonas aeruginosa* (0.4%).

IL-6 is an inflammatory cytokine, which is secreted in response to bacterial infections in body<sup>(21)</sup>. Serum and urinary levels of this protein increase during UTI, and its measurement has been shown to be useful in differentiating between APN and lower UTI<sup>(10)</sup>.

in our study the urine IL-6 levels of children with acute pyelonephritis were significantly (p < 0.05) higher (109.24) pg/ml when compared with non-renal febrile controls group (15.59) pg/ml while seum IL-6 levels of children with acute pyelonephritis were significantly (p < 0.05) higher (28.86) pg/ml when compared with non-renal febrile controls group (7.93) pg/ml as seen in Table ( 3 ). The results of this study demonstrated that both serum and urine IL-6 levels were markedly elevated during the acute phase of a first time febrile acute pyelonephritis in children.

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**Table ( 3 ). level of serum & urine IL-6 in APN**

Group	No.	Urine IL-6		Serum IL-6		T-test value
		Mean	± SE	Mean	± SE	
Patients	26	109.42	± 38.82	28.86	± 19.53	41.762 *
Control	20	15.59	± 4.22	7.93	± 0.33	8.329 NS
T-test value	----	81.372 *		19.313 *		---

\* (P≤0.05) , NS: Non-significant.

Our study in agreement with The study of <sup>(10)</sup> on children of 1-121 months old with UTI showed that the value of inflammatory markers including CRP, WBC, serum and urinary IL-6 and IL-8 in patients with acute pyelonephritis were higher than that in lower UTI patients as in table( 4 & 5). Also, these researches showed that there was a positive significant correlation between acute pyelonephritis, and serum and urinary IL-6, IL-8 and other inflammatory markers. Sheu et al<sup>(10)</sup> concluded that serum IL-6 and IL-8, especially IL-6, are suitable markers for diagnosis of acute pyelonephritis. Other studies confirmed the increase in urinary IL-6 and IL-8 in children with febrile UTI<sup>(22-23)</sup>.

**Table ( 4 ) count of WBCs & Neutrophil in APN**

Group	No.	WBCs count		Neutrophil	
		Mean	± SE	Mean	± SE
Patients	26	14.81	± 1.23	8.92	± 1.07
Control	20	6.71	± 0.46	3.88	± 0.34
T-test value	----	3.358 *		2.915 *	

\* (P≤0.05)

**Table (5) Level of CRP in APN**

No.	CRP : No. (%)		Chi-square value
	+ve	-ve	
26	21 (80.76)	5 (19.23)	26.32**

\*\* (P≤0.01)

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## قياس مستوى الالتهاب IL-6 في المصابين بالتهاب الكلية

### والحويض الحاد للأطفال

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#### الخلاصة

يعد استخدام السايبتوكينات من الوسائل المهمة للكشف عن ومراقبه امراض الجهاز البولي .تم في هذه الدراسة قياس مستوى IL-6 في الإدرار ومصل الدم لأطفال مصابين بالتهاب الكلية والحويض الحاد (APN).

أجريت الدراسة على (95)عينه إدرار ودم جمعت من أطفال تراوحت أعمارهم من (شهرين - 12 سنه) ممن لديهم التهاب المسالك البولية الحاد من حمى ،تكرار التبول ،حرقه البول.

صممت هذه الدراسة على(26)مصاب ب (APN) كذلك (20) طفل من الأصحاء من نفس الأعمار . شخضت الاصابات من قبل الأطباء المختصين ودعم التشخيص بالاختبارات المختلفة التي شملت WBCs,Nutrophili,CRP, فضلا عن السونار .

أظهرت النتائج ارتفاعا ملحوظا في تعداد خلايا الدم البيضاء والعدله كذلك تركيز البروتين الطور الحاد CRP للمصابين بالمقارنة مع مستوياتها لدى الأصحاء (مجموعه السيطرة) .

كما ظهرت فروقات معنوية واضحة بين الذكور والإناث المصابين. إذ كانت معدلات الاصابه لدى الذكور (65.38) اعلي مما في الإناث ( 34.62 ) على مستوى معنوي ( $P < 0.01$ ).

وقد وجدت أيضا اختلافات مهمة في نسب الاصابه في الأعمار المختلف هاذ كانت اعلي نسبه لالتهاب للأعمار أكثر من سنتين وقلها للأعمار بين سنه إلى اثنين .

قدرت تراكيز الالتهاب IL-6 في الإدرار ومصل الدم للمصابين .اذ كانت هناك فروقات معنوية مهمة بين مستوياتها للمصابين والسيطرة إذ كان معدلها للمصابين في الإدرار (109.24)بيكو غرام/مل مقارنة بالسيطرة (15.59)بيكو غرام/مل اما في مصل الدم كان (28.86) بيكوغرام/مل مقارنة بالسيطرة (7.93)بيكو غرام/مل وعل مستوى معنوية ( $p \leq 0.05$ )