

**RESEARCH ARTICLE**

## Metabolic acidosis impairs clearance of UPEC-UTI

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### ABSTRACT:

**Background:** Acute pyelonephritis (AN) which is commonly brought about by the vesicoureteral reflux (VUR) has for decades been a fatal kidney disease mostly affecting the children and it is associated with the metabolic acidosis. All of the past studies which has been carried out have suggested that metabolic acidosis major cause is NH<sub>4</sub>CL supplement common in food, and they hinder clearance of UPEC (*Uropathogenic E. coli*) in the refluxing mouse exemplary. **Objective:** The major aim was to examine the clinical, microbiological, and epidemiological features of cPN and the involved prognosis with a group of patients suffering from the infection. **Patients and Methods:** a prospective examination was carried out in which 1325 consecutive clients below the age of 14 and having been diagnosed with cPN. The analysis of major demographic, clinical and microbiological data, there was evidence of association with links to mortality in univariate analysis in which they were encompassed in the multi-variate logistic regression model. **Results:** The results obtained exhibited that *Escherichia coli* was the major causative agent accounting for nearly half of all the infections. The results obtained after the analysis will be used to treat children across Iraq mostly below the age of ten and suffering from the acute pyelonephritis. **Conclusion:** This draws a conclusion that hindered clearance of UPEC-UTI cannot be simplified by an impact on the urine acidification other urothelial hindrance function. As the metabolic stress linked acidosis hinder the UPEC clearance, the corrective mechanism of acidosis can prevent renal injury linked to pyelonephritis.

**KEYWORDS:** Urinary Tract Infections, *Escherichia coli*, pyelonephritis (cPN).

### INTRODUCTION:

UTI's infections has been widespread, over the last decade it has affected more than 50 million children and women across Iraq. Despite the fact that the infection can attack either male or female, traditional beliefs is that it is more widespread among woman and children, in which it is postulated that half of them will get the infection within their lifespan. Experts have proven an approximate of 25% of the children below age ten to having the first stage of bacterial cystitis, in which it goes to reappear within six months' period. The current study shows that in Iraq therapeutics are sub-optimal due to the predominance of multidrug resistant pathogens increase and also the antibiotics for the prolonged infections does not translate to recurrences<sup>1</sup>.

Children who are suffering from such infections tend to have prolonged health concerns and reduction in their

quality of life diminishing completely with time. The bacterial infections of the tract come with several signs and symptoms of which may cause a lot of organisms. This research will only put emphasis on the uropathogenic *Escherichia coli* commonly referred to as UPEC as the primary etiological agent of UTI. Studies have proven that UPEC accounts for over 80 percent of all cases of community acquired infections<sup>2</sup>.

### PATIENTS AND METHODS:

For this study, it involved an observational study in which 1325 children inpatients were incorporated aged not more than 14 years. These children were suffering from cPN and they had visited Shar hospital between 1 July 2017 and 30 June 2019 located within Sulaymaniyah in Iraq. Some of the patients were excluded from the study due to various reasons i.e. they were postoperative duration after undergoing urological surgery, and had recently had a kidney transplant. Also, the information was gathered using a defined designed procedure<sup>3</sup>. The variable which were recorded are age, gender of the patients, if there was an underlying nephron-urological feature, other predisposing features

such as previous history of the UTIs and chronic renal failures, the period of symptoms, clinical available information, all the past antimicrobial treatment, and physical examination<sup>4</sup>. When the initial diagnosis was carried out, all the selected patients were admitted to the hospital and treated immediately, depending on their clinical status.

**STATISTICAL ANALYSIS:**

All the collected information was fed into SPSS software, in which the results obtained were written either in median or interquartile range and numbers/percentages. Both the non-normally and normally distributed variables comparison was carried out using t-tests and the Mann-Whitney U-tests accordingly<sup>5</sup>. The category variables were examined by the use of X2 tests and also the fisher analysis was used for comparison in some instances. All the obtained measures for association were written as odd ratios having a confidence interval of 95% for the dichotomous variables. Any 2-tailed P value which had a range of 0.05 was taken to be significant statistically. Most of the co-variates which were found to have a strong link with the attributable mortality on univariate analysis in the region of significance p is less than 0.1 were all included in the multi-variate logistic regression model employing the backward selection tactics. It is also worth to note that all patients consent was obtained prior to the study. Secondly, the data and samples were taken from Shar hospital as part of the normal care in the medical industry, and as per the current guidelines<sup>6</sup>.

**RESULTS:**

The 1325 patients (children) whom were included in the study, 52 percent were male while 83 percent were female. The children median age was 8 years. In overall, 84.2 percent of the patients were admitted to the infectious disease department while 14.9 percent were admitted in the Intensive care unit<sup>7, 8</sup>. The other portion which was 11 percent was admitted in various normal wards.

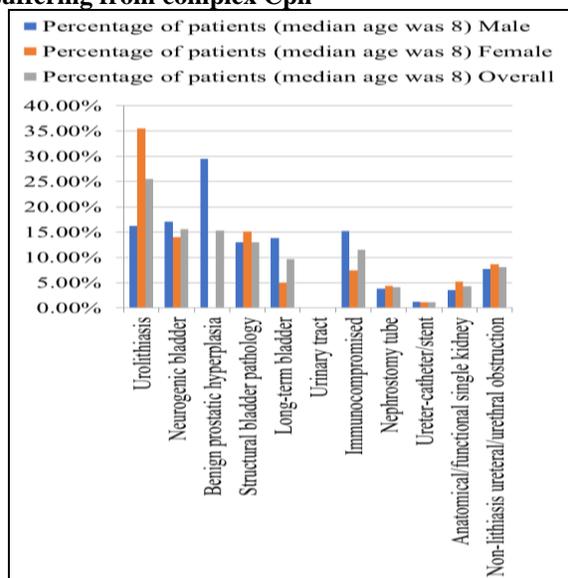
**Table 1: Measures used to classify patients suffering from complex cPN**

	Percentage of patients (median age was 8)		
	Male	Female	Overall
Urolithiasis	16.2%	35.5%	25.5%
Neurogenic bladder	17.1%	14.0%	15.6%
Benign prostatic hyperplasia	29.5%	0	15.3%
Structural bladder pathology	13.0%	15.1%	13.0%
Long-term bladder	13.8%	5.0%	9.6%
Urinary tract	-	-	-
Immunocompromised	15.2%	7.4%	11.5%
Nephrostomy tube	3.8%	4.4%	4.1%
Ureter-catheter/stent	1.2%	1.1%	1.1%
Anatomical/functional single kidney	3.5%	5.2%	4.3%
Non-lithiasis ureteral/urethral obstruction	7.7%	8.6%	8.1%

The first phase of the cPN in which 62.6 percent of the patients were examined, while the remaining 37.3 percent had had contact with the infection in their past.

Observing the phases, 70.9 percent of the infections happened in patients suffering from structural and functional abnormalities occurring at the genitourinary tube. The table below show some of the features on which the sampled patients were reflected to have suffered from the infection. The recurrent UTI was found in 23.3 percent of the patients while 43 percent suffered from other disorders i.e. diabetes or the chronic kidney failure<sup>9</sup>.

**Analysis 1: Measures used to classify patients suffering from complex Cpn**

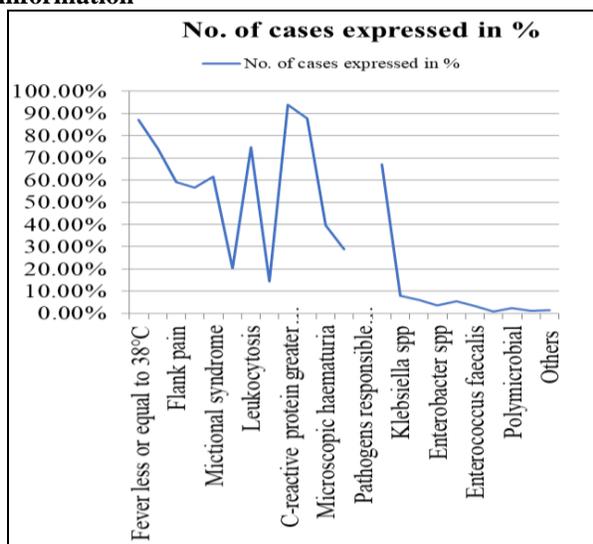


**Table 2: Major clinical, lab, and micro-biological information**

	No. of cases expressed in %
Fever less or equal to 38°C	87.2 %
Chills	74.1%
Flank pain	59.1%
Costovertebral tenderness	56.7%
Mictional syndrome	61.7%
Systolic blood pressure less or equal to 90 mm Hg	20.2%
Leukocytosis	74.7%
Thrombopenia	14.3%
C-reactive protein greater or equal to 6 mg/L	93.9%
Pyuria	87.9%
Microscopic haematuria	39.8%
Bacteriuria	28.8%
<b>Pathogens responsible for episodes of Complicated pyelonephritis</b>	
Escherichia coli	67%
Klebsiella spp	7.9%
Proteus spp	6.1%
Enterobacter spp	3.6%
Non-fermenting GNB	5.4%
Enterococcus faecalis	3.4%
Other Gram positive bacilli	0.9%
Polymicrobial	2.5%
Candida spp	1.1%
Others	1.5%

The median period for all the signs shown prior to patients being admitted was an average of 3 days. 87 percent of the patients exhibited a fever which was greater or equal to 38.3 degrees' while 59.4 percent showed flank pain, and 56.7 percent had costovertebral tenderness. Overall the major biochemical, clinical, hematological, and urinalysis information as depicted by table 2.

**Analysis 2: Major clinical, lab, and micro-biological information**



Before the study can begin, one week prior to the patients' admission, a total of 38.4 percent of them had been given anti-microbial dose. There was also a urine culture which was performed for 1251 patient while the blood culture was carried out in 1076 patients. The examination of the urine culture showed a positive with

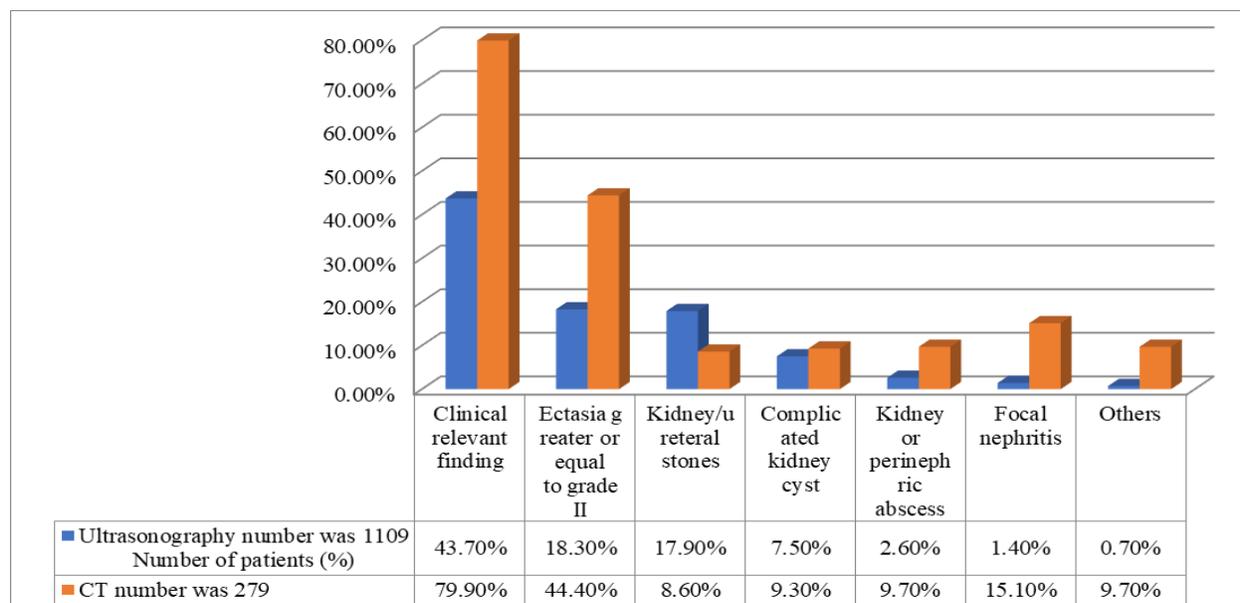
67.7 percent patients while 35.1% of the sampled patients showed clinically significant bacteremia. In the case where blood culture and urine were investigated, 77.9 % of the patients, had 12.2 percentage of the dissenting outcomes: 27.7 percent of these results was as a result of various isolation and 72.3 percent of them was as a result of the isolation which occurred in the urapathogens within the blood culture.

The Escherichia coli accounted for the 67% of the total cases while Klebsiella spp accounted for 7.9% and proteus spp accounted for 6.6 percent. According to table 2. It is evident that the etiological causative agents in the range of 69.3 percent in which the etiology of the cPN was eventually identified.

After the sampled patients had been registered within the Shar hospital, the ultrasonography study was availed 48 hours for 1109 cases. This study exhibited that the pathological findings cases were 58.7%. the CT was carried out among 79.9 percent of the cases, in which the relevant one stood at 36.2 percent and incidental one at 2.5%.

**Table 3 below illustrate the major clinical significant CT and the ultrasound outcomes.**

	Ultrasonography number was 1109	CT number was 279
	Number of patients (%)	
<b>Clinical relevant finding</b>	43.7%	79.9%
Ectasia greater or equal to grade II	18.3%	44.4%
Kidney/ureteral stones	17.9%	8.6%
Complicated kidney cyst	7.5%	9.3%
Kidney or perinephric abscess	2.6%	9.7%
Focal nephritis	1.4%	15.1%
Others	0.7%	9.7%



The first study was a mixed therapy in which 23.6% of all the cases and also there was single therapy in the region of 76.4%. For the case to be taken as a-etiology, it had to be 96.6% appropriate. A lot of sepsis happened among the 25.9 percent of the patients and there was 12.5 percent of the septic shock<sup>10</sup>. The median number of days was 2 allowed before they could attain a pyrexia while the median duration for the stay at the hospital was 9 days. Across the time in which the study was being carried out, nine cases of death were confirmed and attributed to cPN (4.1%). Also, when the selected sample patients were discharged, 1.7% of them failed to return for the review. The cured number of patients stood at 87.6% while 8.0 % suffered from a relapse and 4.3% of them got a reinfection.

### DISCUSSION:

The signs infection within the patients suffering from this disease varies across a wide range in which there are cases of mild lower tract signs to other exhibition such as bacteremia and extreme sepsis. Regardless of whether cPN is termed as a communal acquired disease, its occurrence is still very high. The available little data trying to illustrate its microbiological and clinical features, its prognosis is by far scanty. Many explanations are available for this challenge, with the major one explaining how challenging it is to undertake the systematic evaluation studies owing to the lack of consensus pertaining the true definition of cPN<sup>11</sup>.

Over the past, there has been investigation concerning cPN within a specific selected class of patients, but certainly this is among the most extensive study to have been carried out for children suffering from acute cPN. The selected children were treated within a homogenous structure with clearly defined procedures. Across the findings established from the analysis of the data obtained, it is evident that the cPN occur proportionally in both men and women<sup>12</sup>. Across the study, the median range of symptoms before the patients being admitted was 3 days which was also the same figure posted for the recent evaluation. The outcome exhibited by the urine culture stood at 67.7%, and this was a lower figure in comparison to the uncomplicated PN. Additionally, this study had 34% of the cases exhibiting a clinical significant bacteremia with a figure in the region of 42% as reported in other studies.

Owing to the fact that *Escherichia coli* is among the common aetiological causative agent in UTI, across the infection of cPN it has been established that the occurrence of isolation always does not go above 67%. Other agent such as *Klebsiella* spp and *Proteus* spp they also assume a greater importance. Most of the recent studies which have been carried out concerning *Escherichia coli* have established that the agent account

for 63 percent of all the infections while *Klebsiella* spp account for only 7 percent. This study identified that ESBL manufactures microorganisms with a percentage of 14.1%, this figure is slightly higher in comparison to other reported figures by other researchers. Both the aetiological continuum and the accelerating increase in the portion of ESBL production of resistant microorganisms call for a specific effort on how the cPN is diagnosed and treated<sup>13</sup>.

This study established that CT is superior in comparison to ultrasonography for the urologic diseases. For instance, the CT study showed relevant findings in the region of 79% of all the sampled cases conducted. Nevertheless, has it need to be potentially nephrotoxic distinction improvement as shown in this study, the CT study should be a preserve for those patients and especially children who are experiencing unfavorable and their past ultrasound studies exhibit an inconclusive outcome. Lastly, this study outcome can be relied upon since it encompassed a large sample of patients thus conferring a high degree of external validity for its results.

### CONCLUSION:

To conclude, cPN can be termed as a dominant infection which encompass a greater intake of healthcare services. Also, the infection is associated with extreme clinical procedures accompanied by high mortality rate both for children and old patients, and especially the one who in the process develops a septic shock. The recent time has seen cPN reflected as a disease possessing some clear symptoms for admission, there are also cases which can be managed as outpatients. Further researchers are encouraged so as to explore this topic.

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