



ASSESSING THE UTILITY OF PLATELET PARAMETERS AS A PREDICTOR FOR EARLY DIAGNOSIS AND MANAGEMENT OF URINARY TRACT INFECTIONS IN CHILDREN

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ABSTRACT

BACKGROUND: Urinary tract infections are one of the most common bacterial infections occurring in children that may cause short term morbidity when not treated early or undertreated due to life-threatening urosepsis. Platelet parameters such as MPV are newly emerging markers of inflammation for early diagnosis and management of UTI.

AIM- The purpose of this study is to assess the utility of platelet parameters in the early detection and management of urinary tract infection.

METHODS: This was a cross sectional study carried out in the Department of Paediatrics, Chettinad hospital and research institute between October 2020 and November 2021. Children aged between 6months – 17 years admitted with a clinical diagnosis of UTI were included in this study. Children were further grouped into **Culture positive** and **Culture negative** based on their urine culture reports. Validity of platelet

parameters between the two groups was done and IBM SPSS software version 22 was used for statistical analysis.

RESULTS: A total of 140 cases in each group were included in this study. The mean age was around 3-5years in both the groups. Among the study population, 102 (72.9%) participants were Escherichia coli positive. Only 8 (5.7%) were affected by gram positive organisms. Platelet parameters such as PLC and PCT were significantly higher in the culture positive group when compared with culture negative group ($p<0.001$). ROC curve revealed that platelet count and Plateletcrit can better predict UTI with a relative difference in validity among all the parameters. The area under the curve was more with PLC thus stating that PLC can be considered as a better choice among platelet parameters to predict UTI.

CONCLUSION: The mean values of PLC, PCT, MPV and PDW were within the normal range in the culture positive group but were still higher than culture negative group. Platelet parameters such as PLC and PCT were significantly higher in the culture positive group when compared with culture negative group ($p<0.001$). Among the platelet parameters, Platelet count had a higher specificity of 78.65%, followed by Plateletcrit with a specificity of 34.31% over MPV and PDW in predicting the disease. The area under the curve was more with PLC thus stating that PLC can be considered as a better choice among platelet parameters to predict UTI as per this study.

KEYWORDS: Urinary tract infection, Mean platelet volume, Plateletcrit, Platelet distribution width, C-reactive protein

INTRODUCTION

Infection and inflammation of the urinary system are referred to as "urinary tract infections" or "UTIs" and are confirmed by significant growth of bacteria usually of a single type in urine culture ¹. 80% of paediatric UTI cases are caused by *Escherichia coli*. The prevalence of UTI in patients presenting to hospital with febrile episode is 10% in children, 13.6% in infants and 7% in neonates ². Clinical diagnosis in children is unreliable, hence urine culture is defined as gold standard method for diagnosing the disease and for starting appropriate therapy for UTI. If not treated early and appropriately, it can eventually progress to cause bacteraemia and sepsis finally leading to death ³.

Platelets are important cells in defense mechanism. Platelets play an important part in the inflammatory process by increasing the number of white blood cells and preventing the death of polymorphonuclear cells, eosinophils and monocytes via apoptosis ⁴. Information about platelet indices can be easily obtained with a complete blood count. A change in platelet parameter can be utilized as a predictor of the gram-type of bacterial pathogen causing urinary tract infection (UTI) ⁵. When compared to UTIs caused by gram negative organisms, gram positive bacteria causing UTIs have a marked increase in MPV and PDW.

In developing countries like India where majority of children are deprived of proper access to health care facilities, availability of simple tests for accurate, rapid diagnosis of completely reversible infections like UTI is an absolute necessity ⁶. It was found by some studies that platelet indices could be considered to predict UTI in children as soon as possible without the need to wait for urine culture reports, which takes time to obtain and are even challenging to collect urine samples for. Platelet indices also can be used to find type of bacteria (Gram positive or Gram negative) involved in infection as per certain studies ⁷. In light of the above information, this study has been conducted to find out how these platelet parameters help in identification and management of urinary tract infection in children thus preventing further complications. There are not many studies available in India establishing the use of platelet parameters for the diagnosis of UTI. This study might add on to the literature the efficacy of platelet parameters in predicting UTI in children.

MATERIALS AND METHODS

The present cross-sectional study was conducted in Department of Paediatrics at Chettinad Hospital and Research Institute from October 2020 to November 2021 for a duration of 13 months. Children between the age group of 6 months-17 years attending to outpatient department and those admitted in paediatric ward with symptoms suggestive of Urinary tract infection were included in the study. Children who were diagnosed with any chronic infections, chronic kidney disease, liver disease, hypothyroidism, hematological disorders, with recurrent episodes of UTI and who already had received treatment for the current infection were excluded from the study. The Institutional Human Ethics Committee approved the study. A written informed consent was obtained from parents who were willing to participate in the study.

Demographic characteristics (name, age, and gender), date of presentation to the hospital, presenting features, constitutional symptoms, any underlying disease, and history of any medications used were noted. Children were evaluated for UTI using diagnostic methods such as urine analysis and culture and sensitivity by collecting urine specimens in a sterile manner. A five millilitre of blood sample (venous) is aspirated from the study participants and sent for;

- CBC parameters (Hemoglobin concentration, WBC count, RBC count, platelet count, MPV, PDW and PCT) and blood film.
- C-reactive protein (CRP) was assayed (reference range <0.5mg/L).

The automated cell counter (CELL-DYN Ruby software version 2.0 analyzer S/N: 35863BG) was used to measure platelet parameters (total platelet count, MPV, PDW and PCT) in our institute. The reference ranges at our institute were (155-450*1000 Lac/cmm for platelet count, 6.9-10.6 fL for MPV, 11-16% for PDW and 0.17–0.35% for plateletcrit). The results of urinalysis, urine culture and sensitivity, automated Complete Blood Counts (Hemoglobin concentration, WBC count, RBC count, platelet count, MPV, PDW and PCT) and C-reactive protein (CRP) were collected.

The study population was then divided into two groups based on the urine culture reports:

- **Culture positive group:** This included 140 children diagnosed to have UTI by urine culture
- **Culture negative group:** This included 140 children who were proven to be negative by urine culture.

Statistical analysis was performed with IBM SPSS software version 22. Interpretation of results was done with appropriate statistical tools. P value < 0.05 was considered statistically significant.

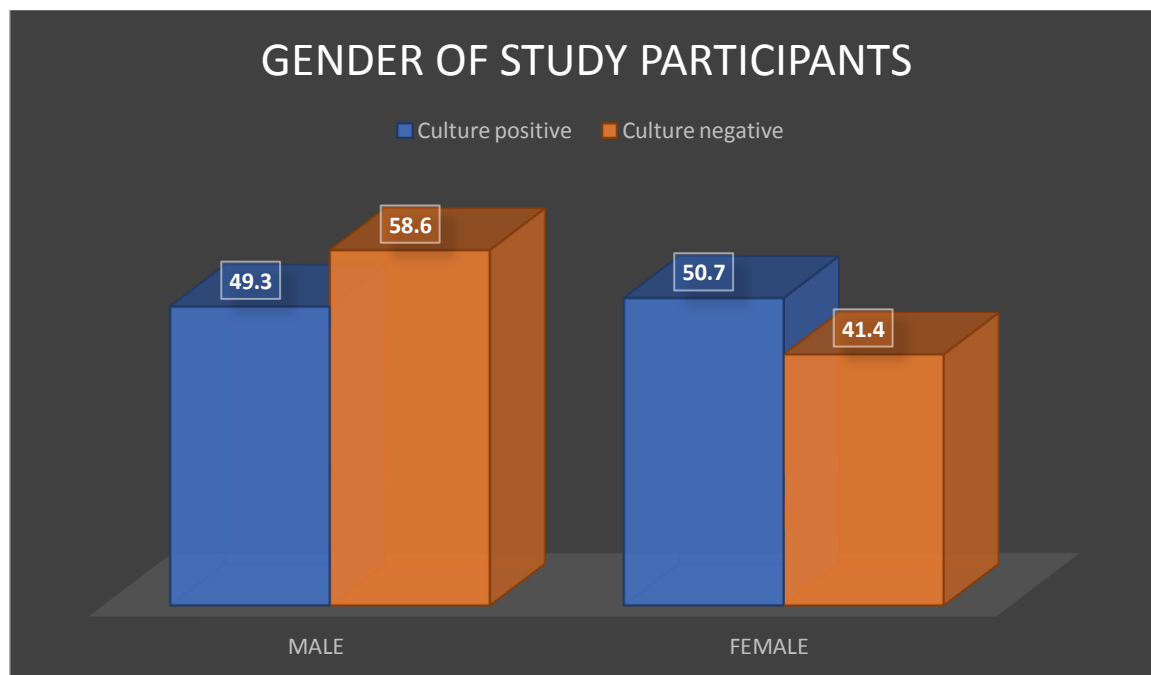
RESULTS

A total of 140 culture positive and 140 culture negative cases were included in this study. The Median age among the Culture positive group was 3 years and that of Culture negative group was 5 years as depicted in Table . Culture positive group had female predilection (50.7%) whereas Culture negative group had a male predilection (58.6%) (Table)

TABLE 1: DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO SELECTED BASELINE CHARACTERISTICS

	Culture positive (n=140)		Culture negative (n=140)		P value
Age group					
	Number	Percentage (%)	Number	Percentage (%)	0.096
<1 year	35	25	17	12.1	
1 - 5 years	56	40	59	42.1	
6 - 10 years	29	20.7	29	20.7	
>10 years	20	14.3	35	25	
Median age	3.0		5.0		
Gender					
	Number	Percentage (%)	Number	Percentage (%)	0.005
Male	69	49.3	82	58.6	
Female	71	50.7	58	41.4	

FIGURE 1:PRESENTS THE DISTRIBUTION OF MALE AND FEMALE PARTICIPANTS IN THE STUDY POPULATION.



According to urine analysis reports, Presence of pus cells in urine was significantly more in the Culture positive group compared to the culture negative group ($p = 0.001$) (Table) Among the study population, 102 (72.9%) participants were Escherichia coli positive, 10 (7.1%) participants were Klebsiella positive, 8 (5.7%) were Enterococcus positive, 5 (3.6%) were Citrobacter positive (Figure 2).

TABLE 2: DISTRIBUTION OF GENERAL URINE FINDINGS IN THE STUDY POPULATION.

Urine routine	Culture positive group (n=140)		Culture negative group (n=140)		P value
	Number	Percentage (%)	Number	Percentage (%)	
Albumin					
Nil	133	95	135	96.4	0.481
Trace	7	5	5	3.6	
Pus cells					
< 5 cells	84	60	112	80	0.001
6-10 cells	16	11.4	21	15	
>10 cells	40	28.6	7	5	

FIGURE 2: SHOWS THE DISTRIBUTION OF CAUSATIVE ORGANISMS OF UTI IN THE STUDY POPULATION (N=140).

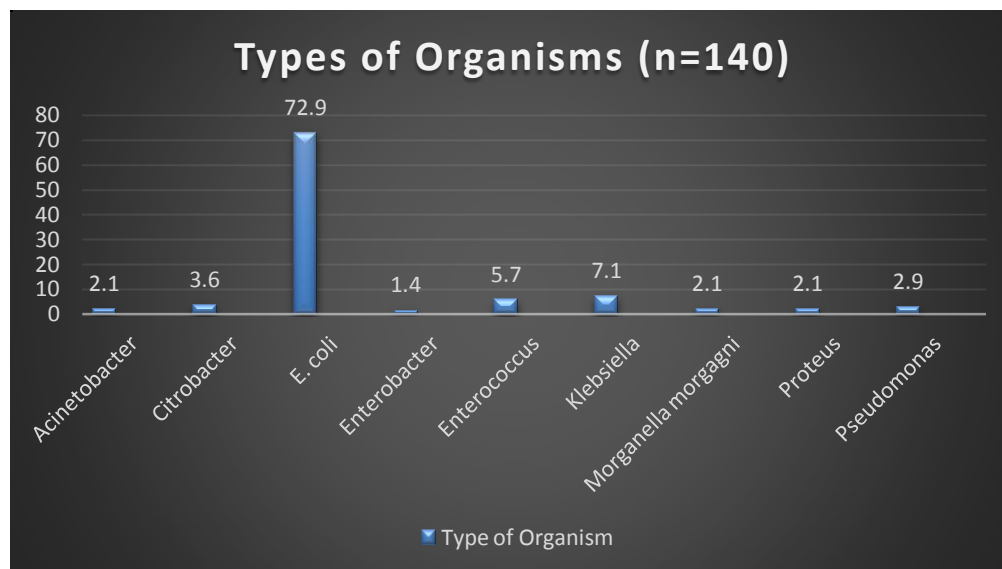


TABLE 3: FREQUENCY OF TYPE OF ORGANISM BASED ON GRAM STAINING CAUSING UTI IN THE STUDY POPULATION (N=140)

Organism	Frequency (n)	Percentage (%)
Gram Negative	132	94.3
Gram Positive	8	5.7
Total	140	100

The mean values of Total leucocyte count, Haemoglobin, platelet count, Plateletcrit, Platelet distribution width and MPV were compared between two groups. The mean Haemoglobin level was significantly higher in the culture negative group when compared with culture positive group. Platelet parameters such as PLC and PCT were significantly higher in the culture positive group when compared with culture negative group ($p < 0.001$) (Table). Among the platelet parameters, Platelet count had a higher specificity of 78.65%, followed by Plateletcrit with a specificity of 34.31% over MPV and PDW in predicting UTI (Table).

TABLE 4: MEAN AND STANDARD DEVIATION OF COMPLETE BLOOD PARAMETERS FROM OUR STUDY POPULATION

Parameter	Culture positive group (n=140)		Culture negative group (n=140)		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
Hb	10.78	1.751	11.38	1.727	0.003*
TLC	10876.64	5401.501	9957.92	4515.218	0.116
PLC	3.57	1.643	3.31	1.609	< 0.001*
MPV	8.40	1.110	7.96	1.120	0.351
PCT	0.284	0.523	0.277	0.113	< 0.001*
PDW	16.52	1.20	12.52	2.52	0.158

TABLE 5: SENSITIVITY, SPECIFICITY, POSITIVE AND NEGATIVE LIKELIHOOD RATIOS OF THE PLC, MPV, PDW AND PCT IN PREDICTING THE DISEASE.

Parameter	Sensitivity	Specificity	Positive likelihood ratio	Negative Likelihood ratio
PLC (95% CI)	88.49% (88.9-89.7)	78.65% (64-83.6%)	1.43 (1.27-1.65)	0.12 (0.07-0.34)
MPV (95% CI)	95.43% (88.9-97.7)	19.32% (14.1-25)	1.11 (1.04-1.25)	0.11 (0.14-0.72)
PDW (95% CI)	96.49% (88.9-95.6)	28.4% (17.2-32.8)	1.2 (1.12-1.39)	0.33 (0.10-0.49)
PCT (95% CI)	98.49% (88.90-97.7)	34.31% (34.55-52.39)	1.45 (1.42-1.91)	0.23 (0.06-0.27)

Urine Culture was considered as gold standard for the patients affected with UTI. Further analysis was performed to assess the validity of the studied parameters in predicting UTI using receiver operating characteristics (ROC) curve which revealed that Platelet count and Plateletcrit can better predict UTI with relative difference in validity parameters. The area under curve was highest for PLC. PLC can be considered as a better choice among the platelet parameters to predict UTI as from our study (

Figure 3)

FIGURE 3: DIAGNOSTIC PROPERTIES OF TLC, MPV, PDW AND PLATELETCRIT USING ROC CURVES WITH REFERENCE TO URINE CULTURE.

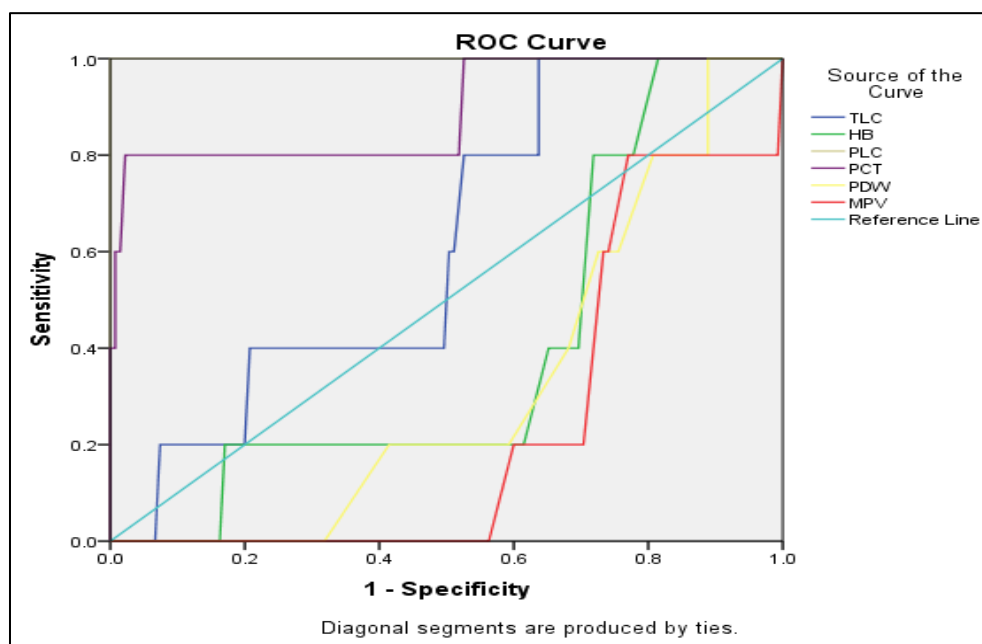


TABLE 6: AREA UNDER THE CURVE.

Test Result Variable(s)	Area
TLC	0.614
HB	0.398
PLC	1.000
PCT	0.890
PDW	0.324

MPV	0.246
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DISCUSSION

The present study validated the use of platelet parameters for diagnosing UTI so that it would help out in treatment plan and thereby finding a new predictor index for the management of UTI cases. The median age of study population was 3years in the culture positive group and 5years in the culture negative group. In this study, there is a female predominance over males in culture positive group. This distribution was comparable with the study done by **Baig MA et al (2015)** ⁴.

Urinalysis revealed that presence of pus cells was significantly more in the Culture positive group compared to the culture negative group ($p = 0.001$). In a similar study done by **Alaaraji et al (2020)** ⁸ it was also found that pus cells were significantly more in the UTI group when compared with control group.

Among the study population, the main causative agent was E. Coli in 72.9%, Klebsiella in 7.1%, Enterococcus in 5.7%, Proteus and Pseudomonas aeruginosa were less frequently reported among the patients with 2.1% and 2.9% respectively. **Chang et al.** ⁹ also found that E. coli was responsible for almost 76% of UTI cases followed by Klebsiella spp in 11.7%, Staphylococcus saprophyticus in 6.4%, and Pseudomonas aeruginosa in 2.2%. Moreover, **Riccabona et al.** ¹⁰ in his study also found that E coli (28%), Proteus mirabilis (16%), Staphylococcus aureus (12%), Pseudomonas aeruginosa and Streptococcus species each 7.4% were the most frequently isolated bacteria in the study group. However, type of causative bacteria varies in different countries and populations and there were some variations among different studies, but almost all studies and literatures proved that E. coli is responsible for major of UTIs among gram negative organisms, followed by gram positive cocci.

The present study found that the PLC and PCT levels were significantly higher in culture positive cases than culture negative cases. The present study had mean values of PLC, PCT, MPV and PDW within the normal range but it was still higher than the culture negative group. Among the platelet parameters, Platelet count had a higher specificity of 78.65%, followed by Plateletcrit with a specificity of 34.31% over MPV and PDW in predicting the disease. In a study done by **Alaaraji et al (2020)** ⁸, it was found that the

platelet count, MPV and PDW levels were significantly higher in UTI cases than controls. However, the mean platelet count of UTI cases was within normal range but was still higher than controls. The value of MPV in the present study is relatively similar to that of **Zayed et al**¹¹ study in which children with urinary tract infection had a mean MPV of 7.804 ± 0.914 but is less than that reported in study by **Srinivasa, S., et al**¹² in which the children diagnosed with urinary tract infections had a mean platelet volume of 12.4. In another study by **Catal, F., et al.**¹³ patients with upper UTI had greater MPV levels than controls. In this study, majority of the study participants were infected with gram negative organisms (94.3%) which may be the cause for normal platelet parameters.

In the present study, ROC curve revealed that platelet count and Plateletcrit can better predict UTI with a relative difference in validity parameters. The area under the curve was more with PLC thus stating that PLC can be considered as a better choice among platelet parameters to predict UTI. In a study done by **Lee et al**¹⁴, they evaluated the efficacy of MPV and PDW in children with lower UTI and compared them to a group of children with acute pyelonephritis and also used the ROC curve to assess the validity of MPV, ESR, CRP, and WBCs. They found that MPV had lower AUC than CRP but it has higher AUC than that of WBC and ESR, hence finally concluding that MPV can act as an acute phase inflammatory reactant in UTI. **Srinivasa and Dhingra**¹² tested the validity of Hb, CRP, Platelet count, MPV and PDW and found higher sensitivity, specificity, and diagnostic accuracy of these parameters except Hb. The higher AUC was produced by MPV (0.990), followed by PDW (0.910) and CRP (0.910) and the MPV had a sensitivity and specificity of 97.1% each.

Keeping in view the current study and the various studies exploring the value of platelet parameters as a marker in diagnosing UTI, it can be summarized that platelet parameters are newly emerging marker of inflammation with good clinical utility. Even though its potential to early diagnose the disease needs further evaluation, its role as a marker of infection can't be ruled out.

CONCLUSION

The median age group of the study population was 3 years with a female predominance in culture positive group (50.7%). Presence of pus cells in urine was significantly more in the Culture positive group. The main causative agent was E. Coli in 72.9% and only 8 (5.7%) were affected by gram positive organisms. Platelet parameters such as PLC and PCT were significantly higher in the culture positive group when compared with culture negative group ($p < 0.001$). The mean values of PLC, PCT, MPV and PDW were within the normal range in the culture positive group but was still higher than culture negative group. Among the platelet parameters, Platelet count had a higher specificity of 78.65%, followed by Plateletcrit with a specificity of 34.31% over MPV and PDW in predicting the disease. Anaemia was present among the culture positive group with a mean value of 10.7g/dL. ROC curve revealed that platelet count and Plateletcrit can better predict UTI with relative difference in validity parameters. The area under the curve was more with PLC thus stating that PLC can be considered as a better choice among platelet parameters to predict UTI as per this study.

LIMITATIONS

1. The universal method of collection of urine sample from the participants either by catheterization or suprapubic needle aspiration was not applied to the study group.
2. The study was done in a single center with a small sample size.
3. It requires data from similar large multicentric studies for the generalization of results.

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Conflict of interest: None

REFERENCES

1. Robinson JL, Finlay JC, Lang ME, Bortolussi R, Canadian Paediatric Society ID, Immunization Committee CPC. Urinary tract infections in infants and children: Diagnosis and management. *Paediatr Child Health*. 2014;19(6):315-325.
2. Tebruegge M, Pantazidou A, Clifford V, Gonis G, Ritz N, Connell T, et al. The age-related risk of co-existing meningitis in children with urinary tract infection. *PLoS One*. 2011;6(11):e26576.
3. Hansson S, Brandström P, Jodal U, Larsson P. Low bacterial counts in infants with urinary tract infection. *J Pediatr*. 1998;132(1):180-182.
4. Baig MA. Platelet indices-evaluation of their diagnostic role in pediatric thrombocytopenias (one year study). Published online 2015.
5. Yeaman MR. The role of platelets in antimicrobial host defense. *Clin Infect Dis an Off Publ Infect Dis Soc Am*. 1997;25(5):951-970.
6. Dr. Radha M, Dr. Vanisri HR. Platelet parameters as an inflammatory marker in children. *Int J Clin Diagn Pathol* 2020;3(2):44-48. DOI: 10.33545/pathol.2020.v3.i2a.223
7. Simões e Silva AC, Oliveira EA. Update on the approach of urinary tract infection in childhood. *J Pediatr (Rio J)*. 2015;91(6 Suppl 1):S2-10.
8. Alaaraji K, Al-obaidy Q, Mahdi S. The utility of platelet indices in diagnosis of urinary tract infection. *Ann Trop Med Public Heal*. 2020;23.
9. Chang SL, Shortliffe LD. Pediatric urinary tract infections. *Pediatr Clin North Am*. 2006;53(3):379-400, vi.

10. Riccabona M. Urinary tract infections in children. *Curr Opin Urol.* 2003;13(1):59-62.
11. Zayed KMS, Abdelhakeem AM, Gafar HS, Eldahshan TAEK. Diagnostic value of platelet parameters versus interleukin-6 in children with urinary tract infection. *Egypt Pediatr Assoc Gaz.* 2016;64(3):142-148
12. Srinivasa S, Dhingra P. Platelet indices in children with urinary tract infection. *Int J Contemp Pediatr* 2018;5(3):953-957.
13. Catal F, Bavbek N, Bayrak O, Uz E, Isik B, Karabel M, et al. Platelet Parameters in Children with Upper Urinary Tract Infection: Is There a Specific Response? *Ren Fail.* 2008;30(4):377-381.
14. Lee SJ, Cha J, Lee JW. Probiotics prophylaxis in pyelonephritis infants with normal urinary tracts. *World J Pediatr.* 2016;12(4):425-429.