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Trend of Erythrocyte Sedimentation Rate in Patients with Symptomatic Urinary Tract Infection Under Treatment

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Abstract

Objectives: The aim of this study was to evaluate erythrocyte sedimentation rate (ESR) in patients with symptoms of urinary tract infection (UTI), and to analyze bacteriological and clinical findings.
Methods: In a prospective study, 187 patients with UTI and suggestive signs and symptoms were included. History of UTI and clinical findings were recorded. Urine specimens were cultured and analyzed for pyuria by sediment microscopy and nitrite using a test strip. The systemic inflammatory response was assessed by ESR, and total white blood cell count.
Results: *Escherichia coli* accounted for 62.2% of the urinary isolates. Most UTI patients showed a decline three days after treatment, whereas some had an increased ESR response at this time (despite improvements in clinical symptoms). Overall, ESR on the sixth day was determined to be a better marker for response to symptomatic UTI treatment than the third day ESR.
Conclusions: This study showed that ESR and clinical findings were not interchangeable indexes of patient's condition, although they are concordant (both normal and both abnormal) in the vast majority of patients. Erythrocyte sedimentation rate is frequently misleading in patients with UTI and is not responsive to changes in the patient's condition. Checking ESR is recommended not earlier than six days after starting UTI treatment, if necessary.

Keywords: Urinary Tract Infections, Signs and Symptoms, Inflammation, ESR

1. Background

Urinary tract infections (UTIs) are amongst the most common bacterial infections affecting all age groups (1). There are some inflammatory biomarkers that may help determine the severity of UTI and predict the patient's condition. An old biomarker is erythrocyte sedimentation rate (ESR). This test is widely used and is a useful marker of inflammation in many conditions (2, 3). Erythrocyte sedimentation rate is a non-protein and an indirect measure of the acute phase reaction and reflects plasma viscosity. Sedimentation rate of red blood cells depends on several physiologic factors such as serum lipid and hemoglobin concentrations, ratio of plasma proteins, and plasma pH (4). Despite this limitation, this test is still used in different clinical settings to indicate disease severity and dynamics. Although there have been abundant publications on the clinical use of ESR in the past several decades, its value in diagnosis of infections has remained unclear (5). The role of ESR in clinical decision-making of chronic infectious diseases has been re-established in different settings, including chronic osteomyelitis and endocarditis (6, 7). In general, ESR rises in acute infections within 24 - 48 hours of the onset of inflammation and falls back slowly with resolution (5).

Bacterial infection in the urinary tract can elevate acute phase reactants, such as ESR (8). Its value lies in the fact that it is a simple and inexpensive laboratory test for assessing inflammation.

2. Objectives

Natural ESR response after UTI treatment could be considered as a proxy of inflammation presence; hence the aim of the present study was to assess the short-term prognostic value of ESR in adult patients with symptomatic UTI, who need hospital admission, and to compare this with current available biomarkers such as blood leucocyte count. The second aim was to assess the changes in clinical findings and ESR in response to treatment of UTI.

3. Methods

3.1. Patients

We conducted a prospective observational study on patients presenting a presumptive diagnosis of UTI. The study was performed as a census with a specified duration of time. The participants were selected among patients with symptomatic UTI in a general hospital (Bou-Ali Sina hospital of Qazvin University of Medical Sciences). In a two-year period (September 2013 to June 2015), all 18-year-old or older patients, who presented symptoms suggestive of UTI and were admitted to the emergency room, infectious or internal medicine wards, were screened without any strict exclusion criteria. The patients had already undergone an empirical treatment for UTI (e.g. treatment based on clinical symptoms or signs). At last, 187 patients were included based on presence of bacteriuria by quantitative culture, or pyuria. Samples were taken from the patients with a minimum of two typical signs or symptoms of lower or upper UTI (such as dysuria, frequency of urination, suprapubic tenderness and urgency). The patients did not have any other known site of infection or inflammation. A detailed clinical history was obtained and physical examinations were performed on admission and also days three and six. Signs, symptoms, concomitant diseases, and medical treatment were recorded. The UTIs were classified as urosepsis or UTI without sepsis.

3.2. Laboratory Procedures

Voided midstream urine samples were obtained for culture prior to treatment (except urosepsis). Urine specimens were examined immediately after collection. The samples were screened for the presence of nitrite by a strip test. Microscopy of spun urine was performed and the number of white and red blood cells per high-power field (HPF) was recorded. Pyuria was defined as at least five leukocytes per HPF. Urine was cultured semi-quantitatively using a calibrated loop that delivers 0.003 mL to the agar plate. All isolates were identified by standard methods. Significant growth was defined as 1:105 colony-forming units (CFU) per milliliters (mL) of urine for gram-negative bacteria, and 1:104 CFU/mL for gram-positive cocci.

Blood samples were obtained before the start of antimicrobial treatment and post-admission days three and six and analyzed for ESR, total white blood cells (WBC) (and polymorphonuclears [PMN]%), hemoglobin and creatinine (Cr) by conventional methods. Also urine analysis and urine culture were done on admission and day three. Urine samples were obtained by midstream method in trained adults and urine catheter in bedridden patients. Cultures driven from midstream samples with only one grown microorganism and a colony count of 10^5 or more CFU/mL were considered positive. Cultures of samples obtained by urine catheter were considered positive if there was concurrent pyuria and growth of one organism with a colony count of 10^5 or more CFU/mL. Pyuria was defined as five or more leukocytes in a high-power field in the urine sediment. Peripheral leukocyte counts (total and differential) were done by automated leukocyte analyzer method, and differential leukocyte count by Giemsa staining. Results of peripheral and differential leukocyte counts were compared with reference ranges for age. The patients were divided to three groups: (1) normal leukocyte count, (2) neutrophilic leukocytosis or leukocytosis with an absolute increase in neutrophil count, (3) isolated neutrophilia (an increase in the percentage of neutrophils without increased absolute leukocyte count). Neutrophilic leukocytosis was defined as a total WBC greater than 11,000/microL in addition to an absolute neutrophil count (ANC) greater than 7700/microL in adults. An ANC above 7700/microL in patients with a total WBC less than 11,000/microL was considered as an isolated neutrophilia.

Erythrocyte sedimentation rate was determined using the automated ESR method. An abnormal ESR was defined as: upper limit of normal considered as 15 and 20 mm/hr for males and females less than 50 years of age, respectively. This increased to 20 and 30 mm/hr for the age of 50 or more (2).

Erythrocyte sedimentation rate was analyzed to find any possible correlation with WBC, clinical sign and symptoms (i.e. body temperature), severity of bacteriuria, nitrite, and urinary tract inflammatory response (severity of pyuria).

3.3. Statistics

Descriptive and analytical tests were performed using the SPSS® software version 21 (SPSS Inc., Chicago, Ill, USA). Continuous variables were summarized as means ± standard deviation (SD) and categorical variables as frequencies and percentages. Fisher's exact test or Chi-square test was used to compare categorical variables. A P value of less than 0.05 was considered statistically significant, and all tests were two-tailed.

4. Results

4.1. Patient Characteristics

In total, 187 patients including 100 males and 78 females were recruited in the study (53.5 vs 46.5%) (Table 1). The age ranged from 18 to 95 years (mean of 66.42 ± 18.97 years) (Table 2). Mean oral temperature of the patients was 38.01°C (± 0.76°C). Patients with abnormal ESR showed more bacteriuria ($P < 0.05$). There were no significant correlations between ESR and urinary tract inflammatory response. Also, no correlation was found between ESR and severity of fever ($P = 0.23$). Tables 1 and 2 depict no significant relations between ESR and signs, symptoms and paraclinical characteristics of UTI patients.

Table 1. Demographic, Bacteriological and Other Related Para-Clinical Features Based on the Results of Erythrocyte Sedimentation Rate of Patients, Categorical Variables

	ESR on Admission (%)			P Value
	Abnormal	Normal	Total	Chi Square Test
Gender				0.151
Male	89 (55.6)	11 (40.7)	100 (53.5)	
Female	71 (44.4)	16 (59.3)	87 (46.5)	
Severity				0.971
Urinary Tract Infection	118 (73.8)	20 (74.1)	138 (73.8)	
Urosepsis	42 (26.3)	7 (25.9)	49 (26.2)	
WBC				0.071
≤11000	81 (50.9)	11 (40.7)	92 (49.5)	
>11000	66 (41.5)	11 (40.7)	77 (41.4)	
≤11000 but ANC > 7700	12 (7.5)	5 (18.5)	17 (9.1)	
Temperature				0.191
Normal	40 (25.0)	10 (37.0)	50 (26.7)	
Fever	120 (75.0)	17 (63.0)	137 (73.3)	
Urine culture				0.854
E. coli	99 (61.9)	16 (59.3)	115 (61.5)	
Other Than *E coli*	38 (23.8)	6 (22.2)	44 (23.5)	
Negative	23 (14.4)	5 (18.5)	28 (15.0)	
Urine WBC				0.672
No Pyuria	30 (18.8)	6 (22.2)	36 (19.3)	
Pyuria	130 (81.3)	21 (77.8)	151 (80.7)	
WBC clump				0.246
Positive	33 (20.6)	3 (11.1)	36 (19.3)	
Negative	127 (79.4)	24 (88.9)	151 (80.7)	
Nitrite				0.335
Positive	30 (18.8)	3 (11.1)	33 (17.6)	
Negative	130 (81.3)	24 (88.9)	154 (82.4)	
Bacteriuria				0.01[a]
Rare	16 (10.0)	0 (0.0)	16 (8.6)	
Few	23 (14.4)	9 (33.3)	32 (17.1)	
Moderate	42 (26.2)	6 (22.2)	48 (25.7)	
Many	79 (49.4)	12 (44.4)	91 (48.7)	

Abbreviations: ESR, erythrocyte sedimentation rate; WBC, white blood cells; ANC, absolute neutrophil count.
[a] chi square for trend.

4.2. Bacteriological Findings and Nitrite Test

Escherichia coli was the predominant urinary pathogen, accounting for 61.5% of the isolates, followed by *Enterococcus* and *Pseudomonas aeruginosa* (both 3.7%) (Table 1). Overall, negative urine cultures were reported in 28/187 (15%) patients. Systolic and diastolic blood pressure was higher in patients infected by *E. coli* ($P < 0.05$) although we didn't find any other significant difference between patients who were infected with *E. coli* or other bacterial species, and those who had negative urine cultures (Table 1). Among low count bacteriuria cases, patients without WBC clumps significantly showed more positive nitrite

Table 2. Demographic, Bacteriological and Other Related Para-Clinical Features Based on the Results of Erythrocyte Sedimentation Rate of Patients, Quantitative Variables

Characteristics	ESR in admission time, Mean (Standard Deviation)			P Value
	Abnormal	Normal	Total	T Test
Age	66.34 (19.17)	66.89 (18.14)	66.42 (18.98)	0.889
Admission period, d	9.42 (4.46)	9.37 (3.79)	9.42 (4.36)	0.952
Systolic blood pressure	124.06 (23.29)	126.78 (20.88)	124.45 (22.92)	0.571
Diastolic blood pressure	74.78 (12.36)	74.74 (12.31)	74.77 (12.32)	0.989
Pulse rate	87.36 (17.41)	86.89 (10.27)	87.29 (16.55)	0.892
Respiratory rate	19.26 (6.22)	20.81 (7.24)	19.49 (6.38)	0.243
Body temperature	38.04 (0.75)	37.85 (0.81)	38.01 (0.76)	0.230
WBC, CBC	10938 (5485)	10992 (4838)	10946 (5383)	0.962
PMN%	77.60 (12.54)	80.89 (11.45)	78.06 (12.40)	0.284
WBC, Urine	53.15 (39.16)	55.07 (41.89)	53.43 (39.46)	0.815

Abbreviations: ESR, erythrocyte sedimentation rate; WBC, total white blood cells; CBC, complete blood count; PMN, polymorphonuclears.

tests than those with WBC clump (38.9% vs. 12.6%; $P < 0.05$). Overall, nitrite positive urine specimens were significantly more common among patients with higher than lower-count bacteriuria (23% vs. 2%; $P < 0.05$).

4.3. WBC and ESR

Data on leukocyte count and ESR (admission time and day three) were available for all cases, yet differential leukocyte count and ESR (day 6) had been checked only in 137 (73.3%) and 54 (28.9%) patients, respectively. Results of leukocyte count were as follow: normal in 92 patients (49.5%), leukocytosis in 77 (41.4%), and isolated neutrophilia in 17 (9.1%). Among the patients, 160 (85.6%) had a raised ESR and only five (3.1%) had a value of 100 mm/h or higher. In patients with a raised ESR, 66 (41.5%) had neutrophilic leukocytosis and 12 (7.5%) had isolated neutrophilia. Only in 78 patients (43.8%), results of both ESR and increased leukocyte count were present.

In our study, the vast majority of patients recovered promptly and did not have any short-term complications. Overall, 99/187 (52.9%) of the patients responded to treatment on day three, however, only 10/187 (5.3%) did not have good clinical signs on day six (Table 3).

On day three, 41/99 (41.4%) of patients responded to treatment, their ESR increased or did not change, however only 14/48 (29.2%) of patients responded to treatment, their ESR increased on day 6 (Table 4).

5. Discussion

This study showed that ESR and clinical findings are not interchangeable indexes of patients' condition in the vast majority of cases, although they are concordant (either normal or abnormal). In our study 14% of the patients had normal ESR on admission. Only 36 (about one fifth) patients had no concomitant disease (possible causes of a high sedimentation rate).

It seems, slow response of ESR to the acute phase reaction leads to false negative results in early phase of an inflammatory process (2).

Although peripheral leukocyte count and ESR are considered simple non-invasive tests and used for diagnosis of invasive bacterial infections, more than a half of the patients with symptomatic UTI did not show a concomitant increase in leukocyte count (absolute or relative) and ESR. In our study, 85.6% of the patients with symptomatic UTI had abnormal ESR. Although moderate elevations of ESR are common in active infections, yet normal ESR cannot exclude infections (9).

In our study, the correlation between an abnormal ESR, presence or absence of patient condition and systemic inflammatory response syndrome (SIRS) criteria were dismally poor. Also, other studies have shown that ESR and leucocyte count don't have a great value in predicting outcome of febrile UTI (10, 11). The results of our study and similar studies demonstrate that ESR changes relatively slowly as the patient's condition improves (12). Peltola and Rasanen studied children younger than 16 years old with a confirmed bacterial infection. In these patients, ESR levels reached a maximum only after several days of admission (13). Peltola et al. compared ESR and fever in septic arthritis cases in a pediatric setting treated by antibiotics. Defervescence occurred more rapidly than ESR normalization (14, 15). Normalization of an elevated ESR may take several

Table 3. Responses to Treatment on Days Three and Six

	Signs on day 6 Count (%)		Total	P Value, Fisher Exact Test
	Improved	Not Improved		
Signs in day 3				0.066
Improved	97 (54.8)	2 (20.0)	99 (52.9)	
Not improved	80 (45.2)	8 (80.0)	88 (47.1)	
Total	177 (100.0)	10 (100.0)	187 (100.0)	

Table 4. Alteration in the Erythrocyte Sedimentation Rate Based on Response to Treatment on Days Three and Six

	Signs and Symptoms Count (%)		Total	P Value Chi Square Test	Odds Ratio (CI 95%)
	Improved	Not Improved			
ESR Day 3					0.98 (0.55 - 1.76)
Decreased	58 (58.6)	52 (59.1)	110 (58.8)	0.944	
No change or increased	41 (41.4)	36 (40.9)	77 (41.2)		
ESR Day 6					1.21 (0.2 - 7.4)
Decreased	34 (70.8)	4 (66.7)	38 (70.4)	0.833	
No change or increased	14 (29.2)	2 (33.3)	16 (29.6)		

Abbreviation: ESR, erythrocyte sedimentation rate.

weeks once an immunoglobulin response has occurred (8).

In our study, ESR was not responsive to rapid changes in the patient's condition. Although serial measurement of ESR level has been advocated for monitoring of disease processes in adulthood infections, most recent studies tend to favor pro-adrenomedullin, procalcitonin, and C-reactive protein over ESR, mainly because of the fact that ESR is affected by a multitude of factors (10).

Escherichia coli accounted for 61% of the urinary isolates, which is consistent with the results of previous studies of patients with community-acquired UTI (16, 17). The second and third common causative agents varied among countries. Isolates of gram-negative bacilli (other than *E. coli*) collected during our study included *Pseudomonas aeruginosa* (3.7%) and *Klebsiella pneumonia* (3.2%) whilst in the Asian-Pacific region they are more commonly responsible for infections [*K. pneumonia* (13.8%), *P. aeruginosa* (7.2%)] (17).

In our study, more than 90% of patients with symptomatic UTI had pyuria and only 27/159 (17%) of urine samples from symptomatic patients with positive urine cultures showed neither nitrite nor pyuria. Therefore, presence of pyuria and/or a positive nitrite test seems to be appropriate for the rapid diagnosis of presumed symptomatic UTI in patients.

5.1. Conclusion

Because of the slow changing nature and several confounders, ESR is frequently misleading in patients with UTI and is not responsive to changes in the patient's condition. Although most patients show a rapid decrease of ESR during three days after treatment, in some UTI cases, ESR rises despite improvements in clinical symptoms. It can also be concluded that most patients with UTI did not show alterations in ESR and leukocyte count concurrently. Also, there is no correlation between systemic inflammatory responses (leukocyte count, ESR, and fever) and urinary tract inflammatory response (pyuria). According to the results, we recommend examination of the ESR not earlier than six days after starting UTI treatment, if necessary.

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Footnotes

Authors' Contribution: Abbas Allami developed the original idea and the protocol, abstracted and analyzed the data, wrote the manuscript and was the guarantor. Navid

Mohammadi and Saeideh Makarem contributed to the development of the protocol, abstracted the data and prepared the manuscript.

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References

1. Bennett JE, Dolin R, Blaser MJ. *Principles and practice of infectious diseases*. **1**. Amsterdam: Elsevier Health Sci; 2014.
2. Osei-Bimpong A, Meek JH, Lewis SM. ESR or CRP? A comparison of their clinical utility. *Hematology*. 2007;**12**(4):353–7. doi: 10.1080/10245330701340734. [PubMed: 17654065].
3. Barati M, Alinejad F, Bahar MA, Tabrisi MS, Shamshiri AR, Bodouhi NO, et al. Comparison of WBC, ESR, CRP and PCT serum levels in septic and non-septic burn cases. *Burns*. 2008;**34**(6):770–4. doi: 10.1016/j.burns.2008.01.014. [PubMed: 18513877].
4. Pawlotsky Y, Goasguen J, Guggenbuhl P, Veillard E, Jard C, Pouchard M, et al. Sigma ESR: an erythrocyte sedimentation rate adjusted for the hematocrit and hemoglobin concentration. *Am J Clin Pathol*. 2004;**122**(5):802–10. doi: 10.1309/8H4L-45F5-G0G1-VKY1. [PubMed: 15491977].
5. Markanday A. *Acute phase reactants in infections: evidence-based review and a guide for clinicians. Open forum infectious diseases*. U.K: Oxford University Press; 2015.
6. Kronig I, Vaudaux P, Suva D, Lew D, Uckay I. Acute and chronic osteomyelitis. *Clin Infect Dis*. 2015;**70**:448.
7. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J*. 2015;**36**(44):3075–128. doi: 10.1093/eurheartj/ehv319. [PubMed: 26320109].
8. Harrison M. Erythrocyte sedimentation rate and C-reactive protein. *Aust Prescr*. 2015;**38**(3):93–4. [PubMed: 26648629].
9. Vajpayee NGS, Bem S. Erythrocyte sedimentation rate. In: McPherson RAPM, editor. *Henry's Clinical diagnosis and management by laboratory methods*. Philadelphia: Elsevier/Saunders; 2011. p. 519–22.
10. van der Starre WE, Zunder SM, Vollaard AM, van Nieuwkoop C, Stalenhoef JE, Delfos NM, et al. Prognostic value of pro-adrenomedullin, procalcitonin and C-reactive protein in predicting outcome of febrile urinary tract infection. *Clin Microbiol Infect*. 2014;**20**(10):1048–54. doi: 10.1111/1469-0691.12645. [PubMed: 25039648].
11. Leli C, Cardaccia A, Ferranti M, Cesarini A, D'Alo F, Ferri C, et al. Procalcitonin better than C-reactive protein, erythrocyte sedimentation rate, and white blood cell count in predicting DNAemia in patients with sepsis. *Scand J Infect Dis*. 2014;**46**(11):745–52. doi: 10.3109/00365548.2014.936493. [PubMed: 25195647].
12. Colombet I, Pouchot J, Kronz V, Hanras X, Capron L, Durieux P, et al. Agreement between erythrocyte sedimentation rate and C-reactive protein in hospital practice. *Am J Med*. 2010;**123**(9):8637–13. doi: 10.1016/j.amjmed.2010.04.021. [PubMed: 20800157].
13. Peltola H, Rasanen JA. Quantitative C-reactive protein in relation to erythrocyte sedimentation rate, fever, and duration of antimicrobial therapy in bacteraemic diseases of childhood. *J Infect*. 1982;**5**(3):257–67.
14. Peltola H, Paakkonen M, Kallio P, Kallio MJ, Osteomyelitis-Septic Arthritis Study Group . Prospective, randomized trial of 10 days versus 30 days of antimicrobial treatment, including a short-term course of parenteral therapy, for childhood septic arthritis. *Clin Infect Dis*. 2009;**48**(9):1201–10. doi: 10.1086/597582. [PubMed: 19323633].
15. Peltola H, Vahvanen V, Aalto K. Fever, C-reactive protein, and erythrocyte sedimentation rate in monitoring recovery from septic arthritis: a preliminary study. *J Pediatr Orthop*. 1984;**4**(2):170–4. [PubMed: 6699158].
16. Hooton TM, Roberts PL, Cox ME, Stapleton AE. Voided midstream urine culture and acute cystitis in premenopausal women. *N Engl J Med*. 2013;**369**(20):1883–91. doi: 10.1056/NEJMoa1302186. [PubMed: 24224622].
17. Lu PL, Liu YC, Toh HS, Lee YL, Liu YM, Ho CM, et al. Epidemiology and antimicrobial susceptibility profiles of Gram-negative bacteria causing urinary tract infections in the Asia-Pacific region: 2009-2010 results from the Study for Monitoring Antimicrobial Resistance Trends (SMART). *Int J Antimicrob Agents*. 2012;**40 Suppl**:S37–43. doi: 10.1016/S0924-8579(12)70008-0. [PubMed: 22749057].