GMR
The Original

EFFECT OF STAPHYLOCOCCUS AUREUS INFECTION ON KIDNEY FUNCTIONS AND RENAL PERFORMANCE

Ghufran N. Abdul-Hur[1], Noor S. Hallab[1], Shatha M. Ali[1], Mohammed M. Sharba[2*], Shamsul Dhuha k. Ramadhan[1], Mayada J. Kadhim[3]

[1] Microbiology Department, College of Science, Al-Karkh University of Science, Baghdad, Iraq
[2] Forensic Evidence Department, College of Science, Al-Karkh University of Science, Baghdad, Iraq
[3]Veterinary Resaechs and Laboratories Department, Veterinary Directorate, Ministry of Agriculture, Baghdad, Iraq
*Corresponding Authors: Mohammed M. Sharba, mohammed.mushtaq@kus.edu.iq

ABSTRACT
Background : ***Staphylococcus aureus*** is a type of Gram-positive bacteria that causes many diseases in humans, moving between the tissues and organs of the human body, including urinary tract infections and skin infections
Methodology : A total of 40 samples were collected, distributed as follows: 10 samples from the control group (healthy individuals), 10 samples from patients with urinary tract infections, 10 samples from patients with Staphylococcus aureus bacteriosis, and 10 samples from patients with Staphylococcus aureus sepsis. Blood was drawn from patients and healthy individuals in all study samples.
Result: Results were different because older people, especially those with urinary catheters, were more susceptible to UTIs. Sepsis patients had higher blood urea and creatinine levels than other groups. The group with Staphylococcus aureus sepsis had significantly higher C-reactive protein, procalcitonin, white blood cell count, and LDH levels. The tests' relationships with each other and with age were likewise strongly correlated.
Aim of study: Assessing the levels of kidney disease tests like urea, creatinine, C-reactive protein, LDL enzyme, procalcitonin, and white blood cells with age and their relationship to Staphylococcus aureus bacteria, which causes urinary tract infections, bacteremia, and sepsis.
Conclusion: This study suggests that Staphylococcus aureus infections start with inflammation and progress to bacteremia. If left untreated or without antibiotics, the bacteria may release virulence factors, causing sepsis and blood poisoning. These illnesses can kill. Kidney function, white blood cell count, and C-reactive protein testing are needed to determine the body's response to the infection and the spread of the bacterial toxin. Important diagnostic information can be gained. Urine protein is another important indicator of illness progression. The stage and severity of the sickness are also determined by biological indicators such procalcitonin and LDH levels. They also help determine the antibiotics that can slow the sickness by considering the bacteria's susceptibility.

KEYWORDS: LDH CRP Staphylococcus aureus Procalcitionin

INTRODUCTION:
Staphylococcus aureus is a type of Gram-positive bacteria that causes many diseases in humans, moving between the tissues and organs of the human body, including urinary tract infections and skin infections. It may reach the blood, causing septicemia and failure in many organs. Staphylococcus aureus secretes a group of toxins and enzymes, in addition to proteins and peptides that have an effect on virulence (1). It has many virulence factors that may cause different diseases, as the bacteria themselves may affect their virulence factors and multiply in areas of infection, leading to an imbalance of the microbiome in the same location, causing the appearance of a group of diseases (2). This bacterium possesses a virulence regulator called AGR and a bacterial count sensor system, which in turn stimulates the production of several toxins and virulence determinants when the bacterial cell count rises to a certain threshold, causing the disease to worsen (3-4). This bacterium plays a pivotal role in the high rate of disease-related complications, including acute kidney injury. Most previous studies investigating acute kidney injury in Staphylococcus aureus bacteria have shown that it leads to an increase in blood creatinine levels compared to baseline creatinine values (5-7). However, these studies did not consider the competing risk factors for acute kidney injury in Staphylococcus patients, nor the dynamics of risk factors such as antibiotic treatment (8, 9, 10, 11). This bacterium is also a major cause of bloodstream infections and infective endocarditis. Although this bacterium causes kidney infection in 0.5-6% of urinary tract infections, leaving treatment for such cases may lead to serious, life-threatening conditions (12).
The risk of urinary tract infections increases with age after the age of 65, as recorded for both men and women, and also after the age of 75, according to (13). They recorded that urinary tract infections are rare in men under the age of 60, but after the age of 75, the rate of urinary tract infections becomes similar between men and women (13). Urinary tract infections are among the most common types of infections in humans (14, 15), affecting all age groups and both

sexes worldwide. Urinary tract infections affect women more than men, with 40-60% occurring within one year. The cause of the infection is often Gram-negative bacteria (16, 17).

METHODS:

Samples were collected from patients with urinary tract infections (urinary tract infections, Staphylococcus aureus bacteriosis, and Staphylococcus aureus sepsis) after general urine examination and confirmation of the presence of pus in the samples. The samples were collected from Yarmouk Teaching Hospital in Baghdad after initial assessment of the infections.

A total of 40 samples were collected, distributed as follows: 10 samples from the control group (healthy individuals), 10 samples from patients with urinary tract infections, 10 samples from patients with Staphylococcus aureus bacteriosis, and 10 samples from patients with Staphylococcus aureus sepsis. Blood was drawn from patients and healthy individuals in all study samples. The blood was separated, and the following tests were performed: measurement of blood urea and creatinine levels; measurement of acute-phase proteins, PCT, and LDH levels using a German-made Roche Cobus 311 analyzer. A blood sample was also collected and placed in an EDTA tube for white blood cell count estimation using a CBC analyzer.

The samples were diagnosed for bacterial infection using a Vitek 2 analyzer.

RESULTS:

Age results were recorded for the four groups included in the study, with a mean score for each group. A highly significant difference was found between the four groups, as shown in Table 1.

The current study showed non-significant difference between ages of patients.

Table 1: Differences between ages of patients groups

Age (Year)				
Groups	Mean	Std. Deviation	Std. Error	P-value
Control	4640.	.716	.22	0.08 NS
UTI	54.9	8.04	2.54	
S. aureus Bacteremia	54.1	7.06	2.23	
S. aureus Sepsis	53.1	9.04	2.86	
One way ANOVA was used to compare between groups NS: Non significant.				

The studies parameters results:

The results of the tests, which were grouped according to their respective levels, showed an increase in the mean arithmetic value of blood urea, creatinine, acute-phase proteins, PCT, and LDH levels in patients with Staphylococcus aureus (SA) infection. A highly significant difference was also observed. Similarly, the mean arithmetic value of white blood cell count was elevated in the SA group, with a highly significant difference found among the four groups. (Table 2)

Table 2: Differences between studied parameters of patients groups

Groups	Mean	Std. Deviation	Std. Error	P-value
BUN				
Control	32.60	2.06	0.65	< 0.001**
UTI	34.60	4.27	1.35	
***S. aureus* Bacteremia**	58.90	12.10	3.82	
***S. aureus* Sepsis**	90.50	11.30	3.57	
Cr				
Control	0.87	0.1	0.03	< 0.001**
UTI	1.64	0.22	0.07	
***S. aureus* Bacteremia**	2.4	0.51	0.16	
***S. aureus* Sepsis**	3.95	1.052	0.33	

eGFR				
Control	92.40	2.6	0.83	< 0.001**
UTI	71.60	5.79	1.83	
***S. aureus* Bacteremia**	54.40	11.49	3.63	
***S. aureus* Sepsis**	33.60	8.42	2.66	
CRP				
Control	3.69	0.36	0.11	< 0.001**
UTI	41.80	12.072	3.81	
***S. aureus* Bacteremia**	92.60	14.90	4.71	
***S. aureus* Sepsis**	133.80	19.24	6.08	
PCT				
Control	0.18	0.01	0.01	< 0.001**
UTI	1.69	0.70	0.22	
***S. aureus* Bacteremia**	6.44	1.30	0.41	
***S. aureus* Sepsis**	13.02	3.08	0.97	
WBC				
Control	6.91	0.17	0.05	< 0.001**
UTI	10.62	0.96	0.30	
***S. aureus* Bacteremia**	14.51	1.72	0.54	
***S. aureus* Sepsis**	19.13	2.47	0.78	
LDH				
Control	169.0	11.4	3.63	< 0.001**
UTI	286.50	18.41	5.82	
***S. aureus* Bacteremia**	364.20	17.93	5.67	
***S. aureus* Sepsis**	444.60	26.46	8.36	
One way ANOVA was used to compare between groups. NS: Non significant., **: Significant difference at 0.01				

Pearson Correlation Results:

Pearson Correlation Results between studied parameters of the three patients group are illustrated in table 3.

The results of the correlation coefficient table between the three patient groups were recorded, and the results were as follows:

There is a direct relationship between age and the percentage of blood urea, creatinine level, acute phase proteins, PCT, white blood cells, and LDH level, while there was an inverse relationship between age and eGFR for the urinary tract infection group. The results of the correlation coefficient between age and creatinine level, eGFR, white blood cells, and LDH were recorded as a direct relationship, while for the bacteremia group, there was an inverse relationship between age and blood urea, acute phase proteins, and PCT. The results of the correlation coefficient between age and blood urea, creatinine level, acute phase proteins, PCT, white blood cells, and LDH were recorded as a direct relationship, while there was an inverse relationship with eGFR for the Staphylococcus aureus sepsis group. table (3) The correlation coefficient between blood urea nitrogen (BUN) and creatinine, acute phase proteins, PCT, white blood cells, and LDH showed a positive relationship for all three disease groups (urinary tract infections, bacteremia with Staphylococcus aureus, and septicemia with Staphylococcus aureus), while the relationship was negative with eGFR for all three groups. Similarly, the correlation coefficient between blood creatinine and acute phase proteins, PCT, white blood cells, and LDH showed a positive relationship, while it was negative with eGFR for all three disease groups. While the correlation coefficient between eGFR showed an inverse relationship with acute-phase proteins, PCT, WBC, and LDH, all other tests showed a direct relationship, meaning they increased with their increase in the three disease groups, as shown in Table 3.

Table 2: Pearson Correlation Results between studied parameters of UTI, *S. aureus* Bacteremia and *S. aureus* Sepsis patients group.

UTI			*S. aureus* Bacteremia		*S. aureus* Sepsis	
Groups	r-value	P-value	r-value	P-value	r-value	P-value
Age *vs*. BUN	0.028	0.93	- 0.056	0.8	0.271	0.4
Age *vs*. Cr	0.22	0.5	0.012	0.9	0.343	0.3

Age *vs*. eGFR	- 0.08	0.98	0.06	0.8	- 0.177	0.6
Age *vs*. CRP	0.28	0.42	- 0.02	0.9	0.208	0.5
Age *vs*. PCT	0.26	0.45	- 0.019	0.9	0.138	0.7
Age *vs*. WBC	0.42	0.22	0.223	0.5	0.143	0.6
Age *vs*. LDH	0.44	0.19	0.39	0.2	0.204	0.5
BUN *vs*. Cr	0.88	0.001**	0.965	0.001**	0.981	0.001**
BUN *vs*. eGFR	- 0.46	0.1	- 0.989	0.001**	- 0.988	0.001**
BUN *vs*. CRP	0.86	0.001**	0.917	0.001**	0.964	0.001**
BUN *vs*. PCT	0.89	0.001	0.771	0.009**	0.858	0.002**
BUN *vs*. WBC	0.67	0.03*	0.887	0.001**	0.754	0.012*
BUN *vs*. LDH	0.63	0.051	0.741	0.014*	0.751	0.012*
Cr *vs*. eGFR	- 0.28	0.41	- 0.922	0.001**	- 0.972	0.001**
Cr *vs*. CRP	0.93	0.001**	0.828	0.003**	0.959	0.001**
Cr *vs*. PCT	0.94	0.001**	0.676	0.03*	0.894	0.001**
Cr *vs*. WBC	0.81	0.004**	0.868	0.001**	0.788	0.007**
Cr *vs*. LDH	0.70	0.023*	0.74	0.014*	0.792	0.006**
eGFR *vs*. CRP	- 0.559	0.09	- 0.917	0.001**	- 0.967	0.001**
eGFR *vs*. PCT	- 0.549	0.1	- 0.774	0.009**	- 0.867	0.001**
eGFR *vs*. WBC	- 0.412	0.2	- 0.860	0.001**	- 0.787	0.007**
eGFR *vs*. LDH	- 0.623	0.054	- 0.707	0.02*	- 0.769	0.009**
CRP *vs*. PCT	0.988	0.001**	0.936	0.001**	0.906**	0.001**
CRP *vs*. WBC	0.844	0.002**	0.897	0.001**	0.879	0.001**

CRP *vs*. LDH	0.789	0.007**	0.826**	0.003**	0.876	0.001**
PCT *vs*. WBC	0.866	0.001**	0.785**	0.007**	0.883	0.001**
PCT *vs*. LDH	0.817	0.004**	0.794	0.006**	0.884	0.001**
WBC *vs*. LDH	0.783	0.007**	0.952**	0.001**	0.992	0.001**

Proteinuria distribution results

The protonuria results for the three groups showed significant variation. In the urinary tract infection group, 50% had no protonuria, 20% had low protonuria, and 30% had mild protonuria. In the bacteremia group, 60% had mild protonuria and 40% had moderate protonuria, while in the sepsis group, 40% had moderate protonuria and 60% had severe protonuria. (Table 4).

Table 3: showed Proteinuria distribution in each three patients groups.

Proteinuria distribution					
Groups	None No. (%)	Trace No. (%)	Mild No. (%)	Moderate No. (%)	Severe No. (%)
UTI	5 (50%)	2 (20%)	3 (30%)	----	-----
S. aureus Bacteremia	-----	-----	6 (60%)	4 (40%)	-----
S. aureus Sepsis	-----	-----	-----	4 (40%)	6 (60%)

DISCUSSION:

Staphylococcus aureus is not a common cause of urinary tract infections (UTIs) in humans, as it is a Gram-positive bacterium and less frequently found, typically comprising less than 1% of urine samples. Numerous studies have been conducted on this topic. A laboratory study in France found that Staphylococcus aureus constituted only 1.3% of urine samples submitted by patients (18). Another community-based study (19) in Britain on this type of bacteria in patient samples showed that it represented only 0.5% of all isolated UTI samples. It has been previously described that the isolation of this type of bacteria is associated with the use of urinary catheters and its spread through the bloodstream, which primarily affects the elderly (20). This study confirms that infection with this type of bacteria is indeed present in the elderly, as demonstrated in the experiment.

The percentage of infected patients was 13%, there was a percentage represented by bacteremia, and the percentage of patients who had a urinary catheter was 53%, according to other studies that were carried out by (21). The study was carried out on 102 patients in a specialized center for the care of veterans who were diagnosed with Staphylococcus aureus bacteria in the urine. The study was evaluated by (21). Previous studies have indicated that staphylococcal infection causing bacteremia ranges between 17% and 40% (22, 23, 24, 25). This decrease is attributed to the presence of acute kidney inflammation, which was accompanied by an increase in blood creatinine levels compared to healthy individuals. This assertion is consistent with the results of the study, which recorded an increase in blood creatinine levels in the group with bacterial bacteremia. Another study has shown that acute renal injury and a decrease in kidney function may result in death as a consequence of septicemia. The rise in deaths is due to these bacteria in the blood, which causes kidney function to cease. Higher antibiotic use, like vancomycin, may also raise the drug's plasma concentration. An additional explanation is that the presence of a high percentage of creatinine in the blood provides an indication of the assessment of multiple organ failure due to septic shock in accordance with the criteria of sepsis (26). Septic shock is considered an indicator of septicemia, which causes an increase in the percentage of creatinine being present in the blood. As a result of this, there is consensus that the increase in blood in the group with septicemia may be explained. Numerous studies have been conducted on measuring procalcitonin and LPG levels in patients with sepsis. One study confirmed that 75% of participants had elevated procalcitonin levels and 92.5% had elevated LPG. This aligns with other studies conducted by Bovo et al. in 1998, which demonstrated a correlation between elevated LPG and procalcitonin levels in patients with severe sepsis (27). This finding is corroborated by the study conducted, which found elevated levels of both procalcitonin and LPG in patients with Staphylococcus aureus sepsis. Several other studies have demonstrated the role of C-reactive protein (CRP). An

elevated CRP immune response indicates an inflammatory infection in the body, specifically in the blood (28). These early tests for detecting sepsis have been considered by some studies to be less accurate in detecting bacterial infections. However, in the study conducted, the sepsis group showed elevated levels. This is noticeable in C-reactive protein levels, and the reason for this is that it is one of the products of the immune response to the entry of foreign bodies, namely bacteria, into the bloodstream. This, in turn, stimulates monocytes to release immune signals and causes the secretion of acute-phase proteins. Therefore, it is elevated in patients with septicemia caused by Staphylococcus aureus bacteria.

While other studies have shown that LDH is a strong indicator of bacterial sepsis, as the latter converts pyruvate to lactate under anaerobic conditions during glucose metabolism, its levels rise in patients with bacterial sepsis due to decreased tissue perfusion, causing oxygen deficiency. This feature was demonstrated by (29). Numerous studies have established a link between protein in urine and urinary tract infections (UTIs), making it a key indicator. Scientific research indicates that the presence of protein in urine is an important criterion for distinguishing between pyelonephritis, acute pyelonephritis, and other types of UTIs (30). Furthermore, studies conducted in 2014 demonstrated that the percentage of protein in the blood during the acute phase ranges between 90.9% and 98.7% (30). Another study showed that the predictive value of protein in the blood is associated with bacterial UTIs, ranging from 5% to 9% (31). Yet another study also demonstrated that the negative predictive value of protein in urine reached 87.8%, meaning that the absence of protein in the urine indicates a low probability of bacterial infection, a view that aligns with this finding.

CONCLUSION:

As a result of this research, the findings suggest that an infection caused by Staphylococcus aureus begins with inflammation and then escalates to bacteremia afterwards. As a result of the bacteria releasing virulence factors, this might ultimately result in sepsis and blood poisoning if it is not treated or if antibiotics are not administered. These are serious infections that possibly result in death. When it comes to identifying the body's reaction to the infection and the degree to which the bacterial toxin has spread, it is essential to monitor kidney function and the amount of white blood cells, in addition to testing C-reactive protein (CRP). Important diagnostic information can be gleaned from this. An other crucial marker for distinguishing between the various stages of illness is the examination of urine protein. Biological indications such as procalcitonin and LDL levels are also essential for determining the stage of the illness and the degree of its severity. Additionally, they assist in determining the type of medicines that can be utilized to retard the course of the illness, taking into consideration the susceptibility of the bacteria to the particular antibiotic.

REFERENCES:

1.Lowy, F.D. *Staphylococcus aureus* infections. *N. Engl. J. Med.* **1998**, *339*, 520–532. [Google Scholar] [CrossRef] [PubMed]

2.Shopsin, B.; Kreiswirth, B.N. Molecular epidemiology of methicillin-resistant *Staphylococcus aureus*. *Emerg. Infect. Dis.* **2001**, *7*, 323–326. [Google Scholar] [CrossRef] [PubMed]

3.Le, K.Y.; Otto, M. Quorum-sensing regulation in staphylococci-an overview. *Front. Microbiol.* **2015**, *6*, 1174. [Google Scholar] [CrossRef] [PubMed]

4.Recsei, P.; Kreiswirth, B.; O'Reilly, M.; Schlievert, P.; Gruss, A.; Novick, R.P. Regulation of exoprotein gene expression in *Staphylococcus aureus* by agar. *Mol. Gen. Genet.* **1986**, *202*, 58–61. [Google Scholar] [CrossRef]

5. Holmes NE, Robinson JO, Van Hal SJ, Munckhof WJ, Athan E, Korman TM, et al.Morbidity from in-hospital complications is greater than treatment failure inpatients with Staphylococcus aureus bacteraemia. BMC Infect Dis 2018;18:107.

6. Joo EJ, Peck KR, Ha YE, Kim YS, Song YG, Lee SS, et al. Impact of acute kidney injury on mortality and medical costs in patients with meticillin-resistant
Staphylococcus aureus bacteraemia: a retrospective, multicentre observational
study. J Hosp Infect 2013;83:300e6.

7. Legg A, Meagher N, Johnson SA, Roberts MA, Cass A, Scheetz MH, et al. Riskfactors for nephrotoxicity in methicillin-resistant Staphylococcus aureus bacteraemia: a post hoc analysis of the CAMERA2 trial. Clin Drug Investig
2022;43:23e33.

8. Westgeest AC, Schippers EF, Delfos NM, Visser LG, De Fijter JW, De Boer MGJ,et al. Acute kidney injury in Staphylococcus aureus bacteremia. Eur J Clin Microbiol Infect Dis 2022;41:431e7.

9. Schumacher M, Allignol A, Beyersmann J, Binder N, Wolkewitz M. Hospitalacquired infections–appropriate statistical treatment is urgently needed. Int JEpidemiol 2013;42:1502e8.

10. Yousefi M, Pourmand MR, Fallah F, Hashemi A, Mashhadi R, Nazari-Alam A: Characterization of Staphylococcus aureus biofilm formation in urinary tract infection. Iran J Public Health. 2016, 45:485-93

11. YOON, Byung Il, et al. Risk factors for recurrent cystitis following acute cystitis in female patients. Journal of Infection and Chemotherapy, 2013;(19)4: 727-731.

12.Martha Medina and Edgardo Castillo-Pino (2019). An introduction to the epidemiology and burden of urinary tract infections TherAdv Urol. 2019 JanDec; 11: 1756287219832172. Published online 2019 May 2.
13.Michel Kengne, AmonTodjimbaideDounia, Julius MbekemNwobegahay . Bacteriological profile and antimicrobial susceptibility patterns of urine culture isolates from patients in Ndjamena, Chad Pan Afr Med J. 2017; 28: 258. Published online 2017 Nov 23.
https://doi.org/10.11604/pamj.2017.28.258.11197
14.Derese B, Kedir H, Teklemariam Z, Weldegebreal F, Balakrishnan S. Bacterial profile of urinary tract infection and antimicrobial susceptibility pattern among pregnant women attending at Antenatal Clinic in DilChora Referral Hospital, Dire Dawa, Eastern Ethiopia. TherClin Risk Manag. 2016;12:251-260
https://doi.org/10.2147/TCRM.S99831
15.Dave V R, Shah V R, Sonaliya K N, Shah S D, Gohel A R. A Study on Epidemiological Profile of Urinary Tract Infections in Perspective of Diabetic Status among Patients Attending Tertiary Care Hospital, Ahmedabad. Natl J Community Med 2018;9(8):594-598
16. Demuth PJ, Gerding DN, Crossley K: Staphylococcus aureus bacteriuria. Arch Intern Med. 1979, 139:78-80. 10.1001/ARCHINTE.1979.03630380056019
17.. Muder RR, Brennen C, Rihs JD, Wagener MM, Obman A, Stout JE, Yu VL: Isolation of Staphylococcus aureus from the urinary tract: association of isolation with symptomatic urinary tract infection and subsequent staphylococcal bacteremia. Clin Infect Dis. 2006, 42:46-50. 10.1086/498518
18.. Goldstein FW: Antibiotic susceptibility of bacterial strains isolated from patients with community-acquired urinary tract infections in France. Multicentre Study Group. Eur J Clin Microbiol Infect Dis. 2000, 19:112-7. 10.1007/s100960050440
19.. Barrett SP, Savage MA, Rebec MP, Guyot A, Andrews N, Shrimpton SB: Antibiotic sensitivity of bacteria associated with community-acquired urinary tract infection in Britain. J Antimicrob Chemother. 1999,
20.N.E. Holmes, J.O. Robinson, S.J. VanHal, W.J. Munckhof, E. Athan, T.M. Korman, *et al.* Morbidity from in-hospital complications is greater than treatment failure in patients with *Staphylococcus aureus* bacteraemia BMC Infect Dis, 18 (2018), p. 107[
21.E.J. Joo, K.R. Peck, Y.E. Ha, Y.S. Kim, Y.G. Song, S.S. Lee, *et al.*
Impact of acute kidney injury on mortality and medical costs in patients with meticillin-resistant *Staphylococcus aureus* bacteraemia: a retrospective, multicentre observational study J Hosp Infect, 83 (2013), pp. 300-306
22.A. Legg, N. Meagher, S.A. Johnson, M.A. Roberts, A. Cass, M.H. Scheetz, *et al.* Risk factors for nephrotoxicity in methicillin-resistant *Staphylococcus aureus* bacteraemia: a post hoc analysis of the CAMERA2 trial Clin Drug Investig, 43 (2022), pp. 23-33
23.A.C. Westgeest, E.F. Schippers, N.M. Delfos, L.G. Visser, J.W. De Fijter, M.G.J. De Boer, *et al.* Acute kidney injury in *Staphylococcus aureus* bacteremia Eur J Clin Microbiol Infect Dis, 41 (2022), pp. 431-437
24.M. Singer, C.S. Deutschman, C.W. Seymour, M. Shankar Hari, D. Annane, M. Bauer, *et al.* The third international consensus definitions for Sepsis and septic shock (Sepsis-3) JAMA, 315 (2016), pp. 801-810
25.Povoa P, Almeida E, Moreira P, Fernandes A, Mealha R, Aragao A, et al. C-
reactive protein as an indicator of sepsis. Intensive care medicine.1998;
24(10):1052-1056.
26. Mimoz O, Edouard AR, Samii K, Benoist JF, Assicot M, Bohuon C. Procalcitonin and C-reactive protein during the early posttraumatic systemic inflammatory response syndrome. Intensive care medicine.1998;24(2):185-188.
27. Zein JG, Lee GL, Tawk M, Dabaja M, Kinasewitz GT. Prognostic signi cance of elevated serum lactate dehydrogenase (LDH) in patients with severe sepsis.
Chest.2004;126(4):873S
28. Sproston, N. R. & Ashworth, J. J. (2018) C-reactive protein at sites of inflammation and infection. Frontiers in Immunology, 9, 754. https://doi.org/10.3389/ fimmu.2018.00754
29. Kang, H. E. & Park, D. W. (2016). Lactate as a biomarker for sepsis prognosis? Infection & Chemotherapy, 48(3), 252-253. DOI: https://doi.org/10.3947/ic.2016.48.3.252.
30-Mohkam M, Shabestami G, Kompani F. Frequency of massive proteinuria in childhood [3]pyelonephritis and the response to antibiotic therapy. J Ped Nephrology. 2014;1(3):121-24.
31-Carter JL, Tomson RV, Stevens PE. Dose urinary tract infection cause proteinuria or [13]microalbuminuria? A systematic review. Nephrol Dial Transplant. 2006;21(11):3031-3