ISSN: 0067-2904

Bacteremia Associated with Pressure Ulcers at Alyarmuk Teaching Hospital in Baghdad

Nuha S. Jassim*, Sameer Abdul ameer Alash
Department of Biology, College of Science, University of Baghdad, Baghdad, Iraq

Received: 7/10/2019 Accepted: 30/11/2019

Abstract

Fifty patients(24 female and 26 male)with pressure ulcersassociated with different diseasesand attending AL-yarmouk Teaching Hospital in Baghdad were selected in this study. The duration of sample collection was from March to December 2018. All blood samples collected from patients were submitted to a blood culturing technique to examine bacteremia. The results showed that12 blood bacterial isolates were obtained. The isolated bacteria were subjected to Vitek-2, which is an accurate identification technique. The results of the blood culturing technique revealed that 33.3% were Gram negative bacteria, while 66.6% were Gram positive. Diagnosis by Vitek-2 showed that 33.3% were*Staphylococcus spp.* , 33.3% were *Enterococcus spp.* , 25.1% were*Serratiamarcescens* and 8.3% comprised *Acinetobacterbaumannii*. The results of minimum inhibitory concentration (MIC)by Vitek-2showed that Trimethoprime –Sulfamethazole concentration at 320 µg\ml was the MIC for *Acinetobacterbaumanni*, while piperacilin, Ticarcillin, and Ticarcillin-Clavulanic acidat 128 µg\ml were the MIC for *Serratia marcescens* . *Acinetobacterbaumannii*showed 100% resistance to all antimicrobial agents, while for the *Serratiamarescence*resistancevalues were 54.55%, 54.55%, and 45.45% for isolate numbers 1, 2, and 3, respectively. Gram positive bacteria recorded NitrofurantionMIC of 256 µg\ml against *Staphylococcus epidermidis*and *Enterococcus spp.*, withboth species showinghigh resistance compared with the others which had a value of87.50%.

Keywords: Pressure ulcers, bacteremia, Blood culture.

تجرثم الدم المرتبط بمرضى قرح الفراش في مستشفى اليرموك التعليمي في بغداد

نهى صلاح جاسم*, سمير عبد الامير علش
قسم علوم الحياة, كلية العلوم, جامعة بغداد، بغداد، العراق

الخلاصة

خمسون مريضا تم اختيارهم في هذه الدراسة يعانون من قرح الفراش ومن امراض مختلفة اخرى (24 انثى و 26 ذكر) المقيمين في مستشفى اليرموك التعليمي في بغداد. كل عينات الدم التي جمعت من المرضى خضعت لتقنية زراعة الدم للتحري عن تجرثم الدم. اظهرت النتائج الحصول على 12 عزلة بكتيرية. تم تشخيص هذه العزل بواسطة جهاز Vitek-2 وهو جهاز دقيق في التشخيص. كشفت نتائج تقنية زراعة الدم 33.3% بكتريا سالبة لصبغة كرام بينما 66.6% تعود الى البكتريا الموجبة لصبغة كرام. أظهر التشخيص بواسطة Vitek-2 .ان نسبة *Enterococcus spp.* بلغت33.3%وكانت *Staphylococcus* 33.3% ولبكتريا*Serratia marcescens spp.* كانت25.1% واخيرا سجلت بكتريا *Acinetobacter*

*Email: Nuhabio91@yahoo.com

أظهرت نتائج الحد الأدنى من تركيز المثبطة (MIC) ان تركيز 8.3%نسبة *baumannii*. Trimethoprime –Sulfamethazole كان 320µg\ml لبكيريا *Acinetobacter baumanni* بينما piperacilin, Ticarcillin, Ticarcillin–Clavulanic acidµg\ml 128لبكتيريا تركيز مضادات *Acinetobacter baumannii* اظهرتبكتريا *Serratia marcescens*. مقاومة لكل انواع المضادات المستخدمة في هذه الدراسة . بينما نسبة المقاومة لبكتريا *Serratia marcescens* كانت ,54.55% 54.55% ,45.45% للعزل البكترية المرقمة 1،2،3 على التوالي.البكتريا الموجبة لصبغة كرام اظهرت MICالمضاد Nitrofurantion كانت 256 µg\ml ضد *Staphylococcus epidermidis* و *Enterococcus spp.*, هذان النوعان يظهران مقاومة عالية مقارنة مع الأنواع الأخرى التي كانت87.50 ٪.

Introduction

Pressure ulcers (PUs) are an injury to the skin or underlying tissue due to unrelieved pressure [1]. It is a serious health problem for the world, specifically toweakened geriatric or bed-bound patients in hospital [2].The symptomstypically range from skin redness to serious injuries to thebones or attached tissues,raisinga significant threat to patients with restricted mobility [3]. The prevalence of developed pressure sore is high in elderly people, appearing within those between the 70s and 80s decades. These ulcers appear in community setting, nursing homes and hospitals, with an incidence varying from 1.2% to 11.2% [4]. Pressure ulcers are generally followed by an inflammatory response andmostly bylocal bacterial colonization or systemic disease[5].

Risksof pressureulcers are correlated with remarkable morbidity and mortality with bacteria, which are the most prevalent complicating factors related with pressure ulcers[6].

PUs can serve as foci for blood infection asthe mostprevalent considerable Infected PUs complication. Patientsare often more probable to develop bacteremia[7].

The association between PUand bacteremia was related with 50 percent mortality rate in hospitalize d patients[8].Septicaemiaor secondary bacteremia can represent complications of the pressure ulcer where both of these situations are correlated with increased death[9]. Precise identification of bacterial isolates from blood at species level as well as accurate identification of portal of entry and/or thesource of infection are essential for the ideal management of such infections[10].

From 1995 to 2002, a database of a hospital in the United Statesrecognizedcoagulase negative staphylococcus (CoNS) as the most prevalent cause, responsible for 31 percent of cases[11].In recent years, the prevalence of *Acinetobacterbaumannii*bacteremia has increased significantly, particularly in immunocompromised populations and intensive care units[12]. Enterococci have recently become one of the most prevalent nosocomial pathogens, with an elevated mortality rate of up to 61% [13].*Serratiamarcescens* is considered as an opportunistic bacterium that causes a variety of human infections, including keratitis ,bacteremia, as well as urinary tract and wound infections [14].

The aim of this study is to detect bacteremia associated with pressure ulcers,along withtesting MIC values of several antibacterial agents.

Materials and methods

Patients

Fifty patients (24 female and 26 male). 40% of patients between 70 and 80 years were included in this study suffering from pressure ulcer and another disease (30% heart disease, 18% lung disease, 16% kidney disease, 16% diabetic patients and the remaining percent for another disease) all these disease with a pressure ulcer were made the patients bed redden at department of medicine\ AL-yarmouk teaching hospital and the patients diagnosed clinically by a physician for pressure ulcer and bacteremia.The duration of study from the march 2018 to December 2018.

Blood sample collection and bacteremia

The following guidelines were implemented rigidly when samples of blood were obtained for blood culture [15]:

Whenever possible, blood sampleswere taken for culture before antimicrobial therapy was administered.ninemillilitres of blood was injected into a sterile bottle containing brain heart infusion broth culture.The same method was repeated to another blood sampletaken from separate sites over a duration of 10 min.Then, the bottles were incubated for 18-24 hours at 37 ° C.The presence of macroscopic alterations such as haemolysis, turbidity, cotton ball like colonies,and gas bubbles were

screened during the next days.Gram staining was performedirrespective to the macroscopic indications of growth,whileblind subcultures ofblood and Macconkyagar were performed after 1,3,and 7 days.

Identification of bacterial isolates

Morphological identification was performed by examiningthe colonieson different mediaand by gram staining. The precise identificationwas achieved throughdiagnosis by vitek-2 system.

Antimicrobial screening of bacterial isolates

Antimicrobial screening test wasperformed by using vitek-2 system, with the susceptibility card for Gram positive bacteria was AST-P580 and that for Gram negative bacteria was AST-222. Interpretation of the results wascarried out using the criteria of the Clinical Laboratory Standards Institute (CLSI, 2018) [16].

Statistical Analysis:

The Statistical Analysis System- SAS (2012) program was used to detect the effects of differentfactors onstudy parameters[17]. Least significant difference –LSD- test was used to compare significant differences between means and Chi-square test was used to compare significant differences between percentages.

Resultsand Discussion

From 50 patients with pressure ulcer, 12 samples (24%) were blood culture positive and different types of bacterial isolates were isolated and stained (33.3%Gram negative bacteria and Gram positive 66.6%), as shown in Table-1. Accurate diagnosis by vitek-2 revealed 33.3% *Staphylococcus sp.*, 33.3% *Enterococcus sp.*, 25.1% *Serratia maresscence*, and8.3% *Acinetobacterbaumannii*, as shown in Table-1. Antimicrobial test was performedfor bacterial isolates.

Table 1-The results of blood culture and identification by Vitek- 2 compact system

NO.	Blood culture	Vitek-2
1	33.3% of *Staphylococcus sp.*	25 % of *S.heamolyticus* 25 % of *S.epidermidis* 50 % of *S.aureus*
2	33.3% of *Enterococcus sp.*	50% of *E.faecalis* 50% of *E.gallinarum*
3	25.1% *Serratia maresscence*	
4	8.3% of *Acinetobacterbaumannii*	

The results demonstrated a significant differencebetween bacterial isolates ($P<0.05$). The highest minimum inhibitory concentration (MIC) achieved usingTrimethoprime-Sulfamethazolewas against*Acinetobacterbaumannii*was 320 µg\ml, whereas for *Serratia marescence*, the piperacilin, Ticarcillin and Ticarcillin-Clavulanic acid showed highest MIC (128 µg\ml),as shown in Table-2 and Figure-1.

Table 2-Theminimum inhibitory concentration for Gram negative bacteria

Bacterial isolate	*Serratia marescence*	*Serratia marescence*	*Serratia marescence*	*Acinetobacter baumannii*
Antimicrobial	MIC µg\ml	MIC µg\ml	MIC µg\ml	MICµg\ml
Cefepime	64 (R)	8 (S)	64 (R)	32 (R)
Ceftazidime	64 (R)	16 (R)	64(R)	64 (R)
Ciprofloxacine	0.25 (S)	0.25 (S)	0.25 (S)	4 (R)
Gentamicin	4 (S)	16 (R)	1 (S)	16 (R)
Meropenem	16 (R)	0.25 (S)	0.25 (S)	16(R)
Minocycline	8 (I)	4 (S)	8 (I)	16 (R)
piperacilin	128 (R)	128 (R)	128 (R)	128(R)
Ticarcillin	128	128	128	128 (R)
Ticarcillin-Clavulanic acid	128 (R)	128 (R)	128 (R)	128(R)

Tobramycin	8 (I)	16 (R)	1 (S)	16 (R)
Trimethoprime-Sulfamethazole	20 (S)	20 (S)	20 (S)	320 (R)
LSD value	16.38 *	`18.24 *	16.55 **	27.93 *
* (P<0.05).				

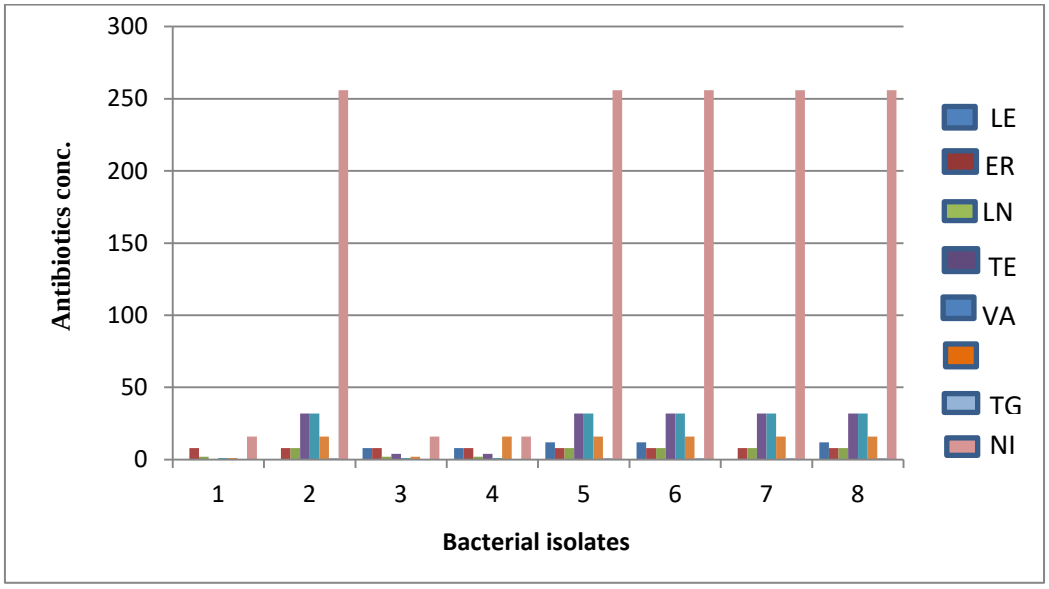

Figure 1-Antibiotics sensitivityto minimum inhibitory concentrations amongbacterial isolates(Gram positive).

1 (*S.aureus*) ; 2 (S. epidermidis) ; 3 (*S.heamolyticus* 1) ; 4 (*S.heamolyticus* 2) ; 5 (*E.fecalis* 1) ; 6 (*E.fecalis* 2) ;7 (*E.gallinarum*1) ; 8 (*E.gallinarum*2).Abbervation : Levofloxcin(LEV),Erythromycin(ERY),Linezolid(LNZ), Ticoplanin(TEC), Vancomycin(VAN) ,Tetracycline(TET), Tigecycline(TGC),Nitrofurantion(NIT).

*Acinetobacterbaumannii*showed 100% resistance to all antimicrobial agents used in this study, while the resistance values for the *Serratiamarescence*were54.55%, 54.55%, and 45.45% for isolates number 1,2, and 3, respectively, as shown in Table-3.

Table 3-The resistance percentages for gram negative bacteria

	Acinetobacter baumannii	*Serratia* marescence(1)	*Serratia marescence* (2)	*Serratia marescence(*3)
Resistant (R)	(100%) (11 \11)	(54.55%) (6 \11)	(54.55%) (6\11)	(45.45%) (5\11)
Sensitive (S)	(0.00%) (0\11)	(27.27%) (3\11)	(45.45%) (5\11)	(45.45%) (5\11)
Intermidate (I)	(0.00%) (0\11)	(18.18%) (2\11)	(0.00%) (0\11)	(9.10%) (1\11)
Total	11*	11*	11*	11*
Chi-Square (χ^2)	15.00 **	9.73 **	12.39 **	11.03 **
** (P<0.01).				

*11 : Is the number of antimicrobial agent used in this study

There was also asignificant differencebetween bacterial isolates (P<0.05), with the highest MIC usingNitrofurantion against *Staphylococcus epidermidis*being256 µg\ml while that for all *Enterococcus spp.*was256 µg\ml,as shown in Table-4 and Figure-2.

Table 4-The MIC values for Gram positive bacteria

Bacterial isolate	*S. aureus*	*S. epidermidis*	*S. heamolyticus*	*S. heamolyticus*	*E. faecalis*	*E. faecalis*	*E. gallinarum*	*E. gallinarum*
Antimicrobial	MIC µg\ml	MIC µg\ml	MIC µg\ml	MIC µg\ml	MIC µg\ml	MIC µg\ml	MIC µg\ml	MIC µg\ml
Levofloxcin	0.12 (S)	0.12 (S)	8 (R)	8 (R)	12 (S)	12 (S)	0.25 (S)	12 (S)
Erythromycin	8 (R)	8 (R)	8 (R)	8 (R)	8 (R)	8 (R)	8 (R)	8 (R)
Linezolid	2 (S)	8 (R)	2 (S)	2 (S)	8 (R)	8 (R)	8 (R)	8 (R)
Ticoplanin	0.5 (S)	32 (R)	4 (S)	4 (S)	32 (R)	32 (R)	32 (R)	32 (R)
Vancomycin	1 (S)	32 (R)	1 (S)	1 (S)	32 (R)	32 (R)	32 (R)	32 (R)
Tetracycline	1 (S)	16 (R)	2 (S)	16 (S)	16 (R)	16 (R)	16 (R)	16 (R)
Tigecycline	0.12 (S)	1 (R)	0.5 (S)	0.5 (S)	1 (R)	1 (R)	1 (R)	1 (R)
Nitrofurantion	16 (S)	256 (R)	16 (S)	16 (S)	256 (R)	256 (R)	256 (R)	256 (R)
LSD value	6.19 *	17.94 *	6.55 *	6.09 *	20.44 *	20.44 *	17.52 *	20.44 *

* (P<0.05).

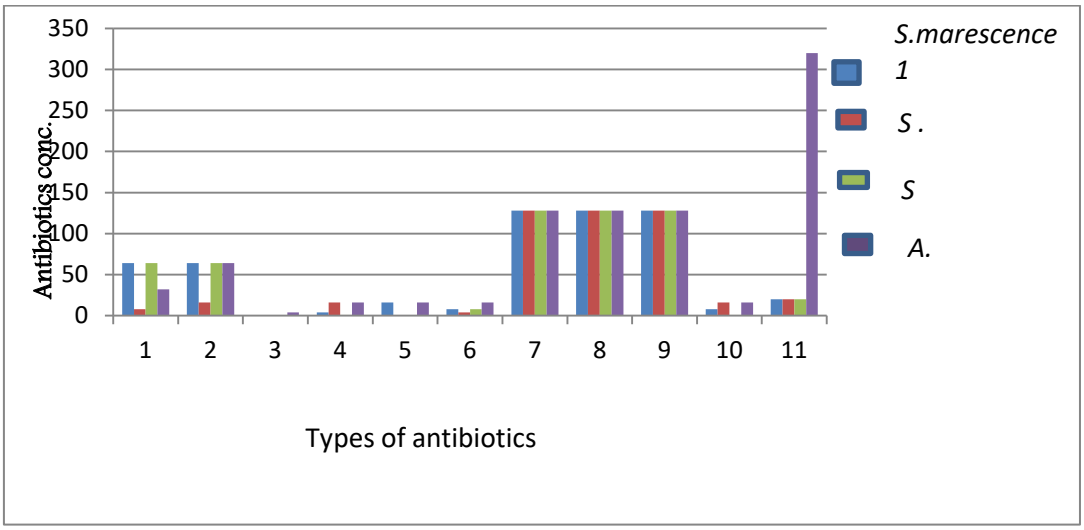

Figure 2-Antibiotic sensitivity variations among Gram negative bacterial isolates (series1 *Serratia marescence*38; series 2 *Serratia marescence*15; series3 *Serratia marescence*7; series4 *Acinetobacterbumannii*). 1-Cefepime;2-Ceftazidime;3-Ciprofloxacine;4-Gentamicin;5-Meropenem;6-Minocycline;7-piperacilin;8-Ticarcillin;9-Ticarcillin-Clavulanic acid;10-Tobramycin;11-Trimethoprime-Sulfamethazole

The bacterial isolate that had the highestbacterial resistance was *S.epidermidis*87.50%,withthe same percentage being recorded for*Enterococcus spp.* , as shown in Table-5.

Table 5-The resistance percentage for Gram negative bacteria

	S. aureus	*S. epidermidis*	*S. heamolyticus*	*S. heamolyticus*	*E. faecalis*	*E. faecalis*	*E. gallinarum*	*E. gallinarum*
R	(12.50%) (1\8)	(87.50%) (7\8)	(25.00%) (2\8)	(37.50%) (3\8)	(87.50%) (7\8)	(87.50%) (7\8)	(87.50%) (7\8)	(87.50%) (7\8)
S	(87.50%) (7\8)	(12.50%) (1\8)	(75.00%) (6\8)	(62.50%) (5\8)	(12.5%) (1\8)	(12.50%) (1\8)	(12.50%) (1\8)	(12.50%) (1\8)
I	(0.00%) (0\8)	(0.00%) (0\8)	(0.00%) (0\8)	(0.00%) (0\8)	(0.00%) (0\8)	(0.00%) (0\8)	(0.00%) (0\8)	(0.00%) (0\8)
*Total	8*	8*	8*	8*	8*	8*	8*	8*
Chi-Square (χ^2)	12.56 **	12.56 **	10.47 **	9.85 **	12.56 **	12.56 **	12.56 **	12.56**
** (P<0.01).								

*8: Is the numbers of antimicrobial agents used in this study.

Discussion

A study published by Thomas (2006) on 21 sepsis syndrome with a attributable to pressure ulcers revealed that 76% had bacteremia resulted from pressure ulcer [18]. Another study by Braga*et al.*(2017) revealed that,amongsixteen patients with infected pressure ulcer, 62.5% developed bacteremia [19]. These results demonstratedhigher proportions of bacteriemic patients than that recorded in our study, which was24%.

The Gram negative bacteria associated with bacteremia:

(Acinetobacterbaumannii and*S. marescence)*

In our study,*A. baumannii* showed resistance to all antimicrobial agents.Thisresultis corresponding with other studies. A study by Yang *et al.*,(2018)showed that77.8% of the patients were multidrugresistant[20].In addition, China's antimicrobial resistance monitoring program has wide ly identified extensive drug resistance to *A. baumannii* (XDRAB)[21].

In another study done by Xu*et al.*, (2016) state that87.7% isolates from bacteremic patients were considered to be XDR[22]. In the same study of Xu*et al.*, (2016) *Acinetobacterbaumannii*isolated from blood was resistant to Cefepime, Ceftazidime ,Ciprofloxacin, Gentamicin and Tobramycin this results correspond the current study results only the different in the isolatewas intermediately resistant to Meropenem, while in a present study was resistant to it [22].

The abilityof*A. baumannii*for the acquisition of genetic resistance determinants is responsible for the development of MDR strains. Other resistance mechanisms include Beta-lactamases, changes in porin canals, efflux pump (responsible for resistance to beta lactam antibiotics), mutations in deoxyribonucleic acid topoisomerase (mediated resistance to quinolone), and genes coding amino-glycoside-modifying enzymes .In addition, oxacillinases and metallo-blactamases (e.g., blaOXA58andblaOXA24\40, blaOXA23,) contribute to the resistance of carbapenem [23].

A retrospective cohort study was also previously performed,were 10 patients with one or more positive blood cultures for *S. marcescens*were recordedin a tertiary care hospital in Seoul, South Korea, from January 2006 to December 2012 [24]. While in the present study, 3 patients with positive blood cultures of *S. marcescens* were recorded for the period from March 2018 to December 2018.

The majority of the isolates in a study by Kim *et al.*, (2015) were susceptible tomeropenem, cefepime, and ceftazidime [24].While in this study, only 2 isolates weresensitive to meropenemsensitive and one isolate was sensitive to cefepime,whereasall isolates were resistant to ceftazidime.

Recent epidemiological analysisdemonstrated an increase in the rate of antimicrobial resistance among isolates of *S.*Marcescens. In contrast, the multidrug-resistant (MDR) strains of *S. Marcescens*were linked with severe outcomes [25].

The Gram positive bacteria associated with bacteraemia

The most common bacteria associated with pressure ulcers were reported to be *Enterococcus faecalis* and *Staphylococcus aureus*[26].

The incidence of MRSA infections, particularly bacteremia, varies worldwide. In 2014, the proportio n of MRSA isolates in Europe ranged from 0.9% in the Netherlands to 56% in Romania[27].In a study on patients with coagulase-negative staphylococci(CoNS), three cases out of 56 (5.4%) of bacteremia were associated with pressure ulcers [28], whereas the proportion of those withCoNS was 10.09% [29]

*Enterococcus spp.*was shown to be responsible for 3.6% of bacteremia associated with pressure ulcers[30].Enterococci have recently become one of the most prevalent nosocomial pathogens, with an elevated death rate of up to 61%.Enterococci are reported as the second most cause of urinary tract and wound infections and the third common cause of bacteraemia[31].In the UK,there were 7066 cases reported of bacteremia by *Enterococcus* species in 2005, reflecting an increase of 8% from 2004. *E. Faecalis*was responsible for 63% of these cases,whereas28% were caused by*E. Faecium.* In addition, 80% of all cases were resistant to antibiotics. Also, it was reported that approximately 12 percent of nosocomial infections in the USA are caused by *Enterococcus* species [32].

Conclusions

Pressure ulcer is a serious health problem andbacteremiacould certainly be one of its dangerous complications. Appropriate antibiotic treatment should be selected in order to eradicate the infection associated with pressure ulcer and avoid bacteremia.

References

1. Bluestein, D. and Javaheri, A. **2008**. Pressure Ulcers: Prevention, Evaluation, and Management. *American Family Physician*.**78**: 1186-1194.
2. Braga , I.A. ; Pirett, C.C.; Ribas, R.M. ; Filho, P.P. and Filho, A. D. **2013**. Bacterial colonization of pressure ulcers: assessment of risk for bloodstream infection and impact on patient outcomes. *Journal of Hospital Infection*. **83**: 314-320.
3. Whittington,K. ;Patrick, M. and Roberts, J.L. **2000**. National study of pressure ulcer prevalence and incidence in acute care hospitals. *J Wound Ostomy Continence Nurs* .**27**: 209-215.
4. Dharmarajan, T. S. and Ugalino, J. T. **2002**. Pressure Ulcers: *Clinical Features and Management*. **1**: 6 4 - 7 1.
5. Anders, J., Heinemann, A., Carsten, L., Leutenegger, M., Pröfener, F. and Renteln-Kruse, W.V. **2010**. Decubitus Ulcers: Pathophysiology and Primary Prevention. *Dtsch Arztebl Int*, **107**: 371–82.
6. Dana , A. N. and Bauman, W.A. **2015**. Bacteriology of pressure ulcers in individuals with spinal cord injury: What we know and what we should know. *The Journal of Spinal Cord Medicine*, **38**: 147-160.
7. Braga, I.A., Pirett, C.C., Ribas, R.M., Gontijo, F. P. and Diogo, F.A. **2013**. Bacterial colonization of pressure ulcers: assessment of risk for bloodstream infection and impact on patient outcomes. *J Hosp Infect.* **83**: 314–320.
8. Reilly, E.F., Karakousis, G.C., Schrag, S.P. and Stawicki, S.P. **2007**. Pressure ulcers in the intensive care unit: the 'forgotten' enemy. *OPUS12 Scientist*. **1**: 17–30.
9. Grey, J. E., Enoch, S. and Harding, K. G. **2006**. ABC of wound care: Pressure ulcers. *BMJ*. **332**: 472-475.
10. Seifert, H. **2009**. The Clinical Importance of Microbiological Findings in the Diagnosis and Management of Bloodstream Infections.*Clinical Infectious Diseases*, **48**: 238-245.
11. Wisplinghoff, H.; Bischoff, T. and Tallent, S.M. **2004**. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. *Clin Infect Dis.* **39**: 309-317.
12. Lee, Y.C. Huang, Y. T., Tan, C. K., Kuo, Y.W., Liao, C.H., Lee, P. I. and Hsueh, P.R. **2011**. *Acinetobacter baumannii* and *Acinetobacter* genospecies 13TU and 3 bacteremia: comparison of clinical features, prognostic factors and outcomes. *J. Antimicrob. Chemother.* **66**: 1839 –1846.

13. Lopes,F. S., Ribeiro, M., Abrantes, T., Marques, M. F., Tenreiro, R. J. J. and Crespo, M. T. B. **2005**. Antimicrobial resistance profiles of dairy and clinical isolates and type strains of enterococci. *Int J Food Microbiol*, **103**: 191–198.

14. Anderson, M. T., Mitchell, L. A., Zhao, L. Mobley, H.L. T. **2017**. Capsule Production and Glucose Metabolism Dictate Fitness during *Serratia marcescens* Bacteremia.*mBio*, **8**: e00740-17.

15. Jawetz, E., Melnick, J. L. and Adelberg, E. A. **1987**. *Review of medical microbiology*. 17th. edition.

16. CLSI. **2018**. *Performance Standards for Antimicrobial Susceptibility Testing*. 28th ed. Wayne, PA: Clinical and Laboratory Standards Institute.

17. SAS**. 2012.** Statistical Analysis System, User's Guide. Statistical.Version 9.1th ed. SAS.Inst. Inc. Cary.N.C. USA.

18. Thomas, D. R.**2006**.The Prevention and Treatment of Pressure Ulcers. *J Am Med DirAssoc* . **7**: 46–59

19. Bragaa, I. A., Britob, C.S., Filhoa, A. D., Filhob, P.P. G.and Ribas, R. M. **2017**. Pressure ulcer as a reservoir of multiresistant Gram-negative bacilli : risk factors for colonization and development.*braz j infect dis*, **21**:171–175

20. Wong, D., Nielsen, T. B., Bonomo, R. A., Pantapalangkoor, P., Luna, B. and Spellberg, B. **2017**. Clinical and pathophysiological overview of *Acinetobacter* infections: a century of challenges. *Clinical Microbiology Reviews*. **30**: 409–447.

21. Yang, S., Sun, J., Wu, X. and Zhang, L. **2018**. Determinants of Mortality in Patients with Nosocomial *Acinetobacter baumannii* Bacteremia in Southwest China: A Five-Year Case-Control Study. *Canadian Journal of Infectious Diseases and Medical Microbiology*.1-9

22. Xu, A., Zheng, B., Xu, Y. C., Huang, Z. G., Zhong, N. S. and Zhuo, C. **2016**. National epidemiology of carbapenem-resistant and extensively drug-resistant Gram-negative bacteria isolated from blood samples in China in 2013 .*Clinical Microbiology and Infection*. 22: 1–8.

23. Ballouz, T., Aridi, J., Afif, C., Irani, J., Lakis, C. and Nasreddine, R. **2017**. Risk Factors , Clinical Presentation , and Outcome of *Acinetobacter baumannii* Bacteremia.**7**: 1-8.

24. Munoz-Price, L.S. and Weinstein, R.A. **2008**. Acinetobacter infection.*N Engl J Med*; **358**: 1271–1281

25. Kim, S.B., Jeon, Y. D., Kim, J. H., Kim, J. K., Ann, H. W., Choi, H., Kim, M. H., Song, J. E. , Ahn, J. Y., Jeong, S. J., Ku, N. S., Han, S. H., Choi, J. Y., Song, Y. G. and Kim, J. M. **2015**. Risk Factors for Mortality in Patients with *Serratia marcescens* Bacteremia. *Yonsei Med J*. **56**: 348-354.(1)

26. Ivanova, D., .Markovska, R., Hadjieva, N., Schneider, I., Mitov, I. and Bauernfeind, A. **2008**. Extended-spectrum beta-lactamase-producing *Serratia marcescens* outbreak in a Bulgarian hospital. *J Hosp Infect*; **70**: 60-5.

27. Dana, A. N. And Bauman, W. A. **2015**. Bacteriology of pressure ulcers in individuals with spinal cord injury: What we know and what we should know.*The Journal of Spinal Cord Medicine*. **38**: 147-160

28. Hassoun, A.; Linden, P. K. and Friedman, B. **2017**.Incidence, prevalence, and management of MRSA bacteremia across patient populations—a review of recent developments in MRSA management and treatment.*Critical Care*, **21**: 211.

29. Toltzis, P. **2018**.*Staphylococcus epidermidis* and Other Coagulase-Negative Staphylococci.Long, S. S.;Charles, G. Prober and Marc,F.(Ed.).*Principles and Practice of Pediatric Infectious Diseases*.Fifth edition .Elsevier Inc.California.Pages 1588-1662

30. Favre B, Hugonnet S, correa S, Sax H, Rohner P, Pittet D. **2005**. Nosocomial bacteremia: clinical significance of a single blood culture positive for coagulase-negative staphylococci. *Infect Control Hosp epidemiol*; **26**: 697-702.

31. Andrés, E. ; Borrallo, M.; Padilla, R.; Garcia-Restoy, E. and Bella, F.2018.Bacteremia associated with pressure ulcers: a prospective cohort study Elena.*Eur J Clin Microbiol Infect Dis*, **37**: 969–975.

32. Opota , O.; Croxatto , A. ; Prod'hom, G. and Greub, G. 2015. Blood culture-based diagnosis of bacteraemia: state of the art. *Clin Microbiol Infect*, **21**: 313–322.