

Sepsis in Burn Patients

Ghassan A. Hassan

Ibn Al- Atheer Hospital /Microbiology Unit / Nineva Health Center

E-mail: ghassansho@gmail.com

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ABSTRACT

One hundred blood samples and burn swabs from septicemic burn patients were collected over a period from July 2017 until may 2018 at Burn Center in Baghdad Teaching Hospital. The age of patients was between one year to sixty years and they were suffering from burn wound sepsis ,the highest number of patients was female among age group 20-29 years old. The highest frequent cause of burn was flame 78% and the least was chemical 1%, it was found that flame burn patients were more vulnerable to sepsis. The mortality rate among male 56%, females 48% and the highest mortality rate was 100% in the age group less than one year and more than sixty years, the least rate of mortality was 27% in the age group 10-19 years old. The number of septicemic patients 36 who is total body surface area (BSA) burned 30-39% and the mortality in this group was 16.6%, however the least number of patients was two of BSA 90-99% with mortality rate 100%. The most frequent aetiological agents isolated from the blood of septicemic burn patients was *staphylococcus aureus* 34(28.1) followed by *Pseudomonas aeruginosa* 25(20.7), *Klebsiella pneumonia* 13(10.8), *Streptococcal pyogenes* 10(8.3), *Escherichia coli* 8(6.6%) and *Serratia marcescense*, *Acinetobacter calcoeticus* were 5(4.1) equally. The incidence of gram negative bacteria was much higher than gram positive bacteria in the septicemic burn cases, most of septicemic attack occur during the first week of admission and especially on the 7th day of staying in hospital and above, and they were much more likely to result from gram positive organism e.g *S.aureus* and *S.pyogene*. After the 1st week the septicemic attack was much more likely to result from gram negative organisms e.g. *P.aeruginosa* *K.pneumonia*, *E.coli*, *Serratia mercescense*, *Acintobacter calcoeticus*, *P vulgaris* and *P. rettger*.

Keywords: Sepsis, Burn, patients.

تسمم الدم لمرضى الحروق

الملخص

تم جمع مئة عينة من الدم مع مئة مسحة من الحروق من المرضى الذين يعانون من تسمم الدم الجرثومي الناتج من الحروق للفترة من تموز 2017 ولغاية ايار 2018 في مستشفى بغداد التعليمي (شعبة الحروق) وكانت معدل اعمار المرضى تتراوح بين اقل من سنة وأكثر من سنتين سنة وكانوا يعانون من تسمم الدم الجرثومي الناتج من الحروق وكانت اعلى نسبة من المرضى هي من الاناث ضمن فئه عمرية (20-29) سنة وكان اعلى سبب للحروق هو اللهب وبنسبة (78%) واقل بسبب المواد الكيميائية (1%) وان الحروق الناتجة من اللهب هي اكثر الحروق عرضه لتسمم الدم الجرثومي. بلغت نسبة الوفيات بين المرضى الذكور (56%) الاناث (48%) وان اعلى نسبة وفيات (100%) حدثت ضمن الفئه العمرية الأقل من سنة واحدة واكثر من 60 سنة واقل معدل بلغ 27% ضمن الفئه العمرية (10-19) سنة. بلغت نسبة الإصابة بالتسمم الجرثومي نسبة 36 عند مرضى الحروق الذين بلغت مساحة الحرق السطحية 30-39% ونسبة الوفيات فيها 16.6% بينما بلغت للمرضى بمساحة الحرق 90-99% اثتان فقط ومعدل الوفيات 100%. أن أكثر أنواع البكتريا المرضية المسببة لتسمم الدم الجرثومي لمرضى الحروق والمعزولة من الدم، *S.aureus* 34(28,1%), *P.aeruginosa* 25(20.7%), *K.pneumonia* 13(10,8%) *S.pyogene*

أظهرت النتائج ان العزلات ألسالبه لصيغة كرام اكثر من العزلات الموجبه لصيغة كرام لمرضى تسمم الحروق. أن معظم حالات تسمم الحروق تحصل خلال الاسبوع الاول من الرقود في المستشفى وخصوصا في اليوم السابع من البقاء في المستشفى بسبب البكتريا الموجبة لصيغة كرام. *S.aureus* , *S.pyogene*.

بعد الأسبوع الأول غالبية حالات تسمم الحروق حدثت بسبب البكتريا السالبة لصيغة كرام , *P.aeruginosa* , *k.pneumonia* , *E.coli* , *Serratia marcescence* , *P.vulgaris* , *P.rettgeri* , *Acinetobacter calcoeticus*

الكلمات الدالة: تسمم الدم، مرضى، الحروق.

INTRODUCTION

The Burn wound sepsis is probably the most serious complication in burns. Invasive sepsis occur when pathogenic organism in the burn wound multiply sufficiently to overcome the body natural defense mechanism and then actively invade the living tissues adjacent to the burn wound. If this advance remains unchecked, septicemia, active grow of organism in the blood, is a highly probable sequel (Muir *et al.*, 2010).

The prognosis of such bacteremia or septicemia may well depend on its prompt recognition by bacteriologic means. Subsequent initiation of specific therapy based on laboratory findings may well prove to be life saving, when the classic syndrome of a septicemia (chills, fever, prostration), due to the presence of actively multiplying bacteria and their toxins in the blood stream is found, it is rarely difficult to isolate the causative organism (Liedberg *et al.*, 2011).

Burn injury produce acute derangement of multiple host function. In generalized burn ,the effect include structural alteration of the gastrointestinal tract mucosa, this damage may predispose burn wounds to infective bacteria.

As invasion and septicemia occur, they are associated with conversion of area of partial thickness burn to area of full thickness burn to lysis and degeneration of granulation tissue with formation of a neoeschar (Pruitt, 2012). This due to damage to the tenuous blood supply caused by vascular invasion and occlusion (Cruickshank *et al.*, 2013).

The onset may be sudden, but more often invasion is superimposed in patient who already has purulent discharge, leukocytosis and fever. Early in the process there may be increased number of non segmented neutrophils in the blood, a further elevation in white cell count, an increase in fever and occasionally chills. As the process advance the patient may become hypothermic, the white cell count may be depressed, the patient may become non responsive and the process progress to death with toxemia (Reig *et al.*, 2001).

A successful outcome of invasive burn wound sepsis require early detection and extremely vigorous therapy. The appearance of the wound and the general condition of the patient is taken into account in the clinical diagnosis (Sanyal *et al.*, 2000).

The prodromal stage of gram negative septicemia may be followed by the sudden onset of septic shock with profound hypothermia, hypotension and multiple organ failure (Curtis *et al.*, 2015). Recovery is still possible if an effective antibiotics is administered, but if treatment is further delayed or is ineffective death will almost certainly supervene (Aladin and Yousif, 2016).

Invasive sepsis and septicemia are rare during the first week post burn but if they do occur they are much more likely to result from gram positive organisms such as *Streptococcus pyogenes* or *Staphylococcus aureus* than from gram negative organisms such as *Pseudomonas aeruginosa*. After the first week, the converse is true (Gang *et al.*, 2000).

Increase risk of septicemia is associated with burn over 30% body surface area (BSA), full thickness skin destruction, infancy and old age, diabetes, cardiopulmonary disease, inhalation injury, obesity and malnutrition, poor blood supply to the wound and moist warm wound environment (Gang *et al.*, 2000; Muir *et al.*, 2010).

No one with major burn is safe from the complication of septicemia until burn wound is completely grafted or has healed, all intravenous catheters are removed and the patient is eating, all antibiotics has been finished, and the patient has no fever for a few days (Bauer *et al.*, 1966).

MATERIALS AND METHODS

A total of 100 patients suffering from septicemic attack after burn were included in this study. The patients include those with infected burn wound who were suffering from septicemia as a complication of burn wound infection. The clinical diagnosis was made depending on the clinical signs and symptoms of the patients. All cases were thoroughly studied from the bacteriological point of view. Each case was carefully assessed regarding isolation and identification of the causative bacterial agents of burn septicemia.

Blood samples were collected from all patients, best time for collection before temperature rise, with adequate volume according to the age of patients. After that the blood transfer to two bottles of culture (brain heart infusion. Blood culture were incubated at 37C and examined daily throughout the first week for evidence of growth. Subculture was performed by using a sterile syringe and needle into two blood agar plate one of them for anaerobic incubation, chocolate agar plate and MacConkey agar plate. In addition, gram stains procedure to determine the presence of microorganism, at the same time subculture was done into a blood agar plate for anaerobic inoculation into the anaerobic jar.

Swabs from infected burn wound were obtained by rubbing the inflamed or discharging area by using sterile disposable swabs were immersed in transport media before antimicrobial topical agent was used. These swabs inoculated on blood agar, MacConkey and chocolate agar at 37c ...

Bacterial identification by Gram staining, cultural characteristics by examining the growth, All biochemical tests, API.

Antimicrobial susceptibility test was carried out as described by Kirby –bauer (1966) and (Higgins, 2014) using different antimicrobial discs and interpretation of zone diameter.

RESULTS

The result showed the highest number of patients was of female 16(16%) among age group 20-29y. The least frequently affected was one female and one male at age group above 60y old. However the highest No. of male patients affected was 9 (9%) among age group 1-9y as shown in (Table 1) and Fig. (1).

Table 1: Distribution of 100 hospitalized septicemic burn patients according to age and gender

Age	Male	Female	Total
	No. (%)	No. (%)	No. (%)
> 1 years	1	2	3(100)
1-9	9	10	19(100)
10-19	7	15	22(100)
20-29	7	16	23(100)
30-39	4	9	13(100)
40-49	4	4	8(100)
50-59	3	7	10(100)
> 60	1	1	2(100)
Total	36(36)	64(64)	100(100)

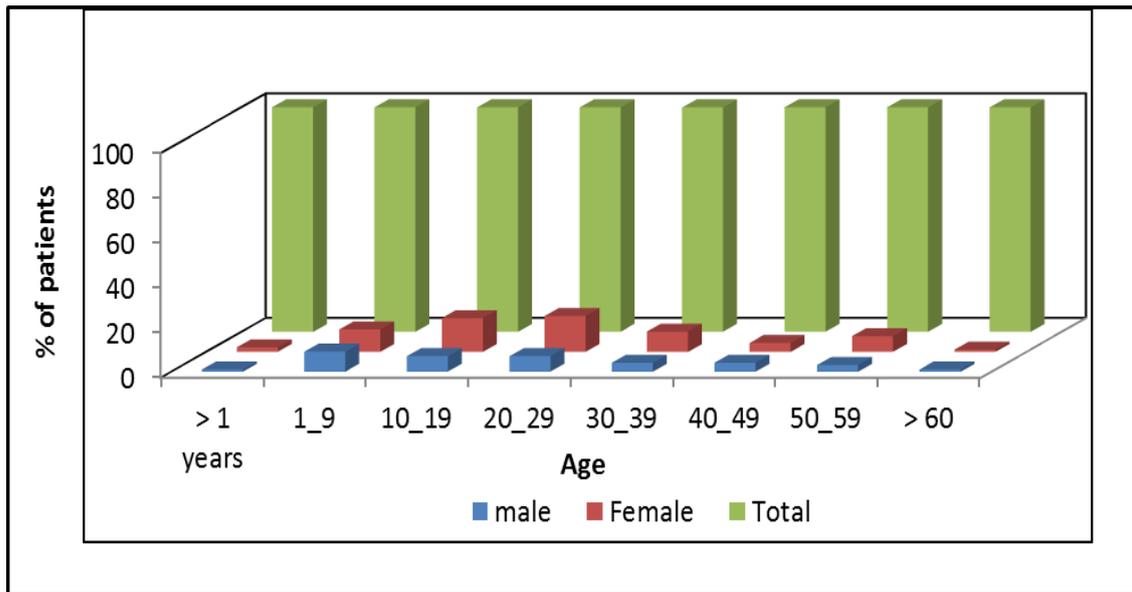


Fig. 1: Distribution of 100 hospitalized septicemic burn patients according to age and gender

The largest number of sepsis burn patients was 53 with 2nd degree of burn depth and the mortality rate was 28.3%, while the patients with the 3rd degree of burn depth was 47 and the mortality rate was 76.96% as shown in (Table 2) and Fig. (2).

Table 2: distribution of septicemic burn patients according to burn degree

Burn Degree	Patients No.(%)	Death No. (%)
1 st . degree	0(0)	0(0)
2 nd . Degree	53(53)	15(28.3)
3 rd . degree	47(47)	36(76.59)
Total	100(100)	51(51)

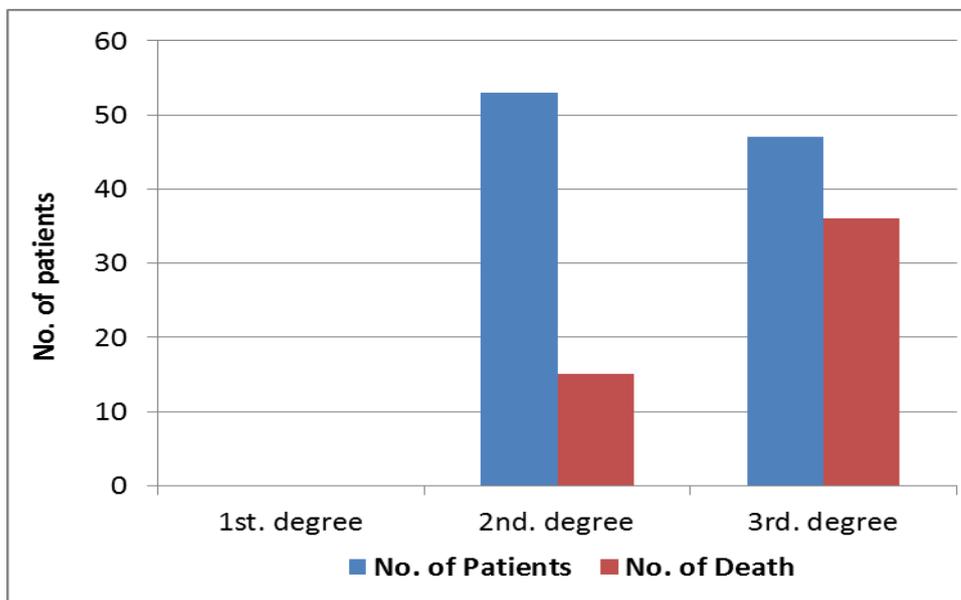
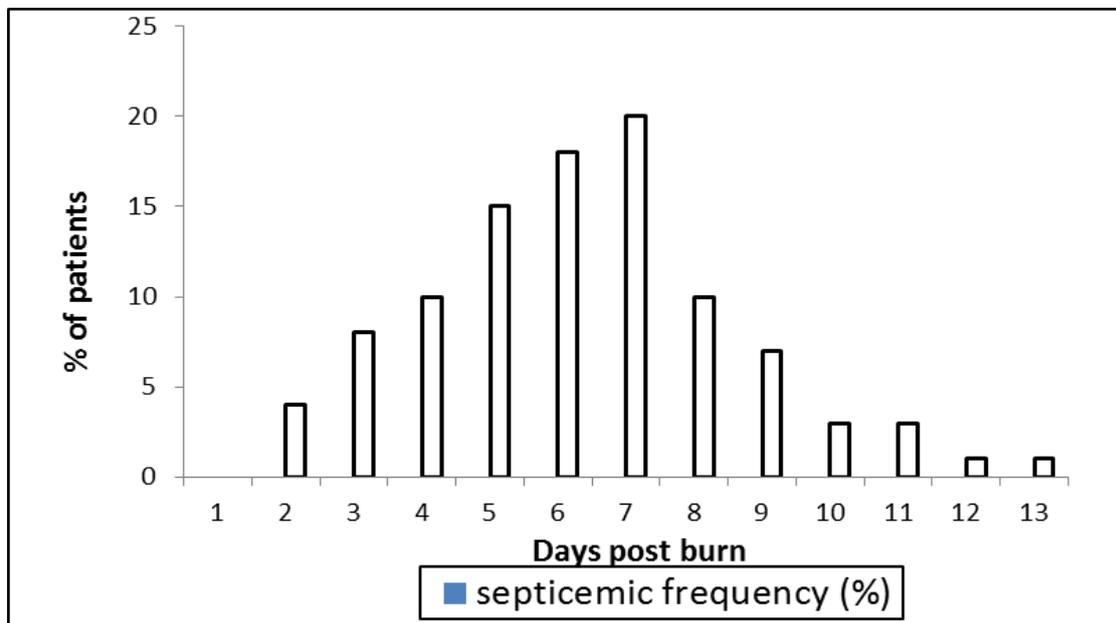


Fig. 2: distribution of septicemic burn patients according to burn degree

Sepsis occurred in burned patients in high percentage 20% at the end of the 1st week of staying in hospital. This declined to 1% in the 12 and 13 days post burn as shown in (Table 3) and Fig. (3) the correlation between the occurrence of septicaemia with the period of staying in hospital (days post burn).

Table 3: Relationship of frequency and percentage of burn septicemia with hospital admission

Hospital admission	Septicemia frequency (%)
1-day	0(0)
2-days	4(4)
3-days	8(8)
4-days	10(10)
5-days	15(15)
6-days	18(18)
7-days	20(20)
8-days	10(10)
9-days	7(7)
10-days	3(3)
11-days	3(3)
12-days	1(1)
13-days	1(1)
Total	100(100)

**Fig 3: Relationship of frequency and percentage of burn septicemia with hospital admission**

The largest number of dead septicemic burn patients were with catheter 37 and ten of them died on the 5th day, while the number of the dead sepsis patients who were without catheter was 14 and four of them died on the 6th day.

Majority of sepsis patients 70% had no medical history while 27% were heavily smokers, 5% of the female patients were pregnant and 3% were alcoholic.

Most common aerobic organism isolated from the blood of septicemic burn patients was *S.aureua* 34(28.1) followed by *P.aeruginosa* 25(20.7%) *K.pneumonia* 13(10.8%), *S.pyogene*

10(8.3%), *E.coli* 8(6.6%), *Serratia marcescense* and *Acinetobacter calcoeticus* 5(4.1%) equally as shown in (Table 4).

Table 4: Bacteria and fungi isolated from blood cultures of septicemic burn patients

Acrobic Bacteria	Index	No.&(%) of isolates from		Total (%)	% of total acrobes (121)
		Male	Female		
<i>S. aureus</i>	1	15(12.3)	19(15.7)	34(28)	28.1
<i>P.aeruginosa</i>	2	11(9)	14(11.5)	25	20.7
<i>K.pneumoniae</i>	3	6(5)	7(5.7)	13	10.8
<i>S.pyogene</i>	4	3(2.4)	7(5.7)	10	8.3
<i>E.coli</i>	5	3(2.4)	5(4.1)	8	6.6
<i>Serratia marcescense</i>	6	2(1.6)	3(2.4)	5	4.1
<i>Acinetobacter calcoeticus</i>	7	2(1.6)	3(2.4)	5	4.1
<i>Chryseomonas meningosepticm</i>	8	1(0.8)	2(1.6)	3	2.4
<i>Candida albicans</i>	9	1(0.8)	2(1.6)	3	2.4
<i>Providencia stuartii</i>	10	1(0.8)	2(1.6)	3	2.4
<i>Pantoea spcies</i>	11	0(0)	2(1.6)	2	1.7
<i>S.typhi</i>	12	0(0)	1(0.8)	1	0.8
<i>Aerononans caviae</i>	13	0(0)	1(0.8)	1	0.8
<i>Enterobacter aerogene</i>	14	0(0)	2(1.6)	2	1.7
<i>S.virdiance</i>	15	2(1.6)	0(0)	2	1.7
<i>P.vulgaris</i>	16	1(1.6)	1(1.6)	2	1.7
<i>P.rettgeri</i>	17	1(1.6)	1(1.6)	2	1.7
Total of aerobic bacteria	18	49(40.4)	72(59.6)	121(100)	100
	19	0(0)	1(100)	1	
Total		49(40.2)	73(59.8)	122	

The total number of aerobic bacteria isolated was 121, representing 72(59.6%) from female and 49(40.4%) from males. One type of anaerobic bacteria was isolated from the septicemic burn patient was *Clostridium welchii* in female patient.

The most frequent combination was that of *P.aeruginosa* and *S. aureus* 3(13.7%) and the impact of seasonal variation upon this pattern was significant with more dispersed distribution over three seasons but mainly in the winter. Next in frequency was *P.aeruginosa* and *E.coli* 2(9.1%) dispersed distribution over two season winter and spring. The largest number of sepsis burned patients occurred during winter 55% and the least number of patients occur during the spring 13%.

The total number of isolated bacteria from the burn wound in male patients was 66(37.7) and from this bacteria 49(40.1%) invade deep to the blood circulation. On the other hand, in female patients 109(62.3%) was isolated from the burn wound and from this 73(59.9%) bacteria invade deep to the blood circulation.

Out of 175 (100%) total number of bacteria isolated from the burn wound for both male and female for all patients 122 bacteria reached the blood.

Out of 39 isolate of *S.aureus* from the burn wound, 34 (87%) of them reached the blood circulation.

Salmonella typhi and *Aeromonas caviae* were isolated from the blood of the septicemic burn patients and not found on the burn wound, indicating an underlying infection.

Serratia plymuthica and *K.oxytoca* were only isolated from the burn wound and did not invade the blood circulation.

The isolated anaerobic bacteria (*Clostridium perfringens*) was isolated from both the burn wound and the blood of the same female patient.

Antimicrobial susceptibility pattern of the isolated bacteria. *S.aureus* isolate were susceptible to vancomycin 31(91.2%) and chloramphenicol 26(76.4%). Amikacin was the most effective agent against all gram negative bacterial isolate, *P. aeruginosa* (68%), *proteus* (75%), *K.pneumonia* (84.6%), *E.coli* (87.5%) and *Enterobacter* (100). Polymyxin B was the second effective antimicrobial agent against *P.aeruginosa* (60%).

DISCUSSION

Burn septicemia is a potentially life threatening clinical emergency that demand urgent diagnosis and treatment and it is probably the most serious complication of burn (Bang *et al.*, 2017).

The usage of large variety of antimicrobial agents in hospitals burn wards, has lead to a change in the etiological agents and their antimicrobial resistance schema along different years (Pruitt and McManus, 2000)

It has been reported that the old age is an important predisposing factor of septicemia. In the present the highest rate of hospitalized septicemic burn patients was 23(23%) in both sexes at age group (20-29) years old. This age represent the age of motility, activity, and much more contact with flame. The least frequent septicemic patients was 2(2%) at the age above 60 years, this may be due to decrease motility, activity and less contact with flame. This results is in agreement with the finding of Bang *et al.* (2017).

In this study the commonest cause of burn was flame (78%), the scaled was (19%) the electrical (2%) and chemical burn (1%) were are this result is in agreement with barrair *et al.*, (2017).

Deep burn are essentially a vascular, so systemic delivery of antibiotics via the blood stream does not substantially affect microbiological growth within the burn wound.

Briar *et al.* (2017) reported that patients with burn more than 60% of total body surface area (TBSA) had 100% mortality, while those with 20-30% of TBSA had 20% mortality. Reported that mortality increase with severity of the burn injury and with increasing age of the patients.

Male septicemic burn patients were more vulnerable to death (56%) from female patients (44%). This finding is constituent with the finding of (Diller, 2001). The mortality rate was increased with the increasing of the burn degree. In 2nd degree septic burn the death percentage was (28%), while 3rd degree it was (76%).

Staphylococcus aureus was the most common isolated bacteria (28.1%) from the blood of patients as a causative agents of septicemic attack followed by *p.aeruginosa* (20.7%). This result was compatible with that of (Lessave *et al.*, 2000) that reported that *S.aureus* has emerged as the most predominant organism and pathogen in resent years causing septicemia in the extensively burned patients.

Pseudomonas aeruginosa was the second most common isolated bacteria from the blood of patients. Nohoba *et al.* (2001) and Gang *et al.* (2000) found that pseudomonas was predominant and the most common organism in causing burn septicemia.

In the currently available drugs, Gentamycin, tobramycin and carbinicillin are the most effective, however there have been increasing numbers of reports of resistance to these antibiotics (Sutter and Hurst, 1999) especially when single drug is employed.

Klebsiella pneumonia was the 3rd bacteria (10.8%) isolated from the blood of septicemic burn patients followed by *B-haemolytic S. pyogene*, *E.coli*, *Serratia marcescence*, *Acinetobacter calcoceticus*, *Chryseomonas meningosepticum*, *Providencia stuartii*, *pantoea*, *Enterobacter aerogene*, *P.vulgaris*, *P.retgeri*, *S.viridance* and *Aeromonas caviae* (Sanyal *et al.*, 2000) reported that the common species isolated were *S.aureus* and *S.pyogene* among gram positive bacteria while *P.aeruginosa*, *K.pneumonia*, *E.coli*, *Serratia marcescence*, *Acinetobacter cacoceticua* and *proteus* species were commonly isolated among gram negative bacteria.

In this study one blood culture sample yielded *S.typhi* in enteric fever and septicemia, blood culture often positive in the 1st week of the disease (Baron and Finegold, 2005). In conclusion this isolated case might be typhoid infection rather than burn septicemia.

Regarding anaerobic bacteria was isolated in single case *Clostridium welchii* this pathogen was isolated from the blood of septicemic burn patient and she was a Kid 4 years old she had gas gangrene in the hand and abdomen after extensive burn.

Clostridium welchii natural habitat is the soil and intestinal tract of animals and human can survive and multiply only in tissue where there is low oxygen tension produce gas gangrene (Simmon, 2001).

Most bacteria which were isolated from the burn wound were isolated also from the blood circulation of the same septicemic burn patients with the same sequence but higher rates for the burn isolate, Bang *et al.* (2017) reported that most virulent pathogenic bacteria have the ability to penetrate the burn wound in extensively burned patients with dysfunction immune system deep to the blood circulation.

This study revealed that there was no difference between the sex distribution in relation to the potency of invading to the bacteria between male and female. This result disagree with that of Nohoba *et al.* (2001) reported that the male burn patients are more resistant to septicemic attack and the invading bacteria are less than that in burn wound, and female patients are more vulnerable to sepsis attack and less resist to invading pathogenic microorganism.

Prophylactic antibiotics treatment vary according to many variables like the extent and depth of burn, age of the patient, general condition of the patient, policy of the department and the issue of availability, antibiotic therapy is very necessary to administered if infection is already exist or the patient is more vulnerable to develop septic complication.

The most common gram positive bacteria was *S.aureus*, this bacteria was susceptible to vancomycin. Most of the *Staphylococcus* isolate were resistant to ampicillin, tetracycline, cephalothin, clindamycin, rifampicin and erythromycin and less resistant against chloramphenicol and cefotaxime. This result in agreement with Jawetz (2001) and Prasanna and Thomas (2002) who reported that vancomycin was the antibiotic to which most methicillin resistant *S.aureus* (MRSA) culture were susceptible.

Most gram negative bacteria isolated during this study were susceptible to amikacin, this may be due to that this antimicrobial agent was not commonly used, so the bacteria did not show any resistance against the antimicrobial agent.

Most gram negative bacteria appeared resistant to most to most of antimicrobial agents e.g ampicillin, cefotaxime, gentamycin, tobramycin, tetracycline, chloramphenicol and rifampicin. This reveal the multiple resistance of such nosocomial infections. This result in agreement with the study reported by (Baron and Peterson, 2005). Who found that multiple resistance is common among hospital strains of gram negative bacteria, those involve in serious nosocomial infections.

In this study *P.aeruginosa* was mostly susceptible to amikacin, polymixin-B but was resistant to other antimicrobial agents.

Barriar *et al.* (2017) found that multi drug resistance was more common with *P.aeruginosa* and the resistance to aminoglycoside had subsequently appeared in *E.coli*.

CONCLUSIONS

The highest mortality rate was among age group above 60 years old in addition at age group less than one year due to septicemic attack, male septicemic burn patients were more vulnerable to death mortality rate from female patients, male patients are less resistant to pathophysiological effect of the burn wound than that from female. The Risks factors (extent and depth of burn, age of patients and medical disease) are important predisposing factors for sepsis development.

All septicemic burn patients showed positive blood cultures inspite of their treatment with antibiotics. The most common isolated organism from the blood of patients as a causative agent of septicemic attack is *S.aureus* followed by *P.aeruginosa*, *K.pneumonia*, *S.pyogenes* and *E. coli*, one type of anaerobic bacteria was isolated in single case which was *C.welchii* infecting the burn wound and

causing gas gangrene. A mikacin was the most effective agent against all gram negative bacterial isolate while vancomycin was the most effective against gram positive.

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