

# Outcome and Management of Sepsis at RozhHalat Emergency Hospital in Erbil –Kurdistan region of Iraq

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**Abstract:** Sepsis is a very common condition in emergency hospitals and presentation is variable, it is under diagnosed with very high mortality rate. All patients with infection are at risk of developing sepsis. Sepsis is a complex condition characterized by activation of inflammatory process and coagulation system in response to microbial insult. An observational prospective study was carried out at RozhHalat emergency hospital in Erbil-Kurdistan region of Iraq between February 2017 to January 2018. The study was approved by the scientific and ethical committee of Kurdistan board of medical specialties. 50 patients aged between (10 - 80) years old presented to this hospital with sign and symptoms of infection were recruited to this study. 50 patients with signs and symptoms of sepsis were recorded in this study. The mean age was 47 with male to female ration of 2:3 (42% male and 58% female). The overall mortality rate was high at 68% with higher rate among female and older age group. The blood culture was positive in 74% of cases of which 52% were gram positive and 22% were gram-negative microorganisms. A Positive blood culture associated with higher mortality rate of 81% compared with 21% if the blood culture was negative. In majority of cases the site of infection was from multiple source (34%) followed by respiratory infection (26%). Skin and soft tissue infection was associated with the lowest mortality of 2.9%. High number of cases (82%) developed complications and 52% of cases developed more than 2 organ failures. All patients received empirical antibiotic therapy however 46% of cases received the wrong antimicrobials. The survival rate was higher

(44%) among patients given the right antibiotics. Similarly patients had better chance of survival if appropriate fluid resuscitation therapy was give. The overall mortality among vasopressor treated patients were 72% compared with 78% chance of mortality if they were not treated with any vasopressor therapy, among those who received inotropic support Noradrenaline associated with higher survival rate(72%). A qSOFA score of more than 2 associated with 86.4 % of mortality compared with 75.5% mortality with similar SIRS criteria. Factors associated with high mortality were: female gender, older age group, positive blood culture, wrong antibiotics therapy, less fluid resuscitation, multisource of infection, multi-organ failure, high lactic acid level and high qSOFA score. This study shows that sepsis is associated with high overall mortality rate of 68% in the RozhHalat emergency hospital and higher rate of death among female and older age group. Negative blood culture, appropriate use of antibiotics and fluid therapy associated with better chance of survival. Vasopressor therapy did not result in better survival outcome except for Noradrenaline. The qSOFA score is as good as SIRS criteria in predicting mortality. High lactate, multi-organ failure and multisource of infection associated with the worst outcome.

**Keywords:** Sepsis, Blood culture, Lactic acid, Vasopressor.

## 1. INTRODUCTION

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to an infection.

Probably the most often related article on the epidemiology of sepsis is the 2001 publication by Angus and colleagues, which used administrative data to estimate that there were 751,000 cases (3.0 per 1,000 population) in the United States each year, resulting in more than 200,000 deaths [1]. More recent research suggests that sepsis causes or contributes to between one-third and one-half of all deaths occurring in hospitals in the United States, with the majority of patients presenting to hospital with sepsis rather than acquiring sepsis in hospital [2].

All available data confirm that sepsis is a major public health problem. In the most recent report, published in 2015, sepsis is considered a cause of death from an infection and death being attributed to the infection that initiated sepsis if not recognized [3]. There is a gradual increase in the frequency of hospital-based sepsis. Extreme age groups, patients with chronic disease, common use of immunosuppressive drugs, and invasive procedures for diagnosis or treatment purposes like central lines or mechanical ventilation, immunocompromised diseases like carcinoma and AIDS increase the frequency of sepsis. Hospitalization for a long time especially ICU admission has more risk to complicated sepsis and septic shock [4]. The definition of sepsis was updated in 2016 following publication of the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) [5].

The 2016 consensus definitions also recommend that the Sequential (Sepsis-related) Organ Failure Assessment (SOFA) criteria and “quick” (q)SOFA criteria to be used to identify sepsis, in place of the currently used systemic inflammatory response syndrome (SIRS) criteria, which was the basis for the previous definition of sepsis [5] [6]. SOFA required multiple laboratory investigations and it is an intensive care unit (ICU) dependent mortality score based on respiratory, cardiovascular, hepatic, renal, and neurological parameters.

The qSOFA is a rapid, shortened version of SOFA for quick sepsis assessment, which designed for use outside the ICU, and parameters of this score are:

1. Respiratory rate of 22 breaths /min and more,
2. Systolic blood pressure of 100 mmHg and less,
3. Altered mental state with a Glasgow Coma scale (GCS) of 14 and less.

The SOFA score is useful in predicting the clinical outcome and effective method to describe organs dysfunction in critically ill patients [7].

The Third international consensus (Sepsis-3) definitions state that the term “severe sepsis” doesn’t necessarily need to be used and no longer recommended. Septic shock has also been redefined as a subset of sepsis in which profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone [5]. Therefore, in sepsis 3 guidelines, patients with sepsis are categorized into 3 groups of: infections, sepsis and septic shock.

In 2016, the UK National Institute for Health and Care Excellence (NICE) published guidance on the recognition, diagnosis, and early management of sepsis and categorize patients into 3 groups according to severity of illness or death from sepsis: high risk; moderate to high risk; or low risk [4].

Depending on guideline of management and outcome of sepsis we can deal with basic therapies that should be completed in the first 24 hour of recognition of sepsis. The following sepsis therapy protocol is known as sepsis 6 resuscitation bundles:

1. High flow oxygen to maintain oxygen saturation more than 94%
2. Taken blood culture before initiation of antibiotic therapy
3. Intravenous empirical antimicrobial therapy
4. Intravenous fluid resuscitation
5. Serum lactate level measurement
6. Monitoring urine output hourly [8].

Blood culture should be obtained before starting empirical antimicrobial therapy to isolate microorganism that caused infection and to detect proper antimicrobial therapy [9].

Early administration (within one hour) of appropriate antimicrobials is central to management of sepsis or septic shock. Each hour delay in administration of appropriate antimicrobials is associated with significant increase in mortality [10].

Earliest possible administration of appropriate IV antimicrobials following diagnosis of sepsis or septic shock causes best result in outcomes [11].

Broad spectrum antimicrobial therapy must be given in order to cover all likely pathogens, the choice of empirical antimicrobial therapy depends on patient’s history, clinical status and local epidemiological factors.

Key patient factors include site of infection, concomitant underlying diseases, chronic organ failures, medications, indwelling devices, the presence of immunosuppression or other form of immunocompromised, recent known infection and Receiving antimicrobials within the previous three months [12].

Fluid resuscitation is another crucial line for management of sepsis and septic shock, sepsis especially in case with tissue hypo perfusion may be manifested by acute organ dysfunction and/or decreased blood pressure and increased serum lactate [13].

Initial fluid resuscitation begins with 30 mL/kg of crystalloid within the first 3 hours. This fixed volume of fluid enables clinicians to initiate resuscitation while obtaining more specific information about the patient and while awaiting more precise measurements of hemodynamic status [14].

Serum lactate is a sensitive marker to defined tissue hypoxia and it is a more objective indicator for tissue perfusion as compare with physical examination or urine output. An increased in serum lactate indicates more severe sepsis and associated with increase in mortality [15,16].

International guidelines recommend norepinephrine and dopamine regarded as first line vasopressor agents in septic shock. phenylephrine, epinephrine, vasopressin and terlipressin are considered second line agents. Norepinephrine shows improved survival and has less adverse effect and hemodynamically more beneficial than dopamine because of these Norepinephrine remain

as a first line vasopressor superior to dopamine for treatment of septic shock [17].

Steroids may be used for those who are on chronic steroid therapy or adrenal dysfunction, but there is no clear evidence for use low dose steroid to prevent or reduce sepsis and septic shock in critically ill patients, a recent large multicenter RCT demonstrated no reduction in the development of septic shock in septic patients treated with hydrocortisone versus placebo [18].

Patients with sepsis and multiple organ system failure have a high mortality rate, although the outcome of intensive care treatment in critically ill patients may be difficult to prognosis accurately, establishing realistic ICU treatment goals is paramount [19].

The aim of the current study is to investigate the management and outcome of sepsis at our local hospital and how it compares with the international standards for sepsis management.

## 2. PATIENTS AND METHODS:

A prospective observational study carried out on 50 consecutive patients of all age groups regardless of gender with signs of life at presentation from the 1<sup>st</sup> of February 2017 to the 31<sup>st</sup> of January 2018. All patients who were admitted to RozhHalat emergency hospital with suspected sepsis were recruited and patient who did not give consent were excluded. Data recorded on a specially designed questionnaire, collected and entered

in the computer and then analyzed using appropriate database system which is called Statistical Package for Social Science (SPSS) version 22 and the result were compared between patients with different variables, with a statistical significance level of <0.05. The results will be presented as rates, ratio, frequencies, and percentages in tables. The chi square test was performed to compare between the groups.

This study was granted approval by the Ethical and Research Committee of Kurdistan Board of medical specialties. Permission to access patient data was obtained from hospital manager and written Informed consent of permission was also obtained from all participants or their next of kin if patients did not have capacity to give consent.

## 3. RESULTS

Overall mortality was high as 34/50 (68%) that shows in figure (1).

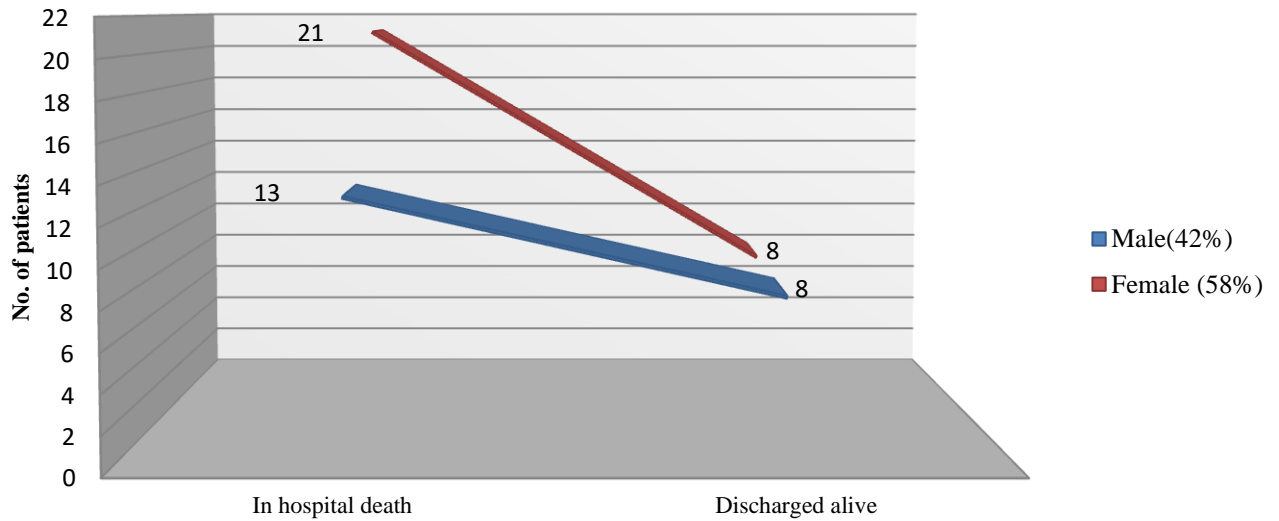
As shown in figure (2) the total study group consisted of 50 consequential patients, 21(42%) male and 29 (58%) female with the male to female ratio of (2:3). patients died in hospital 13 (38.2%) were male and 21 (61.8%) were female.

Figure (3) shows age distribution which the mean age of the participants was (47.14±22.71SD) years old ranging from 10-80 years and the majority of patients 60% (30/50) were above the age of 40 years old.

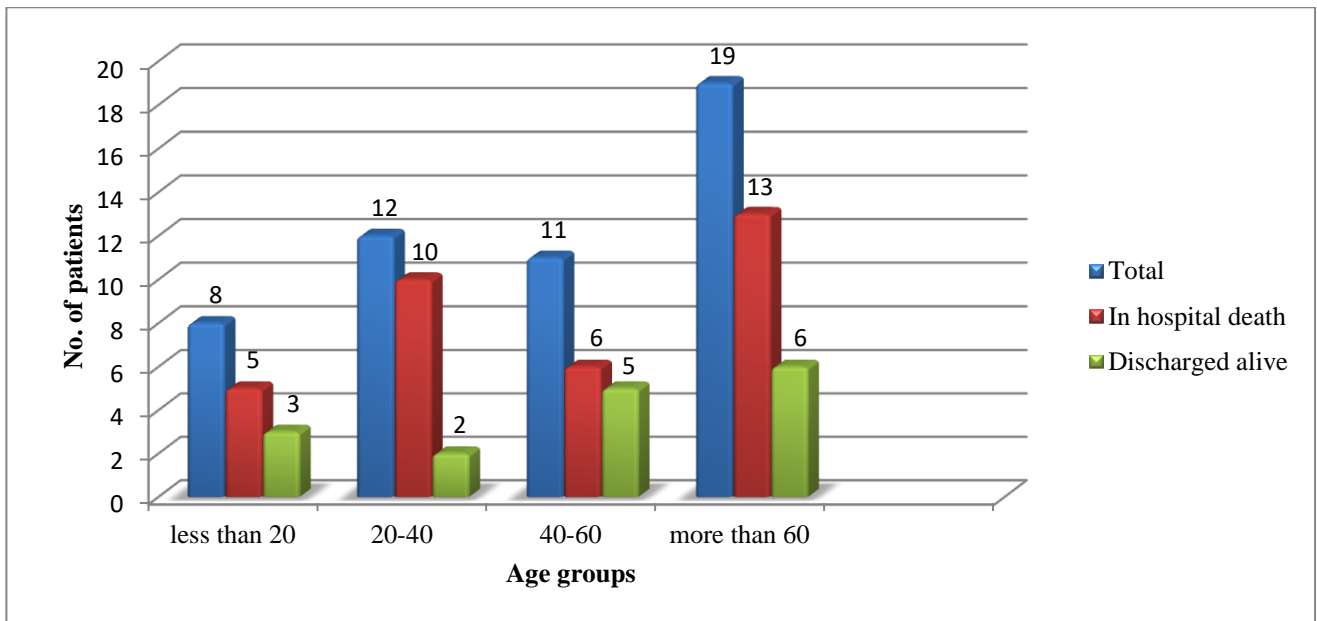
Figure 1: Outcome



**Figure 2: Gender Distribution**



**Figure 3: Age distribution**



As shown in table (1) the qSOFA was as good as SIRS criteria in predicting mortality. A qSOFA score of more than 2 associated with 86.4 % of mortality compared with 75.5% mortality with SIRS score of more than 2. A score of less than 1 for both qSOFA and SIRS criteria

were associated with low mortality rate of 5.9% and 0% respectively. For the qSOFA the highest mortality of 55.9% was with score of 2 while the highest mortality of 47.1% associated with SIRS score of 3.

**Table 1: Scores**

Scores		Outcome		Total
		In hospital death	Discharged alive	
qSOFA p: (0.001)	0	0 0.0%	5 31.3%	5 10.0%
	1	2 5.9%	6 37.5%	8 16.0%
	2	19 55.9%	4 25.0%	23 46.0%
	3	13	1	14

		38.2%	6.3%	28.0%
Total		34	16	50
		100.0%	100.0%	100.0%
SIRS Criteria P: (0.006)		In hospital death	Discharged alive	
	1	0	5	5
		0.0%	31.3%	10.0%
	2	12	5	17
		35.3%	31.3%	34.0%
	3	16	5	21
		47.1%	31.3%	42.0%
	4	6	1	7
17.6%		6.3%	14.0%	
Total		34	16	50
		100.0%	100.0%	100.0%

Lactic acid measured for all patients. Table (2) shows that in 30 patients have lactic acid below 2-mmol/liter, among this group mortality rate was (63%). While 20

patients have lactate 2 mmol/liter and more which 15 patients and mortality was 75%.

**Table 2: Lactate level**

Lactic acid (P: 0.06)	Outcome		Total
	In hospital death	Discharged alive	
< 0.9	0	3	3
	0.0%	18.8%	6.0%
0.9 – 1.9	19	8	27
	55.9%	50.0%	54.0%
2 - 4	14	5	19
	41.2%	31.3%	38.0%
> 4	1	0	1
	2.9%	0.0%	2.0%
Total	34	16	50
	100.0%	100.0%	100.0%

Blood culture was done for all patients by the main investigator and in 30/50 (60%) it was taken before patients received Antibiotics. The blood culture result did not grow any organism in 13 (26%) of patients, while it was positive in the remaining 37(74%) patients of which 26/50 (52%) grew gram positive and 11/50 (22%) gram-negative organism.

The commonest gram-positive organism was streptococcus (24%) followed by staphylococcus (22%) while the E. Coli (12%) was the most common gram-negative infective agent. The overall mortality rate for gram-positive organism was 84.6% compared with 72% for gram-negative causative agents while mortality was lower (31%) if the blood culture was negative.

**Table 3: Blood culture and microorganisms**

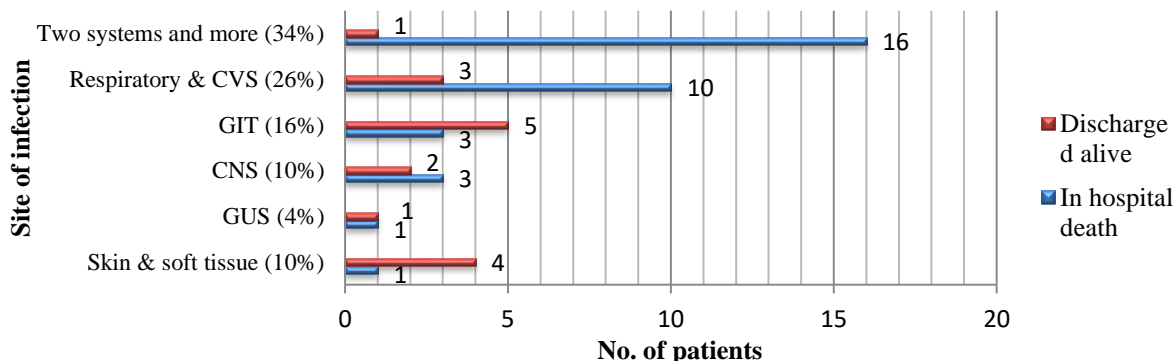
Microorganisms (P:0.04)	Outcome		Total
	In hospital death	Discharged alive	
Negative blood culture	4	9	13
	11.8%	56.3%	26.0%
G+ staphylococcus	9	2	11
	26.5%	12.5%	22.0%
G+ streptococcus	11	1	12
	32.4%	6.3%	24.0%
G+ enterococcus	2	1	3
	5.9%	6.3%	6.0%
G- E.coli	4	2	6
	11.8%	12.5%	12.0%
G- Klebsiella	3	1	4
	8.8%	6.3%	8.0%

G- Acinetobacter	1	0	1
	2.9%	0.0%	2.0%
Total	34	16	50
	100.0%	100.0%	100.0%

Regarding the site of infection (figure 4) the commonest site of infection was from multiple sources (34%) with a high mortality of 47.1%, the second most common site was the respiratory source (26%) with the

overall mortality of (29.4%). The skin and soft tissue sepsis was associated with the lowest mortality rate of 2.9%

**Figure 4: Site of infection**



All patients received empirical antibiotic therapy however 20/50 (40%) received antibiotics before obtaining the blood culture. The patients who received the right empirical antibiotics 27/50 (54%) they had a lower mortality rate

(55.5%) compared with 82% mortality if they did not receive the correct empirical antibiotics 23/50 (46%). Likewise, if the antibiotics were changed correctly after blood culture results the mortality were lower (58.6%) compared with 80% chance of death if the antibiotics were not changed.

**Table 4: Empirical antimicrobials**

Right Empirical antibiotic (P:0.8)	Outcome		Total
	In hospital death	Discharged alive	
Yes	15	12	27
	44.1%	75.0%	54.0%
No	19	4	23
	55.9%	25.0%	46.0%
Total	34	16	50
	100.0%	100.0%	100.0%
Antibiotic change after result of blood Culture (P:0.09)	Outcome		Total
	In hospital death	Discharged alive	
Yes	17	12	29
	50.0%	75.0%	58.0%
No	17	4	21
	50.0%	25.0%	42.0%
Total	34	16	50
	100.0%	100.0%	100.0%

Table (5) reveal that fluid therapy (crystalloid) used at two pattern, the bolus fluid therapy in the first one hour of admission and maintenance fluid in the first 24 hour of admission. Among 47 of patients who received more than one litter

maintenance crystalloid fluids in the first hour, 16 patients (34%) discharged alive. While none of the 3 patients who received less than one litter of maintenance fluids were discharged alive

**Table 5: Fluid therapy**

Bullous dose of IV Fluid (P:0.24)	Outcome		Total
	In hospital death	Discharged alive	
< 250 ml	0	1	1
	0.0%	6.3%	2.0%

250 – 500 ml	26	13	39
	76.5%	81.3%	78.0%
500 – 1000 ml	8	2	10
	23.5%	12.5%	20.0%
Total	34	16	50
	100.0%	100.0%	100.0%
Maintenance dose of IV Fluid (P:0.3)	In hospital death	Discharged alive	Total
0.5 – 1 lit.	3	0	3
	8.8%	0.0%	6.0%
1 – 2 lit.	15	10	25
	44.1%	62.5%	50.0%
> 2 lit.	16	6	22
	47.1%	37.5%	44.0%
Total	34	16	50
	100.0%	100.0%	100.0%

Majority of patients 36/50 (72%) received vasopressor therapy and 14/50 (28%) did not receive inotropics. The overall mortality among vasopressor treated patients were 72% compared with 78% chance of death if they

were not treated with any vasopressor therapy. Noradrenaline therapy associated with the highest survival rate (72%) while combined inotropic use associated with the lowest survival rate.

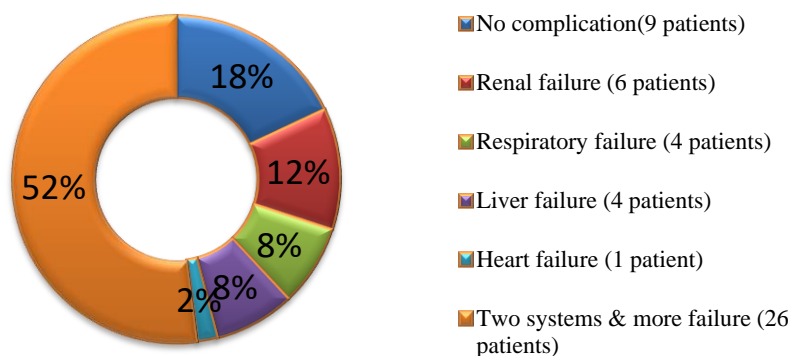
**Table 6:** Vasopressors

Vasopressor (P: 0.005)	Outcome		Total
	In hospital death	Discharged alive	
Not received	11	3	14
	32.4%	18.8%	28.0%
Noradrenaline	3	8	11
	8.8%	50.0%	22.0%
Dopamine	13	4	17
	38.2%	25.0%	34.0%
Dobutamine	0	1	1
	0.0%	6.3%	2.0%
Combination	7	0	7
	20.6%	0.0%	14.0%
Total	34	16	50
	100.0%	100.0%	100.0%

Figures (5,6) shows the rate of complications in this study group. Majority of cases (82%) developed organ failure. The highest overall mortality rate (73.5%) was

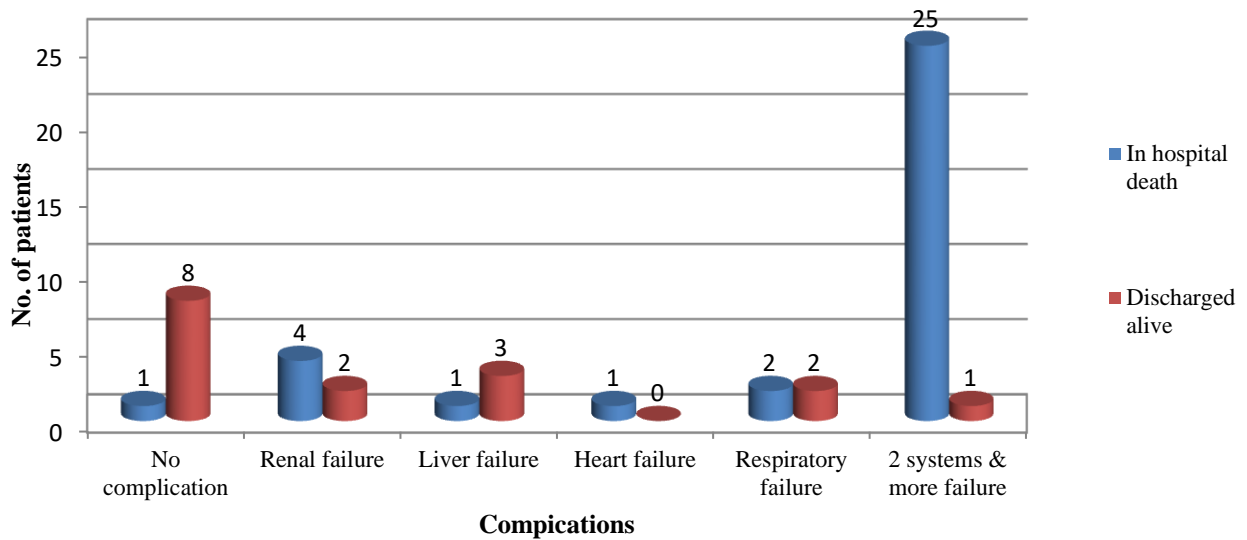
associated with more than 2 organ failures. If there were no complications the survival rate was 88.8% (8/9 cases).

**Figure 5:** Type of complications



**Figure 6:** Outcome of complications





#### 4. DISCUSSION

Sepsis is a serious consequence of infection; it has a high mortality rate worldwide. Septic shock is the most severe and life-threatening complication of sepsis that has irreversible damage that could end up with multi organ dysfunction and death, therefore early recognition and management of septic patients is crucial to reduce mortality rate [5].

The new sepsis definition is designed to identify patients with sepsis with easier criteria's such as qSOFA and categories sepsis into three new main groups of: infection, sepsis and septic shock. Severe sepsis deemed not to be relevant according to the new consensus of sepsis guideline [5].

Adherence to the sepsis 6 bundle of resuscitation is very important to treat sepsis with effective treatment to reduce mortality and morbidity from all categories of sepsis [8].

Multiple international studies revealed that sepsis is more common in the older age group, a study reported in 2006 in the United States shows that 64.9% of patients with sepsis aged more than 65 years of age [20]. Another study reported in India in 2012 shows that severe sepsis and septic shock in elderly patients are not only more common but also associated with higher mortality rate [21], In this study 38% of patients were aged more than 60 years old resulted in 68.4 % of mortality.

In this study female patients were affected more than male to have sepsis and also mortality rate was higher in females compared to male (68.2% and 31.8% respectively) [22] [23].

Three separate studies done in 2017, (USA, Brazil and South Korea) found that qSOFA provided better discrimination than SIRS criteria for predicting mortality. In this study the qSOFA score higher than 2 associated with 86.4% mortality, while similar SIRS criteria score resulted in 75.5% mortality [24] [25] [26]. Serum lactic acid measurement has a predicting rule for mortality in sepsis and recommended in first hour for early recognition of sepsis. In our study mortality rate was high (75%) for those patients whom serum lactate

level more than 2 mmol/liter, this result is comparable to other studies done in Sao Paulo Brazil in 2016 [27], Vancouver Canada in 2012 [28] and Seoul South Korea in 2011 [29].

In our study 26% have negative blood culture which was lower compared to other studies done in Singapore (41.5%) in 2013 [30] and in Spain (35%) in 2008 [31].

Higher mortality rate is seen among gram positive causative microorganism which was 67.4% in this study, a similar result is seen in a study reported in Denmark in 2011 [32].

The finding of this study shows that respiratory infection where the second most common source (26%) for septic patients and mortality rate in patient with respiratory source sepsis was 29.4%. In 34% of patients two or more systems were infected and in those patients mortality rate was very high (47.1%), these results comparable to a similar studies done in Denmark in 2016 [33] and another carried out in Pennsylvania U.S.A. in 2014 [34]. Empirical antimicrobial therapy was proved to be inappropriate among 46% of patient recorded in our study with a high mortality rate of 82.6%. While those with appropriate antimicrobial therapy (54%), mortality rate was less (55.5%), this finding is identical to a study done in Thailand in 2012 [35].

Following blood culture results the antimicrobial therapy were changed in some patients which resulted with lower mortality rate of 58.6%, compared with 80% mortality if the antibiotics were not changed, a study done in Indonesia in 2013 revealed that appropriate empirical antibiotic has better result in outcome for septic patients [36].

In our study the mortality rate was not significantly different if they received vasopressor therapy or not (72% versus 78%). In patients who received noradrenaline as a vasopressor they had higher survival rate (72.7%) compared to those whom received dopamine (23.5%), same result reported in studies done in Belgium in 2012 [37] and in Washington U.S.A in 2015 [38].

Failure of two or more vital organ systems is termed multi-organ dysfunction syndrome and associated with



high mortality. In this study 34% of patients had two or more organ dysfunction and mortality rate among them were 94%. Respiratory failure was detected in 26% of patients and with mortality rate (76.9%), which was highest rate in compare to other study [39].

High mortality rates for sepsis and septic shock in our study was (68%), This figure also has been in other studies in other middle and low-income countries, the overall mortality rate of severe sepsis was (55.7%) in Brazil in 2015 [40], (64.6%) in India in 2007 [41] and (49.7%) in Thailand in 2009 [42].

The poor survival rate in developing countries related to many factors such as lack of resources, lack of standardized sepsis local protocol, unavailability of blood cultures, and lack of awareness. In the hospital that this study was carried out all these factors were present that would explain higher mortality rate compared with the developed countries.

We hope that these findings will lead to development of local and national protocol in the Kurdistan region of

Iraq to manage sepsis with a better standard of care that will lead to reduction of mortality from such a common and deadly condition [43].

## 5. CONCLUSION

This study shows that sepsis is associated with high overall mortality rate of (68%) in the RozhHalat emergency hospital and higher rate of death among female and older age group. Negative blood culture, appropriate use of antibiotics and fluid therapy associated with better chance of survival. Vasopressor therapy did not result in better survival outcome except for Noradrenaline.

The qSOFA score is as good as SIRS criteria in predicting mortality. High lactate, multi-organ failure and multisource of infection associated with the worst outcome.

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