STUDY OF CLINICAL PROFILE, RISK FACTORS AND OUTCOME OF SEPSIS IN ELDERLY

Dr. VENKATARATHNAMMA PN[1], Dr. ARUN VG[2], Dr. PRABHAKAR K[3], Dr. REDDY PRASAD[4]

1. PROFESSOR, DEPT. GENERAL MEDICINE, SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR-563101
2. POST GRADUATE, DEPT. GENERAL MEDICINE, SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR-563101
3. PROFESSOR AND HOD, DEPT. GENERAL MEDICINE SRI DEVARAJ URS MEDICAL COLLEGE,TAMAKA, KOLAR-563101
4. ASST. PROFESSOR, DEPT. GENERAL MEDICINE, SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR-563101

Abstract

Introduction:

Sepsis is the most common cause for hospitalization in the ICU around the world. The clinical presentation of older patients with sepsis is often atypical, leading to a difficult and delayed diagnosis. Prompt diagnosis is crucial to the management of sepsis, as initiation of early-goal-directed therapy is the key to reducing mortality from severe sepsis especially in older patients. Unless antibiotics and life support are delivered quickly, the condition can lead to organ failure and death.

Objectives:

To study the risk factors and clinical profile of sepsis in elderly and to record the primary site of infection and to determine the influence of sepsis on the survival outcome in the elderly.

Materials and methods:

A hospital based observational study was conducted on patients admitted to R.L. Jalappa Hospital & Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar. 100 Patients ≥ 65 years of age admitted with a clinical suspicion of sepsis and those fulfilling the criteria for sepsis by PIRO grading system were studied. Patients were divided into groups based on their age. All patients' clinical presentation, previous medical history and outcomes as death/discharge and duration of hospital stay was recorded and analysed according to the age groups.

Results:

100 subject studied, 64 were males and commonly seen in the age group 65 – 74yrs. Mean hospital stay in pts was 5.1 days with SD 5.2 days. Fever (71%) was the common symptom followed by cough (40%). Diabetes was the most common risk factor followed by hypertension. Only 30% of the patients were found to be febrile at the time of presentation. Most common site of infection was respiratory system (57%) followed by neuroinfection (33%).9 % had no Foci of infection, 42% had one foci, 45% had 2 foci and 4% had 3 foci of infection. 54.7% of Males there were 2 foci of infection and in females 55.6% had one focus of infection. 38% of pts had shock at the time of presentation or during their course in the hospital. There was significant association between Respiratory site, UTI and outcome. Among 23 subjects who died, 73.9% had respiratory infections. 52% of subjects were discharged, 25% Discharged against Medical advice (DAMA) and 23% had mortality.

Conclusion:

Sepsis is more commonly seen in males than in females. Fever being the most common presenting symptom. Elderly patients can develop sepsis even without fever which was seen in 29% of the patients in this study. Respiratory system was found to be the most common site of infection. A significant number of patients developed complications (ICU admission, Ventilator support, acute renal failure and septic shock). There was significant association between Respiratory foci and complications such as Shock and ICU admission and a significant association between ARF and Cellulitis was also seen.

INTRODUCTION:

Sepsis is defined as infection-initiated clinical condition characterized by systemic inflammation. Sepsis is a medical emergency in which an infection overwhelms the body.[1]Sepsis is the most common cause for hospitalization in the ICU around the world. Sepsis is more commonly seen in the geriatric population as compared with their younger counterpart and elderly exhibited significantly elevated mortality as evidenced by earlier studies.[2]

The clinical presentation of older patients with sepsis is often atypical, leading to a difficult and delayed diagnosis.[3] Prompt diagnosis is crucial to the management of sepsis, as initiation of early-goal-directed therapy is the key to reducing mortality from severe sepsis especially in elderly patients.[3]

The progression of sepsis occurs by a loss of homeostasis, characterized by uncontrolled inflammation, oxidative damage to the vascular endothelium and intravascular coagulation. These conditions lead to multiple organ failure and death for a large number of patients.[4, 5]

Vulnerability to various physiological stresses such as infection, inflammation, and oxidative damage increases with age and is causally related to clinical problems in the elderly.[6]

The burden of elderly population presenting with sepsis and septic shock has been on a rising trend in the recent times because of the developments in the medical sciences, extensive use and availability of antibiotics, effective use of intensive care unit, life support and increased awareness of the clinicians about sepsis.[7] It has been estimated that by 2050, globally 21.4% of people will be aged 60yrs or older.[7, 8]

While there is no clear definition of "elderly" in the medical literature, some of the studies classified patients older than 65 years as elderly.[9] Hence we defined elderly patients to be more than 65 years in our study.

There are very few studies are available about the incidence, risk factors, outcome and management of septic patients in elderly age group in rural India. These realities necessitate a heightened level of awareness of the complexities associated with the care of older patients with sepsis.

In this study we examined the symptomatology of patients, role of chronic comorbid medical conditions, the source of infection, and the type of infection as it relates to gender differences in the incidence of sepsis.

PIRO concept

In 2001 the International Sepsis Definitions Conference was organized to develop a practical frame for defining the systemic inflammation caused by infection. A concept for staging sepsis was introduced that is based on the four criteria: **P**redisposition, **I**nfection, **R**esponse to the infectious challenge, and **O**rgan dysfunction (PIRO). However, this concept is not yet used in clinical practice.[10]

AIMS AND OBJECTIVES

To study the risk factors and clinical profile of sepsis in elderly and to record the primary site of infection and to determine the influence of sepsis on the survival outcome in the elderly.

Materials and methods:

A hospital based observational study was conducted on patients admitted to R.L. Jalappa Hospital & Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar. Study was conducted from February 2014 to June 2015. A proforma containing detailed information of each patient, was designed according to the study protocol and ethical clearance was obtained from Institutional Ethics Committee. Patients who were willing to give the written informed consent were included in the study.

Inclusion Criteria

100 patients ≥ 65 years admitted to R.L Jalappa Hospital with a clinical suspicion of sepsis and those fulfilling the criteria for sepsis by PIRO grading system as defined by American college of chest physicians and society of critical care medicine.[10, 11]

- **P** – Predisposing factors.
- **I** – Insult or Infection.
- **R** – Host response.
- **O** – Organ dysfunction.

Exclusion Criteria

1. Trauma with sepsis.
2. Burns.
3. Post-surgical.

Method of Collection of Data:

Informed written consent obtained from all subjects.
Patients were divided into groups based on their age.

(i) 65- 74 years
(ii) 75- 84 years
(iii) > 85 years.

All patients' clinical presentation, previous medical history and outcomes as death/discharge and duration of hospital stay were recorded and analyzed according to the age groups.

Statistical Methods:

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was used as test of significance. Continuous data was represented as mean and standard deviation. p value <0.05 was considered as statistically significant.

Results

100 subjects who met the inclusion criteria with a clinical suspicion of sepsis and fulfilling the criteria for sepsis by PIRO grading system admitted to a tertiary care hospital in Kolar, were included in the study. Out of the 100 subjects 64 were males (64%), 36 were females (36%) and age group distribution as shown in figure 1.

Figure 1: Flowchart showing gender and age groups distribution in this study.

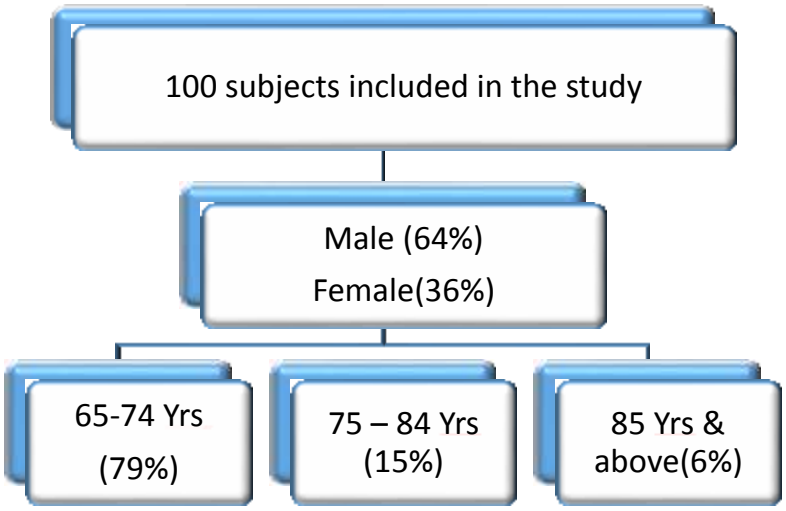


Figure 2: Bar diagram showings Symptoms at Presentation

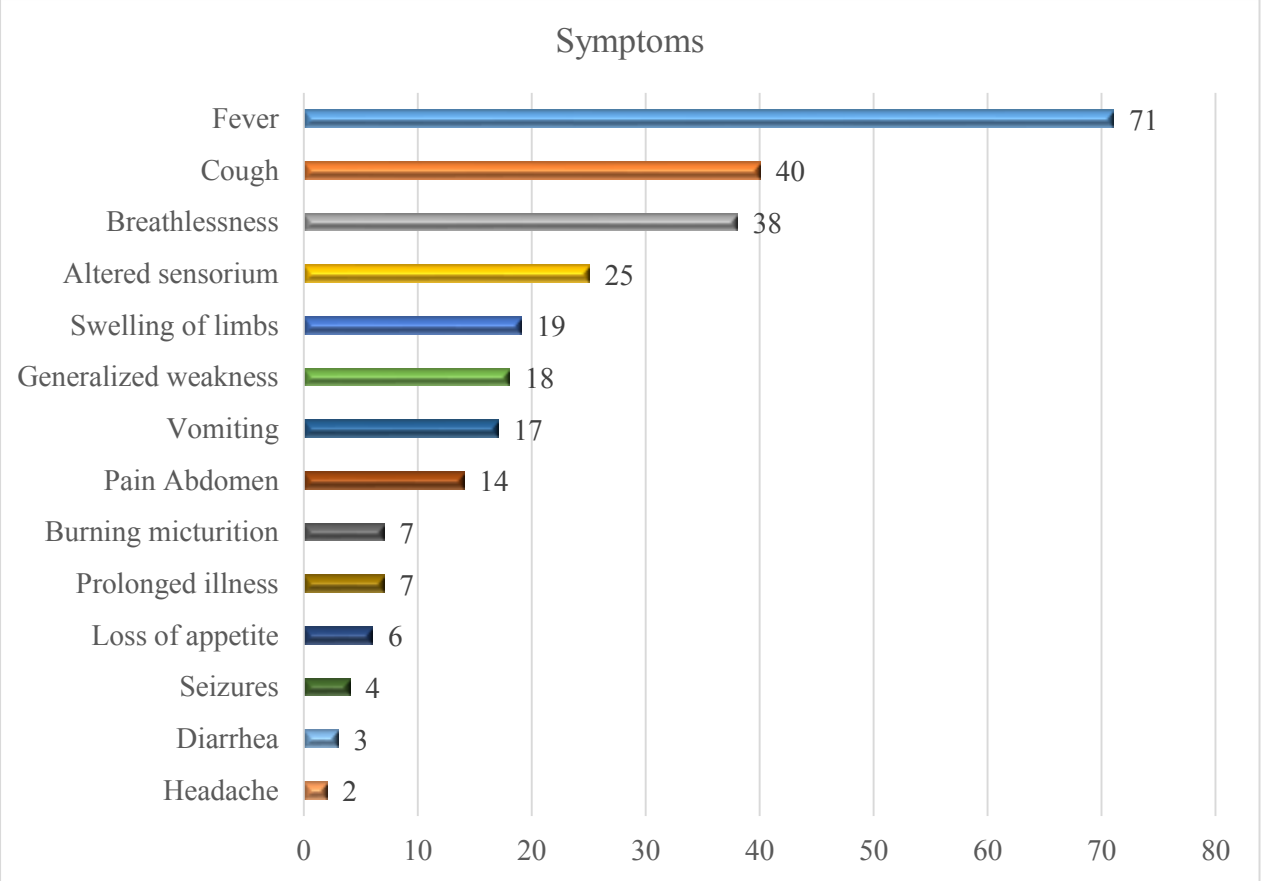
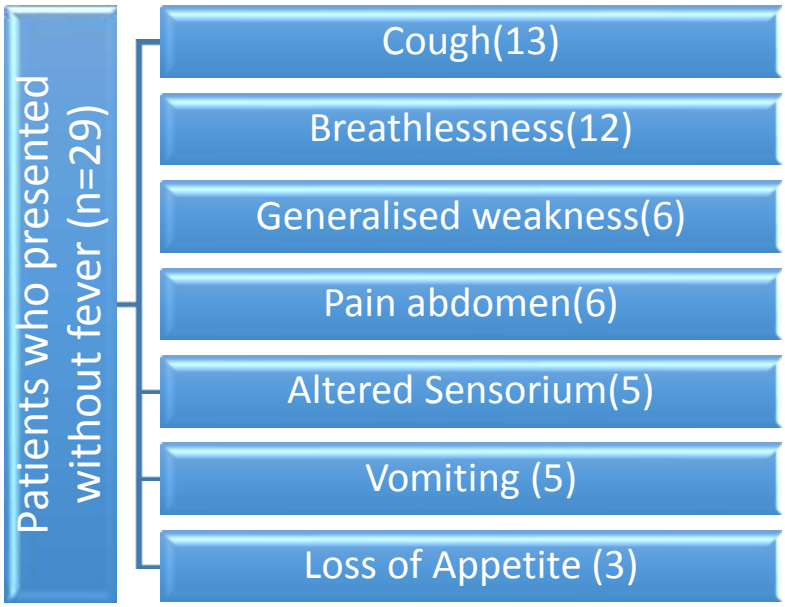
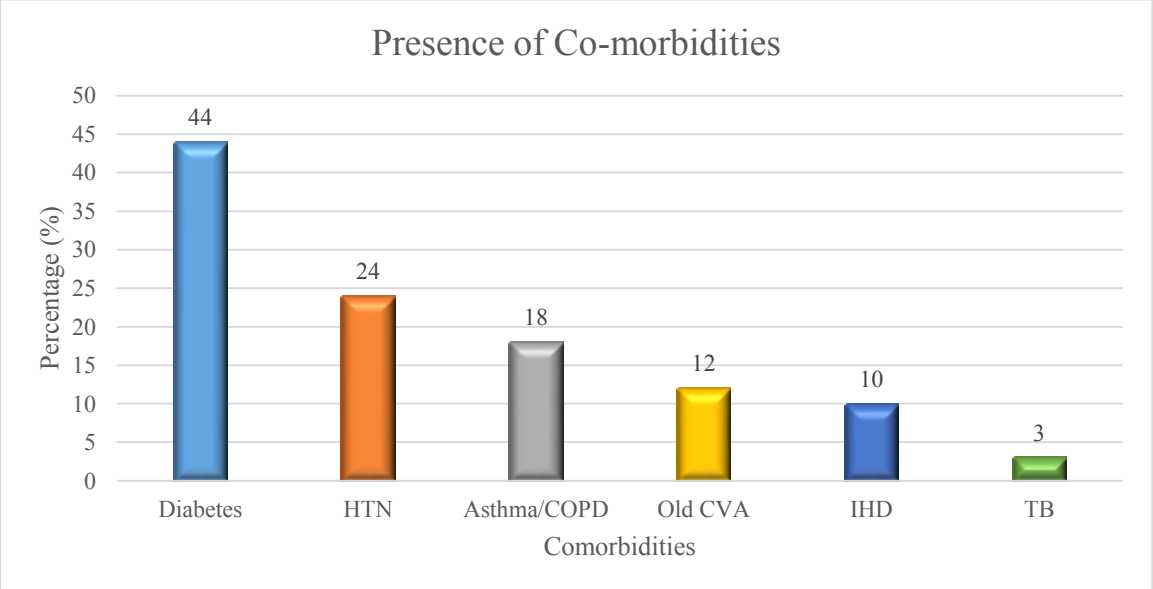


Figure 3: Flowchart showing symptoms at presentation of patients who presented without fever.



Majority (37%) of subjects had 3 symptoms on presentation, 36% had 2 symptoms. The most common risk factor which was associated in patients with sepsis was diabetes (44%) followed by hypertension (24%) and chronic obstructive pulmonary diseases (COPD) (18%) as shown in the table 5 and figure 7.

Figure 4: Bar diagram showing Presence of Co-morbidities in subjects



Other risk factors which were found in patients were smoking (54%) and alcohol (30%). Edema was the most common Finding on GPE (50%), followed by pallor (23%) and others.

Figure 5: Bar diagram showing General Physical Examination Findings in Subjects

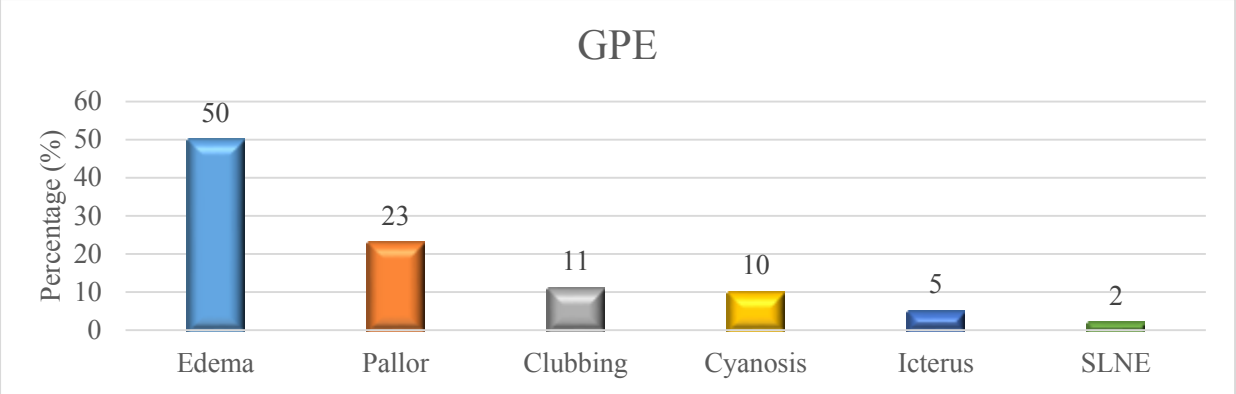
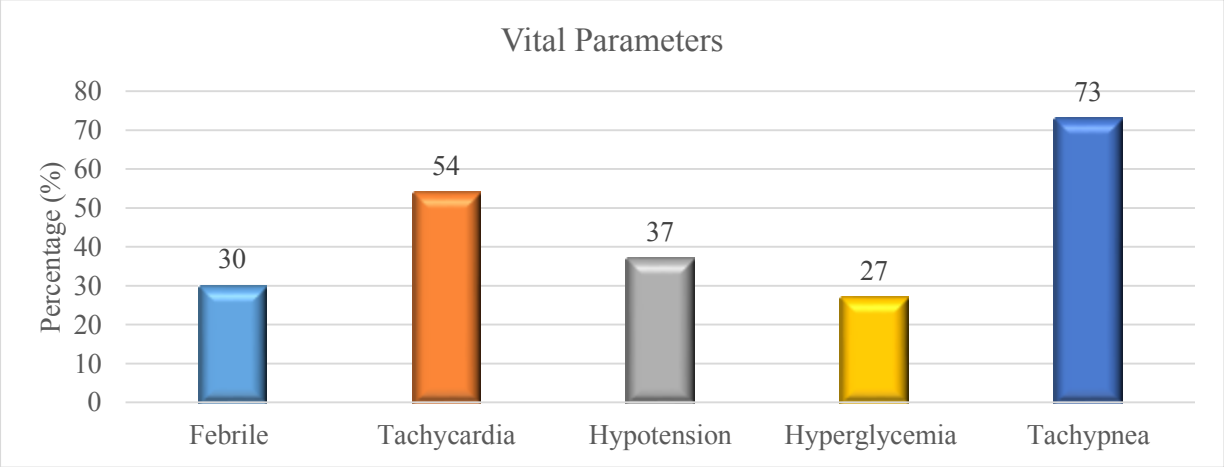


Figure 6: Bar diagram showing Vital Parameters in subjects



Most common site of infection was respiratory system (57%) followed by neuro infection (33%) urinary tract (19%), cellulitis (15%), and bed sores (10%) as shown in the figure.

Figure 7: Site of Infection in subjects

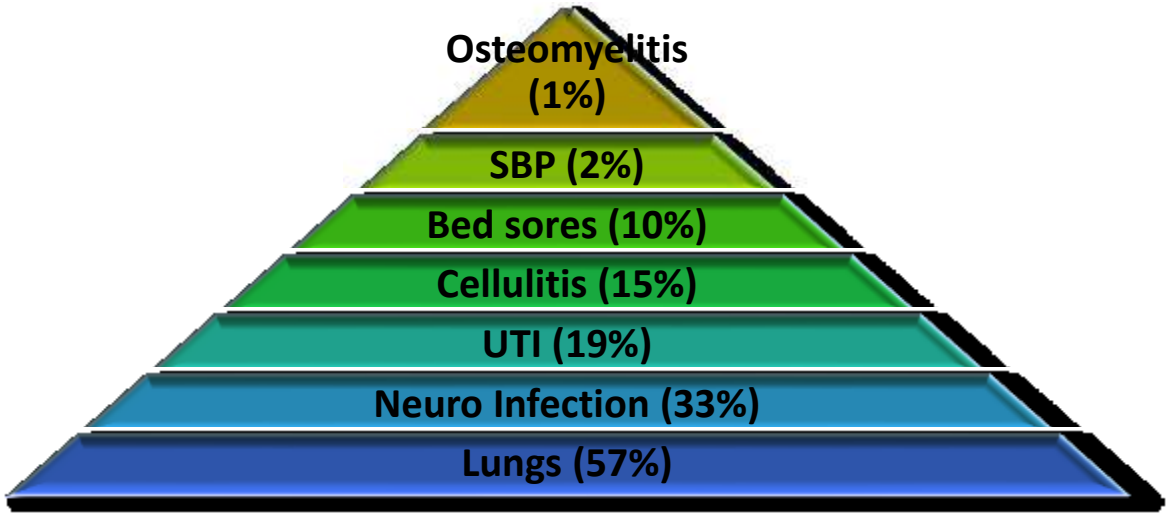


Table 1: No of Foci of Infections in subjects

No. of Foci of infection	Count	%
0	9	9.0%
1	42	42.0%
2	45	45.0%
3	4	4.0%

9 % had no Foci of infection, 42% had one foci, 45% had 2 foci and 4% had 3 foci of infection.

Table 2: Association between Gender and Site of infection

Site of infection		Gender				*p* value
		Males		Female		
		No.	%	No.	%	
RS	No	27	42.2%	16	44.4%	0.827
	Yes	37	57.8%	20	55.6%	
SBP	No	62	96.9%	36	100%	0.097
	Yes	02	3.1%	0	0.00%	
CNS	No	40	62.5%	27	75.0%	0.202
	Yes	24	37.5%	9	25.0%	
UTI	No	53	82.8%	31	86.1%	0.666
	Yes	11	17.2%	5	13.9%	
Bed Sores	No	55	85.9%	35	97.2%	0.071
	Yes	9	14.1%	1	2.8%	
Cellulitis	No	52	81.2%	33	91.7%	0.161
	Yes	12	18.8%	3	8.3%	
Multiple Foci of infection	0	3	4.7%	6	16.7%	0.007*
	1	22	34.4%	20	55.6%	
	2	35	54.7%	10	27.8%	
	3	4	6.2%	0	0.0%	

In the study there was significant association between gender and multiple foci of infections. I.e. in 54.7% of Males there was 2 foci of infections and in females 55.6% of them had one foci of infection. This observation was statistically significant.

Figure 8: Bar diagram showing association between gender and site of infection

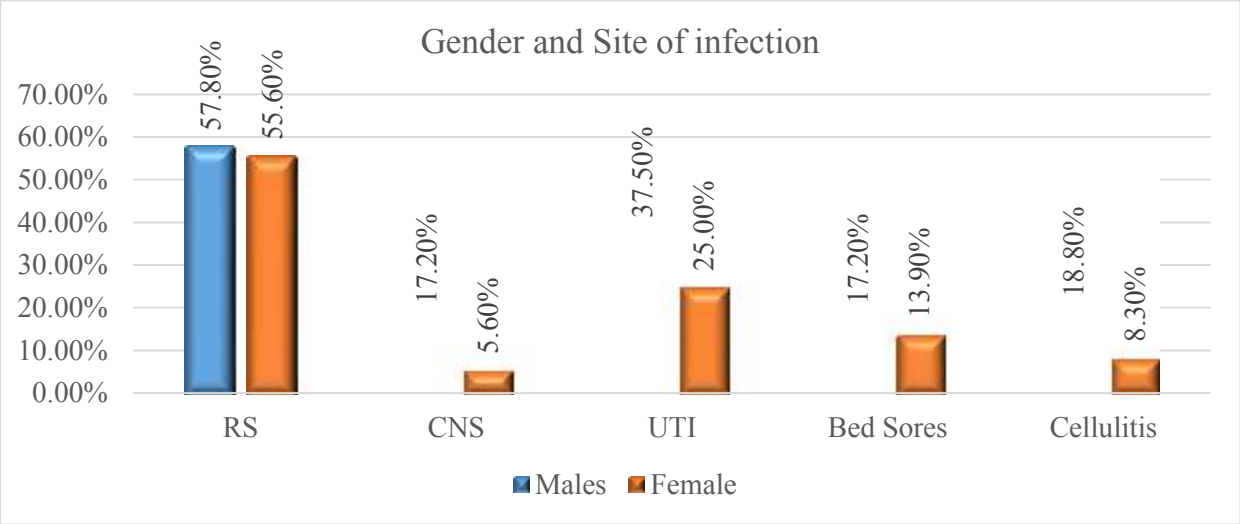
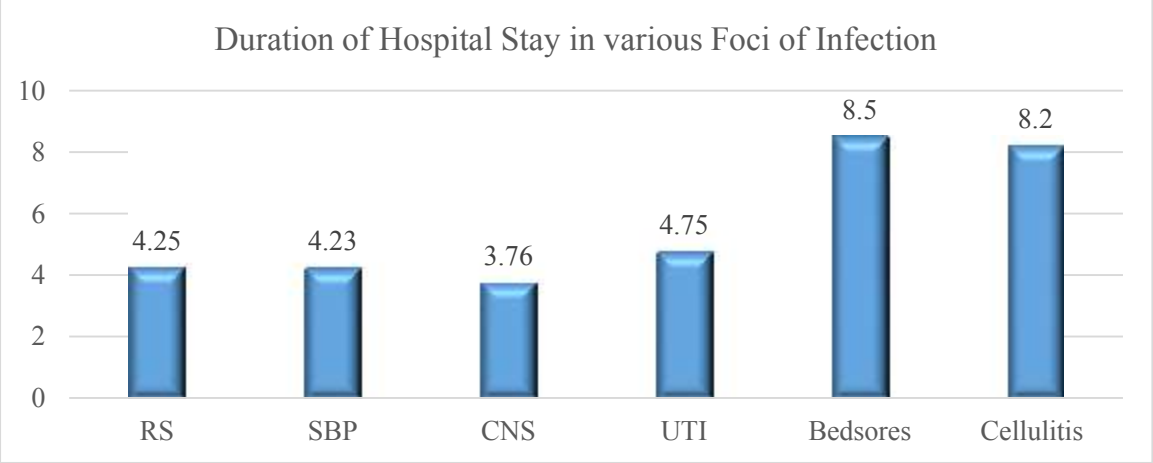


Table 3: Association between Foci of infection and hospital stay

Site of infection	Duration of Hospital stay		*p* value
	Mean	SD	
RS	4.25	3.52	0.061
SBP	4.23	3.27	0.526
CNS	3.76	3.01	0.073
UTI	4.75	1.95	0.773
Bed Sores	8.50	7.34	0.031*
Cellulitis	8.20	6.95	0.013*

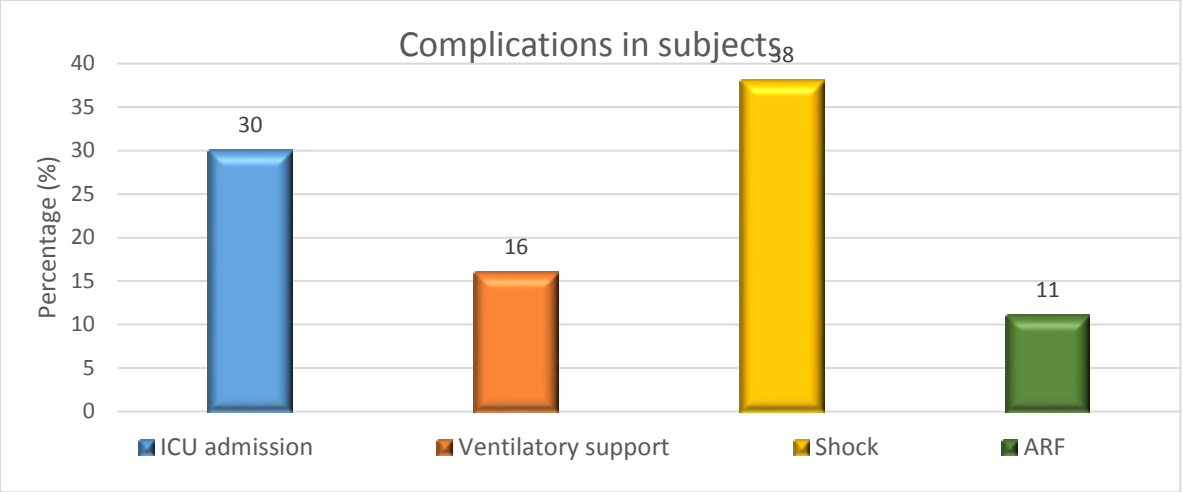
In the study there was significant difference in mean duration of hospital stay in subjects with Bed sores and Cellulitis compared to those who did not have bedsores and cellulitis. With other sites there was no significant difference in duration of hospital stay.

Figure 9: Bar diagram showing Mean duration of hospital stay in various Foci of infection



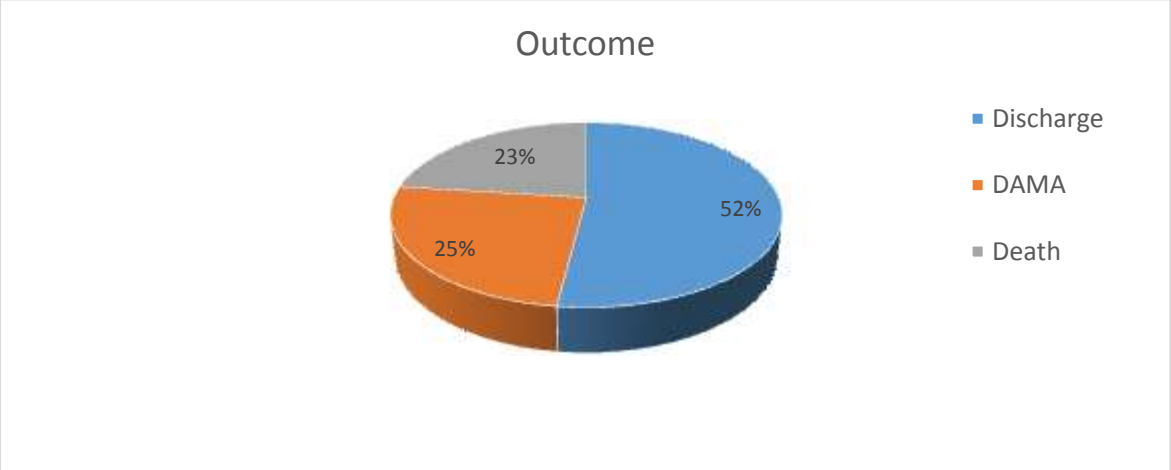
30% were admitted to ICU and 16% were on ventilator support. 53.3% of pts admitted to ICU needed ventilator support. 38% of pts had shock at the time of presentation or during their course in the hospital.

Figure 10: Bar diagram showing complications in subjects



52% of subjects were discharged, 25% Discharged against Medical advice (DAMA) and 23% had mortality.

Figure 11: Pie diagram showing Outcome in subjects



There was no significant association between duration of hospital stay and outcome.

Figure 12: Bar diagram showing association between Duration of hospital stay with outcome

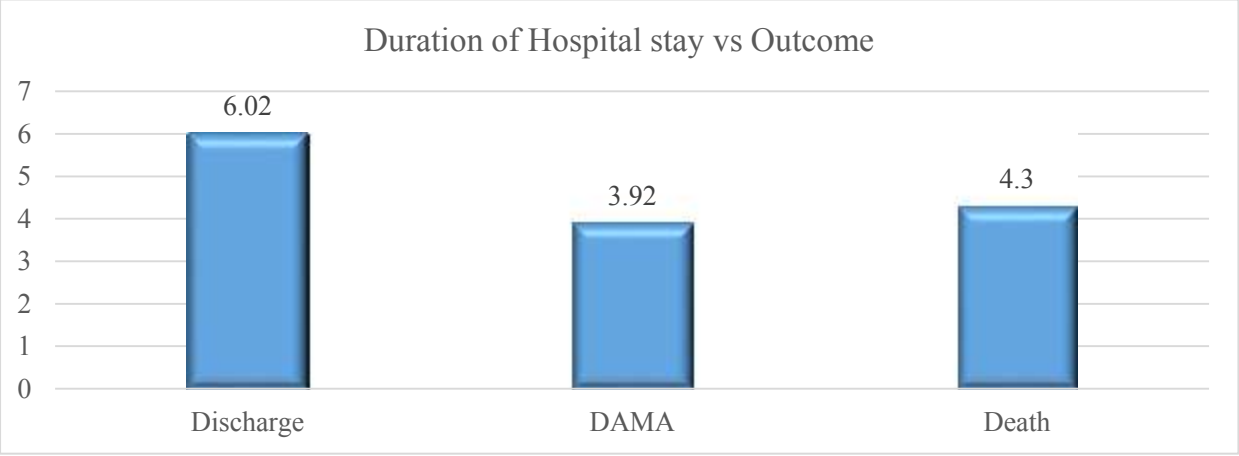


Table 4: Association between Respiratory foci and complications

Complications		Respiratory Infection				*p* value
		No		Yes		
		No.	%	No.	%	
Shock	Yes	10	23.3%	28	49.1%	0.008*
	No	33	76.7%	29	50.9%	
ARF	Yes	5	11.6%	6	10.5%	0.862
	No	38	88.4%	51	89.5%	
Ventilator support	Yes	4	9.3%	12	21.1%	0.113
	No	39	90.7%	45	78.9%	
ICU admission	Yes	6	14.3%	24	44.4%	0.002*
	No	36	85.7%	30	55.6%	

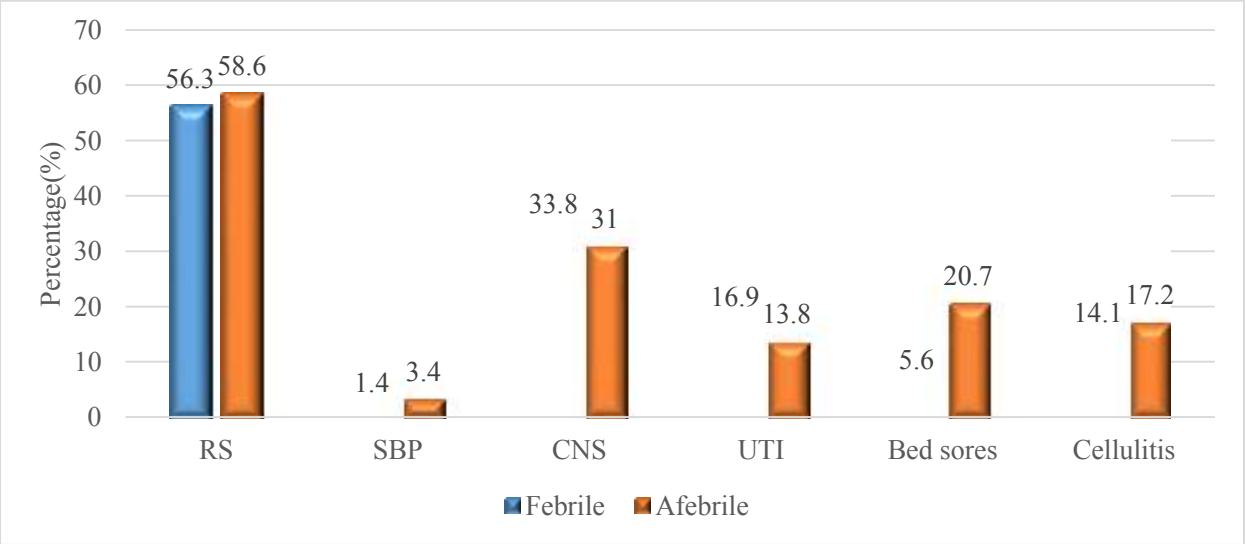
There was significant association between Respiratory foci and complications such as Shock and ICU admission. i.e. Among 57 subjects with respiratory foci 49.1% had shock, and 44.4% Were in admitted to ICU.

Table 5: Association between Cellulitis and complications

Complications		Cellulitis				*p* value
		Yes		No		
		Count	%	Count	%	
Shock	Yes	6	40.0%	32	37.6%	0.863
	No	9	60.0%	53	62.4%	
ARF	Yes	5	33.3%	6	7.1%	0.003*
	No	10	66.7%	79	92.9%	
Ventilator support	Yes	1	6.7%	15	17.6%	0.285
	No	14	93.3%	70	82.4%	
ICU admission	Yes	3	20.0%	27	33.3%	0.306
	No	12	80.0%	54	66.7%	

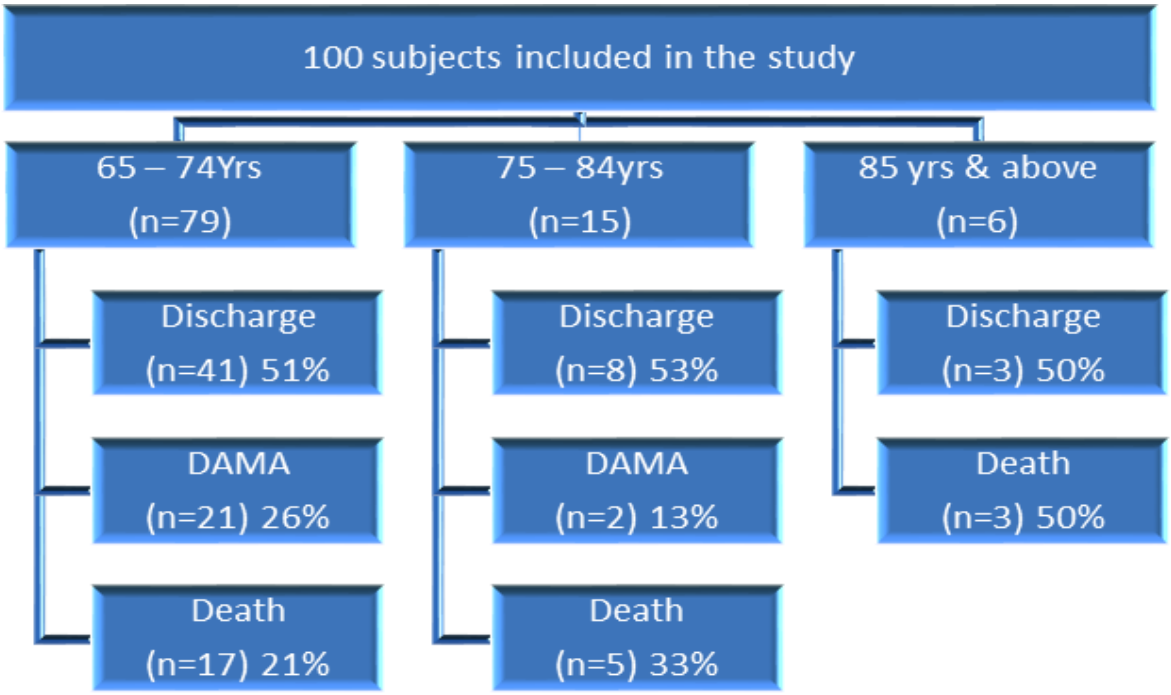
There was no significant association between Cellulitis foci and complications. Except for ARF when there was significant association between ARF and Cellulitis (33.3% of Cellulitis cases had ARF). It was observed that there was no significant association between Fever and Site of Infection. **Except for Bed sores were in among patients with Bed sores only 5.6% had fever.**

Figure 13: Bar diagram showing association between Fever and Site of Infection



No significant association between Fever and outcome.

Figure 14: Flow chart showing outcome and age groups



No significant association between Age and outcome.
In the study there was no significant association between Outcome and Gender.

Figure 15: Flow chart showing outcome and gender

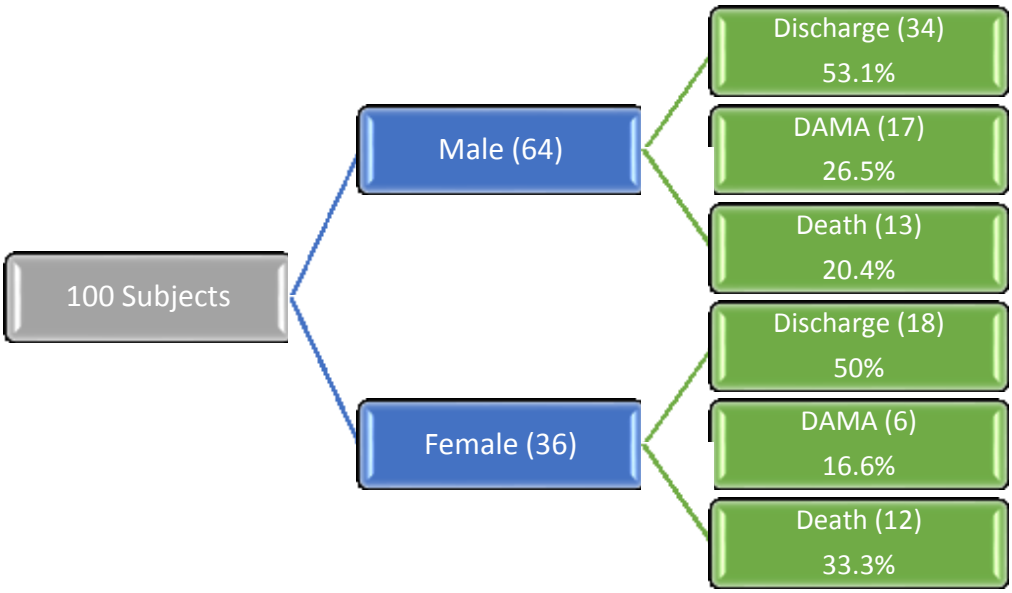
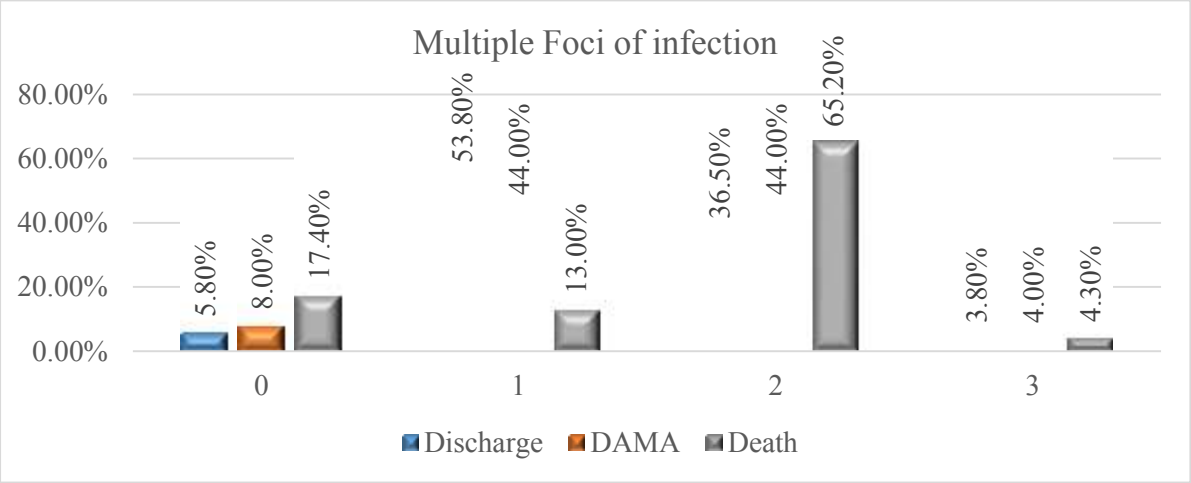


Table 6: Association between Outcome and Site of infection

Site of infection		Outcome						*p* value
		Discharge		DAMA		Death		
		Count	%	Count	%	Count	%	
RS	Yes	23	44.2%	17	68.0%	17	73.9%	0.025*
	No	29	55.8%	8	32.0%	6	26.1%	
CNS	Yes	12	23.1%	12	48.0%	9	39.1%	0.072
	No	40	76.9%	13	52.0%	14	60.9%	
UTI	Yes	15	28.8%	0	0.0%	1	4.3%	0.001*
	No	37	71.2%	25	100.0%	22	95.7%	
Bed Sores	Yes	6	11.5%	1	4.0%	3	13.0%	0.503
	No	46	88.5%	24	96.0%	20	87.0%	
Cellulitis	Yes	9	17.3%	4	16.0%	2	8.7%	0.621
	No	43	82.7%	21	84.0%	21	91.3%	
Multiple Foci of infection	0	3	5.8%	2	8.0%	4	17.4%	0.069
	1	28	53.8%	11	44.0%	3	13.0%	
	2	19	36.5%	11	44.0%	15	65.2%	
	3	2	3.8%	1	4.0%	1	4.3%	

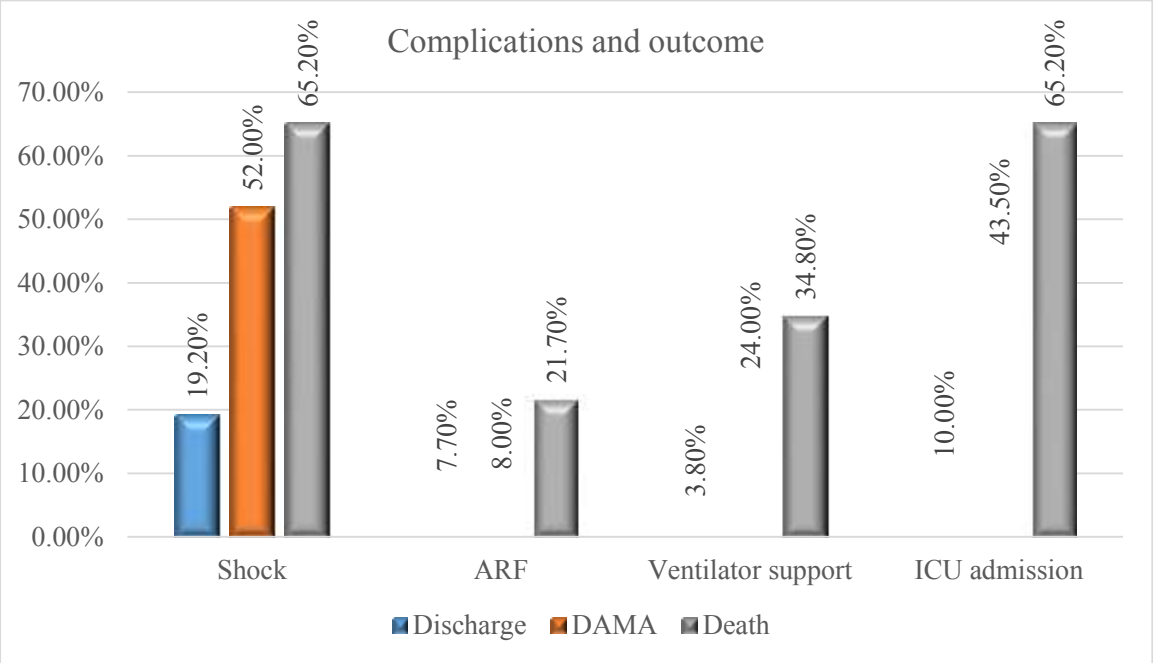
In the study it was observed there was significant association between Respiratory site, UTI and outcome. Among 23 subjects who died, 73.9% had respiratory infections, and in UTI 71.2% were discharged. There was no significant association for other foci of infection and outcome.
There was no significant association between multiple foci of infections and outcome.

Figure 6: Bar diagram showing Association between Multiple Foci and Outcome



In the study there was significant association between complication such as shock, ventilator support, ICU admission and outcome. i.e. among the subjects who had mortality 65.2% had shock, 34.8% were on ventilator support and 65.2% were admitted in ICU. No significant association was observed for ARF and outcome.

Figure 17: Bar diagram showing Association between complications and outcome



Discussion:

Sepsis is a complex interaction of both inflammatory and anti-inflammatory responses, as well as disturbed homeostasis and thrombosis.[12-16] Severe sepsis and septic shock remain a major healthcare burden and are associated with a high mortality.[16] Sepsis is a systemic inflammatory response syndrome (SIRS), provoked by an infection which is associated with high morbidity and mortality, comparable to that of myocardial infarction or stroke. [17] Elderly individuals have an increased risk of developing sepsis, compared with younger patients, because of preexisting co-morbidities and the drugs used for those conditions, frequent instrumentation, declining performance status, and altered immune function. The incidence has increased in the entire Western world during the last decades, yet mortality has decreased only marginally.[18] Despite the high mortality, the severity of sepsis is frequently underestimated.[19]

In this study, 100 subjects were studied who met the inclusion criteria with a clinical suspicion of sepsis and fulfilling the criteria for sepsis by PIRO grading system admitted to a tertiary care hospital in Kolar, were included in the study. Out of the 100 subjects, majority of them (64%) were males as seen in other previous studies.[5,]

Subjects were divided into three groups based on age.

Group 1 → 65 – 74 years,

Group 2 → 75 – 84 years,

Group 3 → 85 years and above.

Subjects were more commonly seen in the age group 65 to 74 years – 79 patients (79%) followed by 75 – 84 years – 15 patients (15%) and 85 years and above – 6 patients (6%) as compared with study done by martin et al.[5] Duration of hospital stay ranged from minimum of 1 day to a maximum of 29 days with an average hospital stay of 5.1 ± 5.2 days. Fever was found to be the commonest symptom (71%) patients presented, followed by cough (40%), breathlessness (38%), and other symptoms which subjects presented with as shown in figure 2.

Inspite of fever being the most common symptom, 29% of the patients did not have a history of fever. Of these 29% of patients, the most commonest symptom were presented as cough(44%) followed by breathlessness, generalized weakness and pain abdomen as depicted in the figure 3. There are no other previous studies available who have analyzed patients without fever.

Generalized weakness and loss of appetite was found to be significant symptom of presentation in patients who presented without the history of fever as shown in the figure 11. Majority of the subjects had 2 to 3 symptoms at presentation.

The most common risk factor which was associated in patients with sepsis in this study was diabetes (44%) followed by hypertension (24%). Smoking was also found to be a significant risk factor especially in males. Prolonged illness (Chronic kidney disease on maintenance hemodialysis, IHD) and bed bound state (Old CVA) was found in 8% of the patients.

At the time of presentation 50% of the subjects had edema and pallor in 23% of the subjects. Inspite of fever being the commonest symptom only 30% of the patients were found to be febrile (Temperature ranging from 99^{o} F to 102^{o} F) at the time of presentation. 37% of the patients had hypotension (Systolic blood pressure < 90mmHg) and 27% had hyperglycemia (known diabetics) at the time of presentation. 73% patients had tachypnea (Respiratory rate above 18).

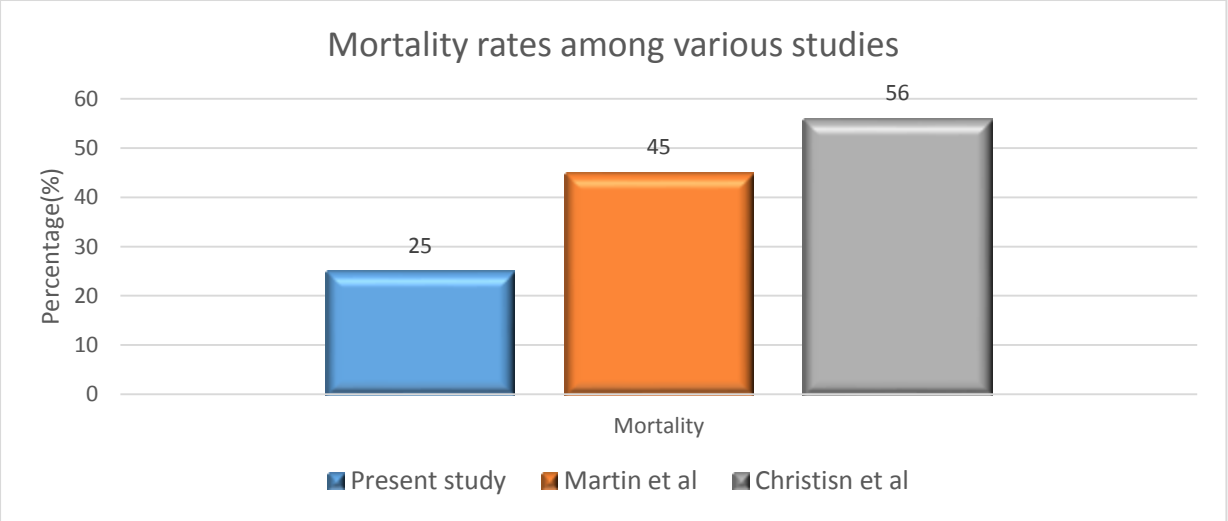
The most common site of infection was respiratory system 57% as compared to previous studies (61%). Second most common site of infection in this study was neuro infection whereas urinary tract infection was found to be the second most common site of infection in the study done by Angus et al.[13,20]

A significant finding found in this study was, 49 % of the patients had multiple foci of infection and 45% of the patients had two foci of infection. Another statistically significant finding in this study was, only 5.6% of patients with bed sores had history of fever.

Complications was seen in 42% of the patients, shock being predominantly seen in 38% of patients. 30% of patients needed ICU management and 53% of them needed ventilator support.

Overall mortality rate in this study was 25% as compared to a study done by Martin et al it was as high as 45% an 56% in study done by Christian et al.[21] Mortality rate was seen higher in the 65 – 74 yr age group as seen in other studies. Male pts had a higher mortality rate 52.2% when compared to female subjects. Same studies also showed a higher mortality in male subjects.

Figure 18: Bar diagram comparing mortality rates in various studies.



Respiratory foci of infection had a higher incidence of admission to ICU, need of ventilator support and increase in mortality when compared to other site of infection. Out of the 100 subjects recruited, 52% got discharged, 25% succumbed to the illness and 23% got discharged against medical advice. Mortality with respiratory foci of infection was 73.9% and least mortality was found with UTI and this finding was statistically significant.

Conclusion

In this study, sepsis is more commonly seen in elderly males. More number of patients belonged to the age group of 65 – 74yrs. Fever being the most common presenting symptom. Elderly patients can develop sepsis even without fever which was seen in 29% of the patients in this study.

Respiratory system was found to be the most common site of infection. A significant number of patients develop complications in the form of ICU admission, Ventilator support, acute renal failure and septic shock.

In 35 subjects (54.7%) of Males there was 2 foci of infections and in 20 female subjects (55.6%) had one focus of infection which was statistically significant.

There was significant association between Respiratory foci and complications such as Shock and ICU admission and a significant association between ARF and Cellulitis was also seen. Among 23 subjects who died, 73.9% had respiratory infections.

The burden of elderly population is on the rise and elderly patients with sepsis and septic shock is expected to be on the rise. Hence infections, sepsis and septic shock are a major threat to health of the geriatric population. Despite the increasing incidence of and significant mortality associated with sepsis in older patients, many elderly patients respond remarkably well to early goal directed management strategies.

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