



1. FCPS
Associate Professor
Department of Medicine
Liaquat University of Medical and
Health Sciences
(LUMHS) Jamshoro
2. MD
Consultant Physician
Department of Medicine, Medical –
III, ward 06
Liaquat University Hospital
Hyderabad / Jamshoro
3. FCPS
Senior Registrar
Department of Medicine, unit-III,
ward 07
Jinnah Postgraduate Medical
Center Karachi
4. Postgraduate
Department of Medicine
Liaquat University of Medical and
Health Sciences
(LUMHS) Jamshoro
5. MBBS
Registrar
Department of Medicine, Medical
unit-III, ward 06
Liaquat University Hospital
Hyderabad / Jamshoro

Correspondence Address:

Dr. Syed Zulfiqar Ali Shah
House No: 279, Doctor's Colony
Hirabad, Hyderabad, Sindh, Pakistan
zulfiqar229@hotmail.com

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SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS); PATIENTS WITH LIVER CIRRHOSIS

Dr. Shuaib Ansari¹, Dr. Irfan Murtaza Shahwani², Dr. Zeeshan Ali³, Dr. Syed Zulfiqar Ali Shah⁴, Dr. Faisal Shahab⁵

ABSTRACT... Systemic inflammatory response syndrome (SIRS) is a generalized disorder, immune response to infection which results in disturbed microcirculation, visceral perfusion and ultimately visceral failure. **Objectives:** To determine the frequency of systemic inflammatory response syndrome in patients with liver cirrhosis. **Design:** Cross sectional descriptive. **Period:** Six months study. **Setting:** At Liaquat University Hospital Hyderabad. **Patients and methods:** All the patients with liver cirrhosis for 06 months duration admitted in the ward were further evaluated for systemic inflammatory response syndrome. The data was analyzed in SPSS 16 and the frequency and percentage was calculated. **Results:** During six months study period, total 100 cirrhotic subjects were studied for SIRS. The mean \pm SD for age in all (100) cirrhotic patients was 45.74 ± 7.537 . The mean temperatures was 40.42 ± 0.32 where as it was 39.72 ± 0.43 and 38.92 ± 0.11 in male and female population respectively. The mean heart beat was 128.42 ± 6.74 where as it was 115.83 ± 8.93 and 120.62 ± 5.53 in male and female population respectively. The mean respiratory rate was 25.31 ± 3.52 where as it was 23.52 ± 2.31 and 26.63 ± 3.21 in male and female population respectively. The mean white blood cell count was 28.81 ± 4.51 where as it was 23.74 ± 4.73 and 30.83 ± 5.73 respectively. The SIRS was observed in 70% subjects of which 47(67.1%) were males and 23(32.9%) were females ($p=0.04$). Majority of SIRS subjects were 30-39 years of age and male population was predominant ($p=0.03$). The gender distribution in relation to severity of liver disease was statistically significant ($p=0.05$) while the SIRS in relation statistical analysis. **Conclusions:** The systemic inflammatory response syndrome occurs in patients with liver cirrhosis.

Key words: SIRS, Cirrhosis, Child-Pugh Score.

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INTRODUCTION

Liver cirrhosis is one of the most frequent cause of hospitalization in Pakistan that cost a major burden on health system and chronic viral hepatitis B and hepatitis C are the most common causes in Pakistan^{1,2}, while the alcohol abuse is the common cause in Western countries.³The history and physical examination of cirrhosis cirrhotic subjects have different findings that needs liver / gastrointestinal work-up to evaluate the cause⁴. The prevalence of liver cirrhosis reported by Kakakhel et al, Nadeem et al and Shaikh et al was 52%, 55% and 51%⁵⁻⁷.

Systemic inflammatory response syndrome (SIRS) is a generalized disorder, immune response to infection which results in disturbed microcirculation, visceral perfusion and ultimately

visceral failure⁸. The mechanism includes platelet aggregation, leukocyte enzyme release, fibrin deposition and coagulopathies⁹. It has been found that SIRS occurs in liver cirrhosis and had worst outcome¹⁰. The inflammation caused by secondary bacterial infection leads to coagulopathy and has a main role to acquire serious complications i.e. hepatic encephalopathy, variceal bleeding and acute hepatic failure¹¹⁻¹³. A study by Thabut et al,¹⁰ shown that inflammation is the major cause of mortality in cirrhotic patients. It has been identified that a imbalance between decreased anti-inflammatory pathway and proinflammatory response is the main root of pathogenesis as far as inflammation is concerned^{14,15}. A study published during 2009¹⁶ shown that the SIRS affects body temperature 87%, heart rate 44%, respiratory rate 64% and white blood cell (WBC) counts 51%, and

reported the prevalence of SIRS in patients with liver cirrhosis was 25%¹⁶.

Therefore this research was conducted to evaluate the frequency of SIRS in cirrhotic subjects that gives knowledge to the health care provider as far as the management strategy of liver cirrhosis is concerned.

PATIENTS AND METHODS

The study was conducted on the patients who met the inclusion as well as exclusion criteria of the study. All the patients with liver cirrhosis for 06 months duration admitted in the ward were further evaluates for SIRS according to the following criteria. (i) Body temperature 100.4 °F or 96.8 °F. (ii) respiratory rate ≥ 20 b/min), (iii) heart rate ≥ 90 b/min) (iv) WBC count $\geq 12,000/\text{mm}^3$ or $\leq 4000/\text{mm}^3$ which was measured by taking 3ml venous blood through a sterile disposable syringe, transfer it in a complete blood picture (CP) bottle and then sent to laboratory for analysis. The patient was considered had SIRS if had at least 02 of the above four criteria. The subjects on antibiotics, hormonal and antipsychotic therapy, had autoimmune disease, malignant hyperthermia, DIC, pregnant women; subjects with malignancy or on chemotherapy, and the individuals with HIV or known cardiac and respiratory disorders were placed in exclusion criteria. All the maneuvers were performed by the collaboration of whole research team and were under medical ethics while data was collected on proforma.

The data of all patients entered and analyze in SPSS 16.00. The frequency and percentage (%) was calculated for gender and SIRS in cirrhotic subjects. The mean \pm SD was calculated for age, duration of cirrhosis, temperature, heart rate, reparatory rate and WBC. The stratification was done for age, gender, duration of cirrhosis and systemic inflammatory response syndrome. The chi square test was applied and statistical significance was considered when the p-value ≤ 0.05 .

RESULTS

During six months study period, total 100 cirrhotic

subjects were studied for SIRS. The identified cause of liver cirrhosis was viral hepatitis i.e. hepatitis C in 85% patients, hepatitis B in 5% patients while 02% patients had concurrent hepatitis B and C infection. Eight percent had non viral cirrhosis i.e. 04% patients had history of alcoholism, Wilson disease was identified in 01% patient whereas no any cause was detected in 03 cirrhotic subjects. The mean \pm SD for age in all (100) cirrhotic patients was 45.74 ± 7.537 while the mean \pm SD for age in male cirrhotic patients was 46.73 ± 10.53 where as in female cirrhotic subjects it was 42.84 ± 11.73 respectively. The SIRS was observed in 70% of which 47(67.1%) were males and 23(32.9%) were females. Regarding the diagnosis of SIRS, 80% patients had 03 criteria, 08% had 02 criteria and 12 had all the four criteria.

The mean temperatures was 40.42 ± 0.32 where as it was 39.72 ± 0.43 and 38.92 ± 0.11 in male and female population respectively. The mean heart beat was 128.42 ± 6.74 where as it was 115.83 ± 8.93 and 120.62 ± 5.53 in male and female population respectively. The mean respiratory rate was 25.31 ± 3.52 where as it was 23.52 ± 2.31 and 26.63 ± 3.21 in male and female population respectively. The mean white blood cell count was 28.81 ± 4.51 where as it was 23.74 ± 4.73 and 30.83 ± 5.73 respectively. The age and gender distribution of subjects is shown in Table: I while the age in relation to severity of liver cirrhosis is mentioned in Table II. The gender in relation to severity of cirrhosis and SIRS is shown in Table III and IV whereas the SIRS in relation to severity of liver cirrhosis is mentioned in Table V.

DISCUSSION

Our study found positive association between SIRS and liver cirrhosis and its severity by Child-Pugh score system. Thabut et al¹⁷ observed that inflammation is the major cause of adverse event in subjects with liver cirrhosis. The cirrhotic subjects are immunocompromised and existence of SIRS in them is may be due to the secondary bacterial infections^{18,19}.

Albillos et al.²⁰ found that cirrhotic individuals with

AGE		GENDER		Total	P-value
		Male	Female		
13-19		4	4	8	0.03*
		5.6%	13.8%	8.0%	
20-29		10	11	21	
		14.1%	37.9%	21.0%	
30-39		25	4	29	
		35.2%	13.8%	29.0%	
40-49		22	5	27	
		31.0%	17.2%	27.0%	
50-59		3	2	5	
		4.2%	6.9%	5.0%	
60 +		7	3	10	
		9.9%	10.3%	10.0%	
Total		71	29	100	
		100.0%	100.0%	100.0%	

Table-I. The age and gender distribution

*P-value is statistically significant

Pearson Chi-square value = 12.28; df = 5

AGE		CHILD-PUGH CLASS			Total	P-value
		A	B	C		
13-19		2	2	4	8	0.91*
		9.5%	4.5%	11.4%	8.0%	
20-29		6	8	7	21	
		28.6%	18.2%	20.0%	21.0%	
30-39		5	14	10	29	
		23.8%	31.8%	28.6%	29.0%	
40-49		5	14	8	27	
		23.8%	31.8%	22.9%	27.0%	
50-59		1	1	3	5	
		4.8%	2.3%	8.6%	5.0%	
60 +		2	5	3	10	
		9.5%	11.4%	8.6%	10.0%	
Total		21	44	35	100	
		100.0%	100.0%	100.0%	100.0%	

Table-II. The age distribution in relation to child-pugh score

*P-value is statistically non significant

Pearson Chi-square value = 4.69; df = 10

GENDER		CHILD-PUGH CLASS			Total	P-value
		A	B	C		
Male		18	33	20	71	0.05*
		85.7%	75.0%	57.1%	71.0%	
Female		3	11	15	29	
		14.3%	25.0%	42.9%	29.0%	
Total		21	44	35	100	
		100.0%	100.0%	100.0%	100.0%	

Table-III. The gender distribution in relation to child-pugh class

*P-value is statistically significant

Pearson Chi-square value = 5.81; df = 2

		SIRS		Total	P-value
		Yes	No		
GENDER	Male	47	24	71	0.04*
		67.1%	80.0%	71.0%	
	Female	23	6	29	
		32.9%	20.0%	29.0%	
Total		70	30	100	
		100.0%	100.0%	100.0%	

Table-IV. The sirs in relation to gender distribution

*P-value is statistically significant

Pearson Chi-square value = 4.52; df = 1

		SIRS		Total	P-value
		Yes	No		
Child-Pugh Class	A	11	10	21	0.05*
		15.7%	33.3%	21.0%	
	B	35	9	44	
		50.0%	30.0%	44.0%	
	C	24	11	35	
		34.3%	36.7%	35.0%	
Total		70	30	100	
		100.0%	100.0%	100.0%	

Table-V. The sirs in relation to severity of the disease

*P-value is statistically significant

Pearson Chi-square value = 5.04; df = 2

ascites have raised lipopolysaccharide binding protein which cause release of TNF α and IL6, both are responsible for systemic inflammation whereas gut decontamination by antibiotics may improves these changes by subsiding the infection. Rosenbloom et al,²¹ observed that WBC activation in SIRS is due to the pro-inflammatory property of IL6. The inflammatory mediators released during acute hepatic necrosis also play a role in the pathogenesis of SIRS^{22,23}. The exact mechanism of pathogenesis is still unknown²³.

In present study the majority of the patients were in 30-39 years of age and the findings are consistent with the study by Abdel-Khalek EE, et al²⁴ whereas the male population predominant in our study as far as SIRS is concerned and the study by Shawcross DL, et al²⁵. also had same observation. In our series the SIRS is related to severity of the liver disease by Child-Pugh score and the finding was also observed by Hong S, et al²⁶.

In current study, 07/70 (10%) patients of SIRS were expired during hospitalization and 03/70 (04%) were during follow up period, all those

subjects were in class B and C of Child-Pugh classification. In a study by Cazzaniga et al,¹⁶ out of 141 cirrhotic patients died during follow up, which included 24% SIRS-positive and 4% SIRS-negative patients,²⁷ while in a study by Behroozian R, et al the mortality rate was 19 out of 109 cirrhotic patients, of which 38% were SIRS-positive and 8% were SIRS-negative²⁸. The mortality rate in our study might have been attributed to the unavailability of advanced medical treatment, such as liver transplants in our centers.

Therefore, the early determination of SIRS also helps to prevent further spread (complication) of the disease as far as systemic inflammatory response syndrome is concerned.

CONCLUSIONS

The SIRS observed in cirrhotic patients and has worst prognosis. It is relatively frequent event in liver cirrhosis, associated with severity of liver disease by the Child-Pugh score and independently and adversely affects the outcome in liver cirrhosis.


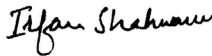

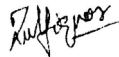
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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Shuaib Ansari	Contribution to conception and design, acquisition of data, analysis and interpretation of data	
2	Dr. Irfan Murtaza Shahwani	Drafting the article and shares its expert research opinion and experience in finalizing the manuscript	
3	Dr. Zeeshan Ali	Contributed in conception and interpretation of data and give his expert view for manuscript designing	
4	Dr. Syed Zulfiquar Ali Shah	Analysis and interpretation of data Contributed in conception and shares its expert research opinion	
5	Dr. Faisal Shahab	Drafting, interpreting and analyzing the data	