

## A Comparative Study on the Cellular Inflammatory Indices among ICU Vs Non ICU Patients of Covid-19 in a Tertiary Hospital

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### Abstract

**Background:** As accumulating evidence has suggested that there is an association of increased levels of inflammatory bio markers in relation to severity of covid -19 illness, the present study was planned to examine the scenario of association between inflammatory markers and severity of covid-19 illness by studying ICU and non ICU patients comparatively. **Research Question:** Is there a positive association between increased levels of inflammatory biomarkers and severely ill patients of covid-19 disease? **The setting** of the study was at Government General Hospital, (State Covid Care Hospital) Vijayawada, Andhra Pradesh. An observational study was conducted during the period from March 2021 to August 2021 on 60 ICU and 40 Non ICU patients of covid-19 by studying their socio demographic profiles and scenario of increased levels of inflammatory Biomarkers in relation with severity of illness of covid-19 disease. **Results:** Maximum about 52% of the admissions were confined to the age group of 41 to 60 years with the mean  $\pm$  2 SD =  $47.4 \pm 24.8$  at 95 CI with 70:30% of sex ratio was observed among study subjects as male & female. High CRP & IL 6 levels were observed among ICU patients when compared to Non ICU patients. Further it was observed that maximum high levels of serum ferritin between 501 to 750 Micrograms/L among ICU admissions of covid-19 significantly with the  $P < 0.01$  when compared to non ICU patients. And also high levels of LDH between 231-600 U/ml were observed among the both groups of ICU & non ICU patients. It was also observed that related to D dimer high levels  $\geq 10,000$  Micrograms/ml were noticed among ICU patients only. It was concluded that high levels of inflammatory Bio markers were associated with older and severely affected covid-19 patients in this study.

**Keywords:** Inflammatory Cellular Indices, CRP (C - reactive protein), Serum Ferritin, IL-6 (Interlukim-6) and LDH (Lactate Dehydrogenase)

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### Introduction

Covid-19 is an infectious disease caused by the SARS-Cov-2 virus. Most people infected with the virus will experience mild to moderate respiratory illness and recover without requiring special treatment. However some will become seriously ill and require medical attention. Older people and those with underlying medical conditions like CVS, Diabetes, Chronic respiratory disease or cancer are more likely to develop serious illness. And anyone can get sick with Covid-19 and become seriously ill or die at any age[1]. Globally by the end of September 2021 there have been 232, 636, 622 confirmed cases of covid-19 and 4762 089 deaths reported to WHO. And in India 33739980 cases of covid-19 and 448062 deaths have been reported. Accumulating evidence has suggested that informatory responses at cellular level play a critical role in the progression of Covid -19[2,3]. Laboratory markers (or) Biomarkers can provide additional objective information which can significantly impact these components of patient care. Covid-19 is localized respiratory infection but a multisystem disease caused by diffuse systemic process involving a complex interplay immunological, informatory and coagulative cascades. The understanding of what the virus does to the body and how the body reacts to it has uncovered a gamut of potential biomarkers[4]. Serum ferritin and IL6 etc. have been reported to be significantly associated with the high risks of the development of severe Covid -19[5,6,7]. Severe Covid-19 and Cytokine release syndrome have been linked to

elevated levels of IL6[8,9] which stimulates the liver to produce CRP, LDH and ferritin[10,11]. And also several studies have suggested that severe disease may be associated with elevated WBC, CRP, PCT and IL6[12,13,14].

So the present study was planned to examine the scenario of association between inflammatory markers and severity of Covid-19 disease by studying ICU and Non ICU patients comparatively.

### Materials and methods

The setting of the study was at Government General Hospital (state Covid Care Hospital), Vijayawada, Andhra Pradesh and the study was conducted during the period from March 2021 to August 2021. At that time as the epidemic curve wave is at peak stage, the covid-19 cases attending the O.P were found to be 50%. So the sample size was calculated by using the formula  $4PQ/L^2$  where  $P = 50\%$ ,  $Q = 100 - P$  i.e.  $50\%$ ,  $L = 20\%$  of  $P$  ie 10 so  $N = 100$ . All the Covid cases admitted in the hospital during the period from March to May 2021 were selected into study as study subjects at the rate of 60:40 [60% ICU cases & 40% Non ICU cases] after received the informed content. The required data about their socio-demographic profiles, clinical signs and symptoms and inflammatory Biomarkers by means of laboratory blood investigations etc was collected during the course of the disease by duly following the Covid protocol.

Prior to beginning of the study the institutional ethics committee clearance was obtained. And the collected data was analyzed by using appropriate statistical techniques like measures of dispersion, Central tendency, percentages, proportions and tests of significance like chi-square test and standard error of mean etc with the help of computer software. The observations were discussed in the light of published work of various authors and basing on the study results conclusions and recommendations were made.

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Result

Table-1: Age & Sex wise distribution of the study subjects

Sl. No.	Age Yrs	Males			Females			Grand Total
		ICU	Non ICU	Total	ICU	Non ICU	Total	
1	20-30	6 (14.5%)	2 (9%)	8(11.4%)	2 (11%)	0	2 (6.6%)	10 (100%)
2	31-40	9 (22%)	5 (17%)	14(20%)	3 (16%)	1 (9%)	4 (13.3%)	18 (18%)
3	41-50	13 (32%)	10 (34%)	23(32.8%)	4 (20.5%)	3 (27.2%)	7 (23.3%)	30 (30%)
4	51-60	7 (17%)	6 (20%)	13(18.5%)	6 (32%)	3 (27.2%)	9 (30%)	22 (20%)
5	> 60	6 (14.5%)	6 (20%)	12(17.4%)	4 (20.5%)	4 (36.3%)	8 (26.6%)	22 (20%)
<b>Total</b>		<b>41(100%)</b>	<b>29(100%)</b>	<b>70(100%)</b>	<b>19(100%)</b>	<b>11(100%)</b>	<b>30(100%)</b>	<b>100(100%)</b>

M ± 2SD = 47.4 ± 24.8 at 95% CI, M ± 2SE =47.4 ± 4.98

- In this study it was observed that maximum 52% of infection was confined to the age group of 41-60 years and the infection was more among males and male verses female ratio is 70:30.

Table-2: CRP levels of ICU Vs Non ICU Covid-19 patients

Sl. No.	CRP mg/l	No. of Covid-19 Patients		Total
		ICU	Non ICU	
1	< 6	1 (1.6%)	31 (77.5%)	32 (32%)
2	7-10	5 (8.3%)	5 (12.5%)	10 (10%)
3	11-20	33 (54.9%)	4 (10%)	37 (37%)
4	> 20	21 (34.9%)	0	21 (21%)
<b>Total</b>		<b>60 (100%)</b>	<b>40 (100%)</b>	<b>100 (100%)</b>

- High CRP levels was observed among ICU patients when compared to Non ICU patients significantly

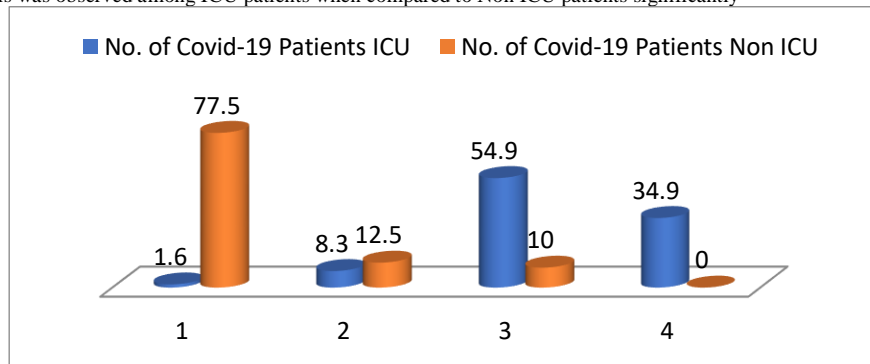


Fig 1: CRP levels of ICU Vs Non ICU Covid-19 patients

Table-3: LDH levels of ICU & Non ICU patients

Sl. No.	LDH U/L	No. of Patients in		Total
		ICU	Non ICU	
1	< 230	6 (9.9%)	16 (40%)	22 (22%)
2	231-450	32 (53.3%)	22 (55%)	54 (54%)
3	461-600	9 (14.9%)	2 (5%)	11 (11%)
4	> 600	13 (21.6%)	0	13 (13%)
<b>Total</b>		<b>60 (100%)</b>	<b>40(100%)</b>	<b>100(100%)</b>

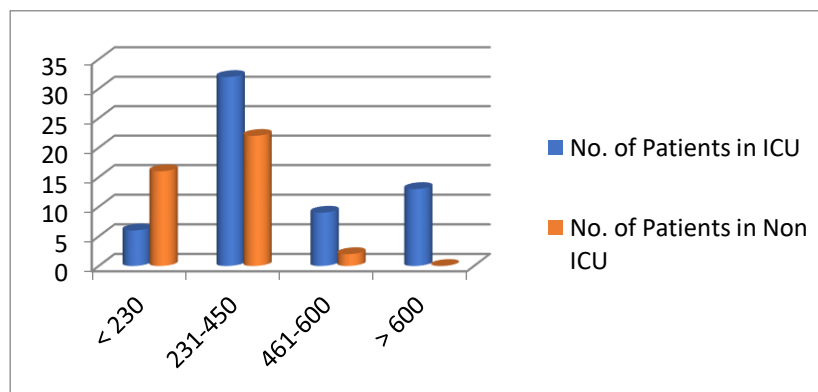


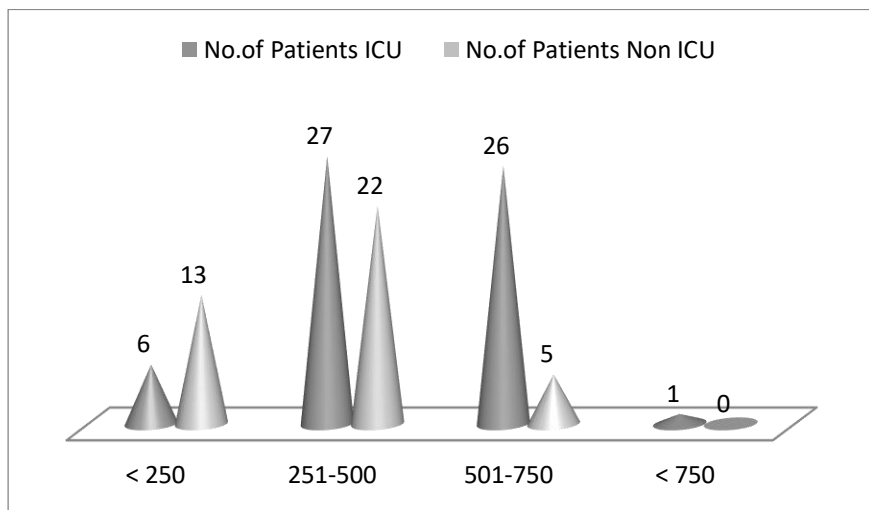
Fig 2: LDH levels of ICU & Non ICU patients

- High levels of LDH were observed among the both ICU & Non ICU admissions in this study

**Table-4: Serum Ferritin levels among ICU & Non ICU Covid-19 patients**

SI. No.	Ferritin ng/l	No. of Patients		Total
		ICU	Non ICU	
1	< 250	6 (9.9%)	13(32.5%)	19 (19%)
2	251-500	27 (44.9%)	22(55%)	49 (49%)
3	501-750	26 (43.3%)	5(12.5%)	31 (31%)
4	< 750	1 (1.6%)	0	1 (1%)
<b>Total</b>		<b>60(100%)</b>	<b>40(100%)</b>	<b>100(100%)</b>

- It was observed that maximum high levels of Serum Ferritin between 501-750 mg/l among ICU admissions of Covid-19 significantly with the P<0.01 when compared to Non ICU admissions



**Fig 3: Serum Ferritin levels among ICU & Non ICU Covid-19 patients**

**Table-5: IL6 Values among ICU Vs Non ICU patients of Covid-19**

SI. No.	IL6 pg/ml	No. of Patients		Total
		ICU	Non ICU	
1	< 15	22 (13.2%)	40 (100%)	62 (62%)
2	15.1-30	27 (16.2%)	0	27 (27%)
3	30.1-45	5 (3%)	0	5 (5%)
4	45.1-60	5 (3%)	0	5 (5%)
5	>60	1 (0.6%)	0	1 (1%)
<b>Total</b>		<b>60 (100%)</b>	<b>40 (100%)</b>	<b>100 (100)</b>

- In this study IL6 levels were also increased significantly among ICU patients when compared to Non ICU patients

**Table -6: D-Dimer Levels of ICU & Non ICU Covid -19 Patients**

SI. No.	D-Dimer Micrograms/ml	No. of Patients		Total
		ICU	Non ICU	
1	<500	0	6 (15%)	6 (6%)
2	501-1000	0	3 (7.5%)	3 (3%)
3	1001-2500	5 (8.3%)	13 (32.5%)	18 (18%)
4	2501-5000	15 (24.9%)	14 (35%)	29 (29%)
5	5001-10000	37 (61.6%)	4 (10%)	41 (41%)
	>10000	3 (4.9%)	0	3 (3%)
<b>Total</b>		<b>60 (100%)</b>	<b>40 (100%)</b>	<b>100 (100)</b>

- High D-Dimer levels between 2501-10000 mg/ml were observed among 86 % of ICU and 45% of Non ICU patients significantly.

**Discussion**

In our study it was observed that 70% of the study subjects were males and 30% were females which correlate with the figures of Jian-Min Jin et al study[15] in which males were 70.3% & females were 29.7% and also the infection was higher among males when compared

to females in Farhaan S et al study[16]. Further it is observed that in majority of the Covid-19 studies infectivity was high among males when compared to females. And in this study related to age maximum about 52% of the infection & admissions were belong to the age group between 41-60 years which means that the infectivity &

severity of the disease covid-19 was directly proportional to the increasing age. Similar finding was observed in study of Biswas M et al[17] where patients with the age  $\geq 50$  years were associated with increased risk of mortality when compared to the age  $< 50$  years. In also Md Abdul Berek et al study[18] where male cases and cases with an age of  $\geq 50$  years were severely affected by SARS Cov-2, and in Jian-Min Jin et al study[15] where severity & mortality was high among older age patients. Naila Shoaib et al study where high infectivity as well as severity was associated with increasing age and Bart G Pigils et al study[20] patients aged 70 & above were associated with higher infection rate, higher risk for severity, higher need for ICU and a higher risk of death. So it is understand that higher infectivity, severity, need for ICU admission and mortality was associated with older age patients of Covid-19 when compared to young age. Significantly in our study high CRP leves were observed among ICU patients when compared to Non ICU patients which correlates with the findings of the Furog Zeng et al study, Roshan kumar Mahat et al study, Wang G et al study, Huang I et al study, Guam HJ et al study, and Ji Pan MD et al study respectively. And also it was observed significantly that maximum high levels of Serum Ferritin between 501-750 among ICU admissions of Covid-19 with the  $P < 0.01$  when compared to Non ICU admissions which was comparable to the findings of Furong Zeng et al study, Roshan kumar Mahat et al study and high ferrin levels could predict severe disease and mortality in Wan G et al study and Huang I et al study. In this study IL6 levels were also raised significantly among ICU patients when compared to Non ICU patients. Chen R et al Ji Pan MD et al Roshan kumar Mahat et al and Furong Zeng et al were also associated with high IL 6 levels among severely affected patients and non survivors.

And it was observed that majority of the ICU patients (66%) in this study showed high levels of LDH i.e. between 251-600 U/L which was comparable to the figures of Guan WJ et al study[25] (41%) & Terpose E et al(40%). Basing on these findings we could understand that strong association of high LDH levels were observed among severely ill patients of Covid-19.

Further it was also observed that D-dimer levels were also increased abnormally with the high values between 5001-10000 mg/ml among ICU patients (86%) which indicates the need of anticoagulation therapy and which was also noticed by Aggarwal M et al in his study.

#### Conclusions and recommendations

As it was observed in the study that the high infectivity & severity was associated with the gender male & older age patients of both sex, it is important to focus on this high risk group towards early testing and timely measurement of inflammatory cellular indices which facilitates effective initiation of treatment.

It is remember today that timely measurement of the inflammatory cellular indices will help the treating doctor towards decision making for admission into hospital (ICU & Non ICU) to trigger the protective therapies like anticoagulation, steroids initiation with other supportive therapies and giving chance to monitoring of patients so that it is possible to improve the overall survival rate of Covid-19 patients in the hospital.

And it is necessary to educate the public regarding the importance of not only early testing of Covid-19 but also to undergo timely measurement of inflammatory biomarkers which allows the physician for better clinical evaluation in order to provide proper clinical care.

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