RESEARCH ARTICLE

THE STUDY OF EPIDEMIOLOGICAL, CLINICAL AND BIOCHEMICAL CHARACTERISTICS OF COVID 19 NON SURVIVORS IN A TERTIARY CARE HOSPITAL OF SOUTHERN INDIA

Dr. Greeshma Manu[1], Dr. Harshavardhan L.[2], Dr. Ravichethan Kumar A.N[3] and Dr. Suneetha D.K[4]

1. Resident, Department of General Medicine, Mysore Medical College and Research Institute, Irwin Road, Mysore, Karnataka.
2. Associate Professor, Department of General Medicine, Mysore Medical College and Research Institute, Irwin Road, Mysore, Karnataka.
3. Associate Professor, Department of General Medicine, Mysore Medical College and Research Institute, Irwin Road, Mysore, Karnataka.
4. Professor, Department of General Medicine, Mysore Medical College and Research Institute, Irwin Road, Mysore, Karnataka.

……………………………………………………………………………………………………....

Manuscript Info

…………………..

Abstract

………………………………………………………………………………

Background: Severe acute respiratory syndrome coronavirus 2, which causes COVID-19 pandemic has affected more than 90 million people and more than 1.9 million deaths. Despite extensive study, the prognostic role of various clinical, haematological and biochemical parameters remains unclear.

Objective: To study the epidemiological, clinical and biochemical characteristicsof covid 19 non survivors and to study the variations in vital parameters, hematological and biochemical parameters at the time of admission and before death.

Materials and Methods: Retrospective study, data was collected, from files of 100 COVID 19 nonsurvivors admitted in second peak of COVID in tertiary care hospital, MYSURU.

Results: The mean age was 59.48 and majority in age group of >61years. Sex preponderance was as follows males 66% and females 34%. The major comorbidities in our study subjects was hypertension in 43% and diabetes in 45%. 16% were alcoholics and 20% smokers. 91% patients presented with hypoxemia and 90% of the patients needed non-invasive ventilation by 5th day. 7 patients needed ICU admission. The maximum number of patients (40) had a hospital stay of 13 hours to 3days. There was significant tachycardia(122/minute), hypotension(90/60mmHg), tachypnoea(34/minute) with desaturation (78%) even with oxygen support in all 100 patients .Most of the patients had worsening trend in the mean values of TLC(10,688cells),NLR(12.5),thrombocytopenia(61,453/mm³),urea(1mg/dl),creatinine(2.35mg/dl),total bilirubin(2.18mg/dl), LDH(940mg/dl), d-dimer(2075ng/dl), ferritin(690mg/dl), and trop-T(49mg/dl).

Conclusion: In our study most of the patients hadrespiratory failure andcytokine mediated damage to other organs renal, hepatic, cardiac and haemorrhagic was also critical and hence should be monitored. The

Corresponding Author:- Dr. Ravichethan Kumar A.N
Address**:-** Associate Professor, Department of General Medicine, Mysore Medical College and Research Institute, Irwin Road, Mysore, Karnataka.

biochemical parameters and vitals at time of admission should be monitored frequently can be used as prognostic, predictive and risk stratifying factors of mortality.

………………………………………………………………………………………………….....

Introduction:-

Coronavirus disease 2019 was first reported in Wuhan city, Hubei, China, in the last week of December 2019[1].The disease reported in a cluster of atypical pneumonia cases and primarily transmitted through respiratory and body contact. Patients with coronavirus disease demonstrated a series of clinical symptoms, including raised body temperature, cough, headache, nausea, vomiting, anorexia, diarrhoea, dyspnea, multiple organ dysfunctions[2]. A large proportion of infected patients reported mild symptoms of the disease and recover. Some patients progressively develop serious complications, including sepsis, acute respiratory failure, metabolic acidosis, heart failure, kidney injury, hypoxic encephalopathy, and eventually die of the illness[3].

Considering the high transmission and infectivity patterns, World Health Organisation announced it as an emergency of public health concern on March 31, 2020[4]. In the initial phase of the disease outbreak, the mortality ranged from 2 to 5%, much higher in the elderly[3]. The mortality in coronavirus cases admitted in Wuhan city reached 7% in the outbreak's initial days. Early identification of severe illness risk factors can help clinicians facilitate appropriate remedial measures and help control mortality[5].

Earlier existing literature on laboratory-confirmed coronavirus cases reported changes in the patients' biochemical parameters, including lymphocyte count, neutrophil count, and D-dimer status. Another study reported changes in inflammatory markers in patients with COVID-19, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and Interleukin-6(1). Further, laboratory findings of COVID-19 deaths also demonstrated an increase in urea, cardiac troponin, creatine kinase, D-dimer, C-reactive protein (CRP), lactate dehydrogenase (LDH), IL-6, and lower level of lactic acid levels and lymphocytes.

The severity of illness is defined by WHO according to clinical management of severe acute respiratory infection. Critical illness is defined as patients with ARDS or sepsis with acute organ dysfunction. Severe illness is designated when patients have fever or suspected respiratory infection, plus one of the following, respiratory rate >30 breaths/min, severe respiratory distress or pulse oximeter oxygen saturation [2]

This study about the epidemiological, clinical and biochemical characteristics of COVID 19 non survivor patients was done so that , it may guide clinicians to identify severe cases initially and facilitate appropriate supportive management.

Method:-

This was a retrospective observational study conducted in K R Hospital, Mysuru. This study included COVID 19 positive non survivor patients admitted between August 2020 and August 2022 K R hospital in Mysuru, Karnataka. The demographic, clinical information, laboratory results, and treatment details of COVID-19 patients were collected from medical records department.

Sample size calculated using the formula $n = 4pq/d^2$ with 95% confidence interval and 5% level of significance of (Standard Deviation)=35.95 and absolute allowable error of 7%.The sample size is 100.

All patients in the age group of more than 18 years who were diagnosed with COVID-19 by the reverse transcription–polymerase chain reaction or rapid antigen testing method were included in the study.

Ethical approval

Ethical approval was obtained from Mysore medical college and research institute Ethics Committee and the ethical protocols of the declaration of Helsinki (1967) including the ethical principles of informed consent, voluntary participation and withdrawal, privacy and confidentiality, were followed.

Data analysis and statistics
Data obtained from the study has been entered in excel sheets and analyzed using SPSS(Statistical package for social sciences) software version 20. and has been presented as descriptive statistics in the form of frequency, tables, figures and graphs.

- Descriptive statistics of the explanatory and outcome variables were calculated by mean, Standard deviation for quantitative variables, frequency and proportions for qualitative variables.
- Inferential statistics like-
1) Chi-square test was applied for qualitative variables.
2) Independent sample t test will be applied to compare the quantitative variables between the groups. The level of significance is set at 5%.A 'p' value of <0.05 is considered statistically significant.

Results:-
Characteristics of Study Population-
The mean age of our study population was 59.48 and majority were in the age group of >61years. The sex preponderance was as follows males 66% and females 34%. The major comorbidities found in a significant proportion of our study subjects was hypertension in 43% and diabetes in 45%. There were 16% alcoholics and 20% smokers.

The duration hospital stay was as follows-
a) <30 minutes (6 patients)
b) 30 minutes – 12 hours (12 patients),
c) 13 hours- 3 days (40 patients),
d) 3 days- 10 days (35 patients)
e) >10 days (7 patients).
ICU requirement for the patients were as follows- on admission (7 patients), by 48 hours (28 patients) and by 72 hours (65 patients). 91% patients required oxygen at the time of admission.

Clinical Features at The Time Of Admission
Fever was seen in 76 %, fatigue in 25%, dry cough in 56%, sputum production in 7%, breathlessness in 75%, anorexia in 13%, chills in 5%, headache in 2%, myalgia in 22%, sore throat in 9% and altered sensorium in 4%.

FEVER 76%	**FATIGUE 25%**	**DRY COUGH 56%**	**SPUTUM PRODUCTION 7%**
BREATHLESSNESS 75%	**ANOREXIA 13%**	**CHILLS 5%**	**HEADACHE 2%**
MYALGIA 22%	**SORE THROAT 9%**	**ALTERED SENSORIUM 4%**	

Table 1:- Clinical

Vital Parameters
The vital parameters which included the mean values of pulse rate, systolic blood pressure, respiratory rate and oxygen saturation at the time of admission and before death were compared. There was a significant tachycardia, hypotension, tachypnoea and desaturation with oxygen support before the time of death.

VITALS	AT TIME OF ADMISSION	BEFORE DEATH	P VALUE
PULSE (beats/minute)	107.99 ± 14.55	122.6 ± 10.49	0.002
SBP(mmHg)	121.81 ± 10.49	97.55 ± 11.82	0.001
RR (cycles/minute)	28.33 ± 4.45	34.1 ± 3.09	0.001
SPO2 (%)	64.87 ± 15.53 at room air	78.4 ± 8.13 with oxygen support	0.002

Table 2:- Vitals.

Hematological and Biochemical Parameters
The hematological parameters included haemoglobin, total cell count, neutrophil percent, lymphocyte percent, neutrophil lymphocyte ratio (NLR) and platelets. There was a slight drop in the mean haemoglobin values of at the time of admission and before death. There was an increase in the mean total cell count with neutrophilia and lymphocytopenia with a raised neutrophil lymphocyte ratio (NLR) when compared at the time of admission and

before death. There was a significant thrombocytopenia observed before death when compared to the mean value pf platelet at the time of admission.

The biochemical parameters included renal function tests, liver function tests, random blood glucose, coagulation markers and inflammatory markers. The mean values of urea and creatinine showed a significant increase when compared with the values of at the time of admission and before death. The mean values of total bilirubin, SGPT, SGOT and ALP also showed an increment. Majority of the study subjects had a persistent increase in random blood glucose values. There was a raise in the mean values of PT INR and d dimer when compared with the values at the time of admission and before death. There was also a rapid increase in the before death mean values of inflammatory markers that included LDH, ferritin and trop- t when compared to that of at the time of admission.

Chi square test of independence indicated a significant correlation of the mean values of haemoglobin, platelets, urea, creatinine, total bilirubin, SGOT, SGPT, ALP, GRBS, PT INR , d dimer, LDH, ferritin and Trop T since the p values of the following parameters were <0.05.

PARAMETER	AT TIME OF ADMISSION	BEFORE DEATH	P VALUE
HEMOGLOBIN(gm/dl)	12.16 ± 2.09	10.11 ± 1.78	0.003
TLC (cells/mm³)	9644.7100 ± 4905.3375	10688.4500 ± 4665.4792	0.122
NEUTROPHIL %	84.66 ± 8.15	85.10 ± 8.47	0.693
LYMPHOCYTE%	11.54 ± 7.93	10.93 ± 7.78	0.590
NLR	11.15 ± 7.08	12.5 ± 9.77	0.240
PLATELET (cells/mm³)	191810.000 ± 73317.345	121604.5300 ± 61453.1482	0.002
UREA (mg/dl)	56.48 ± 35.99	91.00 ± 34.31	0.001
CREATININE (mg/dl)	1.77 ± 1.86	2.35 ± 2.28	0.001
TOTAL BILIRUBIN(mg/dl)	0.72 ± 0.54	2.18 ± 6.377	0.001
SGPT (U/L)	38.63 ± 27.89	61.62 ± 33.27	0.001
SGOT (U/L)	58.16 ± 35.95	77.24 ± 39.4	0.001
ALP (U/L)	112.76 ± 54.66	158.92 ± 68.89	0.001
GRBS (mg/dl)	211.33 ± 104.76	263.89 ± 105.40	0.001
PT INR	1.15 ± 0.23	1.25 ± 0.43	0.001
D DIMER (ng/ml)	1405.23 ± 1184.73	2075.59 ± 1800.33	0.001
LDH (U/L)	940.79 ± 905.66	1355.79 ± 1055.04	0.001
FERRITIN (ng/ml)	536.65 ± 437.40	690.88 ± 501.95	0.001
TROP T (ng/ml)	31.65 ± 21.48	49.26 ± 30.30	0.001

Table 3:- Laboratory Parameters.

Discussion:-
The purpose of this study was to study about the epidemiological, clinical and biochemical characteristics of COVID 19 non survivor patients admitted in KR Hospital, Mysuru.

This study had maximum number of patients in the age group of more than 60 years and the mean age was 59.48 years with a male preponderance of 66%. In the study conducted by Vinay Bharat et al (2) on COVID 19 non survivor patients, males were more commonly affected with most common age group being 51-60 years

This study shows that among 100 non survivor patients, 45% had diabetes mellitus and 43% had hypertension as comorbidities. In the study conducted by Sharavanan E Udayar et al (6) among 452 patients, (35.7%) had co-morbidities such as diabetes and (9.7%) had hypertension.

This study shows that the maximum duration of hospital stay among non survivors were 13 hours- 3 days. In a study conducted by Tamoghna Ghosh et al (3) the maximum duration of hospital stay was 2.4 days.

This study shows that the most common clinical presentations were fever (76%), breathlessness (75%), dry cough (56%) and fatigue (25%). In the study conducted by Anil Gurtoo et al (5), fever (51.1%), cough (49.4%) and

breathlessness (48.3%) were the commonest symptoms, and frequency of all the three increased with severity of COVID-19.

This study shows that all the vital parameters at the time of admission can predict the risk for mortality such as hypotension, tachycardia, tachypnoea, and desaturation. In the study conducted by Ahmed Sameer Ikram et al (7) the non-survivors demonstrated a significantly lower admission oxygen saturation (87%) and diastolic BP [70.79 mmHg], and high admission respiratory rate [24 breaths/minute].

This study showed a significant drop in haemoglobin, with increased total cell count, neutrophilia, lymphocytopenia and high NLR with thrombocytopenia. In the study conducted by MukeshBairwa et al (1) blood cell analysis showed that neutrophil counts were significantly higher in the non survivors (P <0.05)along with a decline in the lymphocyte count and platelet count (P<0.05).

This study shows a significant raise in the random blood glucose levels, renal function tests, liver function tests, coagulation profiles and inflammatory markers. In the study conducted by AnilGurtoo et al (5) significantly higher values of blood urea and creatinine values were observed in non survivor patients. The AST and ALT values were abnormal in 57-58% of non survivors with a significant P value of 0.003. In the study conducted by Tilak N et al it showed that there was a significant raise in D dimer, LDH, ferritin and trop t values in non survivor patients.

Conclusion:-
In this study it was observed that older age group and male patients with medical comorbidities were more likely to develop severe disease and even die from SARS CoV 2 infection.

In this study most of the patients had respiratory failure as the main cause of death but the virus itself and cytokine mediated damage to other organs renal, hepatic, cardiac and hemorrhagic was also critical and hence should be monitored.

For the pertinent diagnosis and treatment management of COVID 19 , the laboratory medicine plays a pivotal role. The SARSCoV2 infection is characterised by several biochemical and hematological alterations that help clinicians to clinch requisite clinical monitoring for an ameliorate clinical outcome .The biochemical parameters and vitals at time of admission can be used as prognostic, predictive, risk stratifying factors of mortality.

Limitations:
Our study comprised a relatively small sample size. Ever since, newer strains of virus have emerged with postulated differences in behavior, this study may not represent characteristic of the current and/or future strains of SARS-CoV-2. This again, stresses the need for continued research of such nature.

Funding:
None declared

Conflict of interest:
None declared.

Ethical Approval:
The study was approved by the Institutional Ethics Committee

References:-
1. MukeshBairwa et al in their study (Hematological profile and biochemical markers of COVID-19 non-survivors: A retrospective analysis)(Clinical Epidemiology and Global Health 11 (2021) 100770)
2. Vinay Bharat et al in their study(Comparison of Clinical, Haematological, Biochemical Findings and Significance of Co-morbidities amongst COVID-19 Positive Survivors and Non Survivors) (Journal of Clinical and Diagnostic Research. 2021 Apr, Vol-15(4): EC22-EC26)
3. Tamoghna Ghosh et al in their study (Impact of various hematological and biochemical parameters on mortality in coronavirus disease 2019 (COVID-19): A single-center study from North India) (Lung India • Volume 39 • Issue 3 • May-June 20220)

4. Matthew J Cummings et al in their study (Epidemiology, clinical   course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study) (Lancet 2020; 395: 1763–70)

5. Anil Gurtoo et al in their study (The Syndromic Spectrum of COVID-19 and Correlates of Admission Parameters with Severity-outcome Gradients: A Retrospective Study) (Journal of The Association of Physicians of India ■ Vol. 68 ■ December 2020)

6. Sharavan E Udayar et al in their study (Clinicoepidemiological profile of COVID-19 patients admitted at a teaching institute in a hilly area of India during the second wave—A retrospective observational study) (Journal of Family Medicine and Primary Care, Volume 11 : Issue 5 : May 2022 , 2172-8)

7. Ikram and Pillay et al in their study((Admission vital signs as predictors of COVID-19 mortality: a retrospective cross-sectional study)(BMC Emergency Medicine (2022) 22:68) https://doi.org/10.1186/s12873-022-00631-7

8. Li Q, Guan X, Wu P, et al. Early transmission dynamics in wuhan, China, of novel coronavirus–infected pneumonia. New England Journal of Medicine. 2020;382: 1199–1207. https://doi.org/10.1056/NEJMoa2001316

9. Kumar R, Singh V, Mohanty A, Bahurupi Y, Gupta PK. Corona health- care warriors in India: knowledge, attitude, and practices during COVID-19 outbreak. J Educ Health Promot. 2021;10(44):1–8. https://doi.org/10.4103/jehp.jehp_524_20.

10. Saxena S, Manchanda V, Sagar T, Nagi N, Siddiqui O, Yadav A, et al. Clinical characteristic and epidemiological features of SARS CoV-2 disease patients from a COVID 19 designated Hospital in New Delhi. J Med Virol 2021;6. doi: 10.1002/ jmv.26777

11. Marimuthu Y, Kunnavil R, Anil NS, Nagaraja SB, Satyanarayana N, Kumar J, et al. Clinical profile and risk factors for mortality among COVID-19 inpatients at a tertiary care centre in Bengaluru, India. Monaldi Arch Chest Dis 2021;91. doi: 10.4081/monaldi.2021.1724

12. Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, et al. Risk factors of critical and mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect 2020;81:e16–25

13. Sherwal BL, Makkar N, Jain A, Dogra V, Prasad S, Sachan A, et al. Trends and clinico-epidemiological profile of COVID-19 patients at a designated COVID-19 hospital in Delhi, North India. J Family Med Prim Care 2020;9:6261-6.

14. Salinas M, Blasco Á, Santo-Quiles A, Lopez-Garrigos M, Flores E, Leiva-Salinas C. Laboratory parameters in patients with COVID-19 on first emergency admission is different in non-survivors: Albumin and lactate dehydrogenase as risk factors. J Clin Pathol2021;74:673-5.

15. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet 2020;395:1054-62

16. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020; published online March 13. DOI:10.1001/ jamainternmed.2020.0994.