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RESEARCH ARTICLE

RETROSPECTIVE ANALYSIS OF BIOCHEMICAL AND HAEMATOLOGICAL PARAMETERS IN COVID-19 PATIENTS ADMITTED TOINTENSIVE CARE UNIT (ICU) IN A TERTIARY CARE HOSPITAL IN MIZORAM, INDIA

Belinda L.Vangchhia, SairengpuiiHnamte, Jitendra K. Chaudhary, J.C Zothanzauva, LalrinawmiHrahsel, Lalremruati and Nirensingh Koch

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Abstract

Background: This study aims to assess the effects and significance of both biochemical and haematological parameters on COVID-19 patients admitted to the intensive care unit (ICU) during the peak second wave of the infection (May to August 2021) in a designated COVID-19 hospital in Mizoram, India.

Methods: All existing data on COVID-19 patients admitted during the period of May to August, 2021 was collected from Medical Record department of Zoram Medical College/ State Referral Hospital (ZMC/ SRHF), Falkawn, Mizoram.

Results: Out of one hundred eighty-seven (N = 187) COVID-19 positive ICU patients admitted to Zoram Medical College/ State Referral Hospital (ZMC/ SRHF),Falkawn from May to August, 2021, 111 (59.4%) were males and 76 (40.6%) were females of which 125 (66.8%) patients died while 62 (33.2%) survived. Mortality rate was comparatively higher in male patients (41.7%) than in female patients (25.1%). Majority of patients belonged to the elderly aged group (65 years and above) with 70 (37.4%) cases and no patients belonging to children age group (below 18 years) were admitted to ICU. Statistical significance was observed in haematological parameters like total RBC and WBC (monocytes, polymorph/neutrophils, leucocytes) count, platelet count, erythrocyte sedimentation rate (ESR), neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR). In addition, clear significance was also noted in immunological parameters like C-reactive protein (CRP), blood glucose and biochemical parameters like serum creatinine, blood urea and aspartate amino transferase (AST).

Conclusion: Our findings suggest the vitality of closely monitoring biochemical parameters like kidney and liver function tests (blood urea, serum creatinine, potassium, bilirubin, albumin, direct and indirect conjugated bilirubin, SGOT/ AST), CRP and haematological tests like total RBC, WBC, platelet counts, ESR, NLR and PLR to enhance immediate clinical interventions. Prognosis of these parameters and prompt treatment can potentially aid in further delay towards the onset of several other severe symptoms and may lead to eventual cure.

Corresponding Author:- Nirensingh Koch

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Introduction:-

The ongoing COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) often lead to serious life-threatening cases requiring intensive care (Li et al., 2020). In a number of instances, patients affected by the virus succumb to the infection resulting in demise even after provision of extensive critical care (Bairwa et al., 2021). COVID-19 is highly infectious and the infection promptly spread throughout the world, the World Health Organization (WHO) announced COVID-19 asPublic Health Emergency of International Concern (PHEIC)on 30thJanuary, 2020 and was declared a global pandemic on 11thMarch, 2020 (WHO, 2020). This global pandemic has posed a severe threat to the well-being of individuals worldwide and is associated with increased mortality and morbidity (Swetha et al., 2022). During the course of COVID-19 disease, various clinical features and continually changing laboratory parameters undergo to make the disease more deadly (Ketenci et al., 2022). COVID-19 has continued even till date, has extended its second & third wave, with an upsurge in the infection rate and has been affecting the lives of millions of people worldwide (Wang et al., 2020). On 27thJanuary 2020, COVID-19 first case in India was detected in Kerala and it rapidly scattered throughout the country (WHO, 2020).

In Mizoram, the peak second wave of COVID-19 was witnessed during the months of May to August 2021 which was later identified to be caused by the SARS-CoV-2variant B. 1.617. During these months, highest rates of hospitalization was witnessed with several patients exhibiting severe symptoms leading to eventual admission to ICU. The most common symptoms in ICU patients include recurrent fever and cough, chills, sore throat, headache, shortness of breath, sepsis and acute respiratory distress often resulting to multiple organ failure eventually leading to mortality (Kumar et al., 2021). Several studies found that advanced age, male gender and co-morbidities including renal disease, malignancy, immunodeficiency, cardiovascular diseases, chronic lung disease, coronary artery disease, diabetes, systemic hypertension and obesity were the risk factors associated with COVID-19 mortality (Ghany et al., 2020, Kumar et al., 2021, Bairwa et al., 2021). Early diagnosis and prompt management can substantially reduce morbidity and mortality (Swetha et al., 2022).

The disease is diagnosed through laboratory tests, clinical symptoms, epidemiological history and radiological investigations (Letelier et al., 2021). For better understanding of the pathogenesis of COVID-19, it is significant to investigate laboratory parameters including haematological, biochemical, and serological abnormalities during SARS-CoV-2 infection (Leticia et al., 2020). The virus generates a systemic inflammatory response that leads to the release of different mediators and activate the immune response. Therefore, results in changes in the levels of various biochemical and haematological parameters (Mallappa et al., 2022). Due to the different nature of the virus, various medication options have been explored (Mohandas et al., 2021). The remedial treatments used in the management of COVID-19 include antiviral drugs (remdesivir, lopinamir, ritonavir), antimalarial drug hydroxychloroquine and immunosuppressants(Yousefi e al., 2020).

Moreover, the infectivity rate of COVID-19 is alarmingly high and troublesome. In a close-knit society as seen in Mizoram, the contagiousness proves to be more hazardous. The spread in a smaller community eventually often leads to the spread in the next locality and so on. In fact, Mizoram remained the state with the 2nd highest Covid cases in India for quite a length of time. Also, the public health system in the state is still in the developing phase with various ways for improvement. In such instances, the importance of rapidly analyzing biochemical and haematological parameters arises, in a way that clinicians may be assisted in understanding the in-depth condition of patients before the onset of more complicated symptoms of the disease and its simultaneous association with several other co-morbidities (Wang et al., 2020, Bairwa et al., 2021).

This study serves as the first of its kind in the state of Mizoram, where in-depth statistical analysis of available laboratory data including immunological, biochemical and haematological parameters in correspondence with clinical symptoms are evaluated. It aims to understand the demographic and clinical characteristics of patients admitted, treated and discharged from Zoram Medical College/ State Referral Hospital (ZMC/ SRHF), Falkawn from May to August, 2021 infected with SARS-CoV-2 in ICU patients. As there is less study/research of COVID-19 or precise scientific documentation in Mizoram, this research will be helpful in impartingin-depth knowledge on COVID-19 to the society.In addition, the study design is in lieu with several previous studies where elevated results of certain biochemical tests like blood urea, serum creatinine, immunological test like C-reactive protein (CRP), blood glucose and elevated haematologicalprofiles like ESR with low lymphocyte count, have been proven to have major significance in disease understanding and provision of treatment by clinicians (Bairwa et al., 2021).

Materials and Methods:-

Data collection

Data was collected between the months of May, 2021 to August, 2021 which was during the peak second wave outbreak in Mizoram. All ICU patients' data was obtained from Zoram Medical College/ State Referral Hospital (ZMC/ SRHF), Falkawn, Mizoram which is the only COVID-19 designated hospital in the state.

Biochemical parameters like liver function tests (including total protein, globulin, bilirubin, albumin, aspartate amino transaminase (SGOT/AST), alanine transaminase (SGPT/ALT), direct conjugated and indirect unconjugated bilirubin, alkaline phosphatase concentrations), kidney function tests (blood urea, uric acid, serum creatinine, potassium, sodium), and immunological parameters like C-reactive protein (CRP) were tested and collected.In addition, haematological parameters like haemoglobin (HB) level, blood grouping, complete blood count (CBC) including red blood cells (RBC) count, white blood cells (WBC) count, DLC, polymorph/ neutrophil, lymphocyte, eosinophil, monocyte, basophil, platelet count, and erythrocyte sedimentation rate (ESR) were tested and collected from ICU patients. All these parameters were taken into consideration for correlation and comparison with respect to the mortality of the patients i.e., discharge status (Alive/ Dead). The status of patient during discharge also corresponds to the severity of the disease in the ICU patients.

Statistical Analysis

Different statistical approach was used for analysis of collected data and was interpreted by SPSS Statistics 25 tools. The mean of different haematological, immunological and biochemical parameters was compared between two groups (Aliveand Dead group) by using independent t-test. Data were expressed and presented as mean standard deviation (±SD) and p value ≤ 0.05 was selected as the threshold of significance.

Chi-square test of significance is used in this study to reveal that there is statistical significance between (discharge status i.e. Alive or Dead) and (Profile list) ($P<0.05$) at 95% Confidence Level. Hence this suggest that there is association/ dependence between discharge outcome and the different profile list. Conversely,no statistical significance between (discharge status) and (Profile list) ($P>0.05$) at 95% Confidence Level suggests that there is no association/ dependence between discharge outcome and the following (profile list).

Monte-Carlo Exact Test is also used to find statistical significance for tables not fulfilling Chi- square test criteria. Result of Monte-Carlo Exact Test reveal that that there is statistical significance between (discharge status) and (Profile list) ($P<0.05$) at 95% Confidence Level. This in turn suggestthe association/ dependence between discharge outcome and different profile list. Conversely, no statistical significance between (discharge status) and (Profile list) ($P>0.05$) at 95% Confidence Level indicates there is no association/ dependence between discharge outcome and the different profile list.

To compare the means of various parameters between the two groups- Alive and Dead, an independent t-test is conducted. In Levene's Test for Equality of Variances Sig values, if Sig > 0.05, it means Equal variances assumed i.e.,there are equal variances between the two groups- Alive and Dead. Hence, we look at Sig. (2- tailed) for Equal variances assumed in t-test for Equality of Means for finding statistical significance. In t-test for Equality of means, if Sig. (2-tailed) >0.05, it means there is no significant difference between the means for Alive and Dead. If Sig. (2-tailed) < 0.05, it means there is statistical significant difference between the means for Alive and Dead groups.

On the otherhand, in Levene's Test for Equality of Variances Sig values, if Sig < 0.05, it means Equal variances not assumed i.e., there are no equal variances between two groups- Alive and Dead. Hence, we look at Sig. (2- tailed) for Equal variances not assumed in t-test for Equality of Means for finding statistical significance. In t-test for Equality of means, if Sig. (2-tailed) >0.05, it means there is no significant difference between the means for Alive and Dead groups. If Sig. (2-tailed) < 0.05, it means there is statistical significant difference between the means for Alive and Dead groups.

Results:-

One hundred eighty-seven (N = 187) COVID-19 positive ICU patients admitted to Zoram Medical College/ State Referral Hospital (ZMC/ SRHF), Falkawn from May to August, 2021 were considered for the study. Out of this, 125 (66.8%) patients succumbed to their illness and died while 62 (33.2%) patients survived of which 111 were males and 76 were females. Of 111 male patients, 33 (29.7%) survived and 78 (70.3%) died. Of 76 female patients, 29

(38.2%) survived and 47(61.8%) died. There were more cases of male patients dying (41.7%) as compared to female patients' mortality (25.1%). Biochemical, immunological and haematological parameters or markers of 187 patients who were confirmed to have COVID-19 and met the criteria for admission to the ICU were divided to Alive and Deadgroup and compared for further statistical analysis.

In the present study, the majority of patients belonged to the elderly aged group i.e., the age group ranging from 65 years and above with 70 (37.4%) cases, followed by young adult (19 to 44 years) with 59(31.6%) cases and middle age (45 to 64 years) 58(31.0%) cases respectively. COVID-19 ICU patients were more commonly found to be males 111(59.4%) than females 76(40.6%) (Table 1).Using independent t-test, it is found that there is significant difference (-2.123(96), p =0.036) in age where mean age for Alive (M=52.19, SD=16.2130) is lower than Dead (M=61.039, SD=17.1183). The magnitude of the difference in the means (MD= -8.8485, 95% CI: -17.1235 to -.5735) is significant. Hence, it is found that there is a significant statistical difference in age between the two groups (Dead vs. Alive) as represented in Table 2.

Vaccination statuses between Alive and Dead groups were compared among unvaccinated, partially vaccinated and fully vaccinated. Among alive (N = 62) patients, 32 (51.6%) were not vaccinated, 23 (37.1%) received 1st dose and 7 (11.3%) were vaccinated with full dose. Meanwhile, out of 125 dead patients, 88 (70.4%) were unvaccinated, 27 (21.6%) were vaccinated with 1st dose and 10 (8.0%) were fully vaccinated. Hence, the mortality percentage in unvaccinated patients was higher (70.4%) compared to unvaccinated patients who survived (51.6%). Among dead patients, completely unvaccinated were highest in numbers compared to partially vaccinated and fully vaccinated (Table 1).

Haematological parameters

Table 3 represents the comparison results of hematological parameters between Alive and Dead groups. A significant difference in hemoglobin (HB) levels between Alive and Dead groups is observed. Using independent t-test, it is found that there is significant difference (p=0.05) in HB where HB mean for Alive (M=12.938, SD=2.017) is higher than Dead (M=12.255, SD=2.659). The magnitude of the difference in the means (MD= .682, 95% CI: -.0112 to 1.376) is significant (Table 2). Hence, there is statistical significant difference in HB between Alive and Dead groups.Our findings also state that using t-test, there is a significant increase in the platelet count mean values among Alive patients (M=261.56, SD=18.9317)compared to the Dead patients (M=215.22, SD=10.92988) with p=0.025. There is a significant difference in RBC count between Alive and Dead groups where RBC count for Alive (M=4.43, SD=0.588) is higher than Dead group (M=4.13, SD=0.893) with p value 0.008. Furthermore, our findings also showed that there is a significant increase in monocytes in Alive group (M=4.55, SD=2.302)compared with Dead group (M=3.74, SD=2.317) with p value of 0.026. The mean values of WBC showed statistically significant decrease in Alive patients (M=8898.387, SD=565.24) thanDead patients (M=14830.4, SD=1043.15)with p value of 0.000. Significantly decreased Differential Leukocyte Count (DLC) was observed in Alive (M=75.66, SD=12.151) compared to Dead group (M=82.35, SD=12.382) with p value of 0.001.

In addition, complete blood count analysis showed that neutrophilcounts were significantly decreased in Alive (M=2.42, SD=0.497) compared with Dead groups (M=2.62, SD=0.505), p value 0.013 and lymphocyte counts were found to be significantly increased in Alive (M=16.26, SD=10.499) thanDead group (M=12.20, SD=9.418) with p value of 0.008. Erythrocyte sedimentation rate (ESR) was found to be statistically significant with Alive group showing lower mean values (M=66.68, SD=3.687902) compared to Dead group with lower mean value (M=70.504, SD=2.741453) and p=value of 0.000.However, there was no statistically significant difference observed in eosinophils between the two groups i.e., Alive and Dead. Besides, our results showed that Neutrophil to Lymphocyte ratio (NLR) in Alive group (M=8.22, SD=7.715) was significantly lower than Dead patients (M=15.78, SD=18.271) with p value of 0.000 and subsequently, Alive patients (M=24.08788, SD=2.487391) showed a significantly lower Platelet to Lymphocyte ratio (PLR)mean value than Dead patients (M=36.59334, SD=3.692486) with p value of 0.000 (Table 3).

Inflammatory markers and Biochemical parameters

C-reactive protein (CRP) is an independent risk factor determinant in ICU COVID-19 patients. In our study, there was significant difference in CRP level between Alive and Dead groups with p value of 0.013, using Chi square test.In addition, blood glucose was found to have statistical difference between Alive group with lower mean value (M=151.0161, SD=10.0925) compared to Dead group with mean value (M=173.632, SD=8.1131) and p-value of 0.000 (Table 4). Kidney function test such as serum creatinine was found to be statistically significant using

independent t-test with p value 0.007and the mean is lower in Alive (M=1.163, SD=1.137) compared to the Dead group (M=1.808, SD=2.065). The magnitude of the difference in the means (MD= -.6451, 95% CI: -1.2007 to -.0895) is also significant. Hence, there is statistical significant difference serum creatinine between Alive and Dead groups (Table 2 and 4).

There is a significant difference in blood urea between Alive and Dead groups. Using independent t-test, it is found that there is significant difference (p =0.003) in blood urea wherein mean for Alive (M=41.69, SD=42.703) is lower than Dead (M=61.16, SD=40.650). The magnitude of the difference in the means (MD= -19.466, 95% CI: -32.135 to -6.798) is significant. In addition, significant difference is observed in potassium levels (p=0.006), wherein mean for Alive (M=4.068, SD=0.512) is lower than Dead group (M=4.339, SD=0.8007), with significant magnitude of difference in the means (MD= -.271, 95% CI: -.462 to -.0805) (Table 2 and 4). Hence, there is statistical significant difference in both blood urea and potassium values between Alive and Dead groups.There was no statistical difference in sodium between the two groups.

As represented in Table 4, Liver function tests such astotal bilirubin mean values were considerably lower in Alive group (M=0.676, SD=0.1771) than Dead group (M=1.149, SD=1.8138) and found to be statistically significant with p value of 0.042.Mean albumin levels were higher for Alive patients (M=3.377, SD=0.5123) compared to Dead patients (M=3.200, SD=0.6129) with p value of 0.039. Direct conjugated and indirect conjugated bilirubin were found to be significantly different between Alive and Dead groups with p value (0.041 and 0.036) respectively. Decrease in mean was found in Alive (M=0.302, SD=0.1079) than Dead group (M=0.692, SD=1.4923) in direct conjugated bilirubin, and also decreased in indirect conjugated bilirubin in Alive group (M=0.368, SD=0.1252) compared to Dead group (M=0.558, SD=0.7054). Furthermore, our results displayed that aspartate amino transferase (SGOT/AST) mean was significantly lower in Alive group (M=67.21, SD=5.09036) than Dead group (M=93.92, SD=7.40944) with p value 0.003. There was no significant difference in several Liver Function tests, namely total protein, globulin,alkaline phosphatase and alanine transaminase (SGPT/ALT) between the two groups (all p>0.05) (Table 4).

Table 1:- Percentage on Age-wise and vaccination status distribution of ICU patients with Alive or Dead outcome.

Age-wise and vaccination distribution of ICU patients with alive or dead outcome					
			Discharge Status		
			Alive	Dead	Total
AGE	Young adult (19-44)	Count	27	32	59
		Percentage within Discharge Status	43.5%	25.6%	31.6%
	Middle age (45-64)	Count	20	38	58
		Percentage within Discharge Status	32.3%	30.4%	31.0%
	Elderly age (65 and above)	Count	15	55	70
		Percentage within Discharge Status	24.2%	44.0%	37.4%
Total		Count	62	125	187
		Percentage within Discharge Status	100.0%	100.0%	100.0%
Vaccination status	Unvaccinated	Count	32	88	120
		Percentage within Discharge Status	51.6%	70.4%	64.2%
	Partially vaccinated (1st dose)	Count	23	27	50
		Percentage within Discharge Status	37.1%	21.6%	26.7%
	Fully vaccinated (2nd dose)	Count	7	10	17
		Percentage within Discharge Status	11.3%	8.0%	9.1%
Total		Count	62	125	187

	Percentage within Discharge Status	100.0%	100.0%	100.0%

Table 2:- Levene's test for equality of variances and independent t-test for equality of means representing both haematological and biochemical patients in Alive and Dead group of ICU patients.

Independent Samples Test										
		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	T	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Hospital Days	Equal variances assumed	1.344	.248	4.485	185	.000	6.301	1.405	3.529	9.072
	Equal variances not assumed			4.259	106.648	.000	6.301	1.479	3.368	9.233
HB	Equal variances assumed	6.679	.011	1.770	184	.078	.6825	.3855	-.0781	1.4431
	Equal variances not assumed			1.944	152.025	.054	.6825	.3511	-.0112	1.3762
RBC	Equal variances assumed	12.862	.000	2.343	184	.020	.29539	.12608	.04664	.54414
	Equal variances not assumed			2.688	168.021	.008	.29539	.10990	.07843	.51235
WBC	Equal variances assumed	15.742	.000	-3.466	185	.001	-6817.613	1967.217	-10698.676	-2936.550
	Equal variances not assumed			-4.643	160.996	.000	-6817.613	1468.270	-9717.166	-3918.060
DLC	Equal variances assumed	.172	.679	-3.500	185	.001	-6.691	1.912	-10.462	-2.919
	Equal variances not assumed			-3.523	123.856	.001	-6.691	1.899	-10.450	-2.931
Polymorph/Neutrophil	Equal variances assumed	.142	.707	-2.521	185	.013	-.197	.078	-.351	-.043
	Equal variances not assumed			-2.533	123.332	.013	-.197	.078	-.350	-.043
Lymphocytes	Equal variances assumed	.623	.431	2.669	185	.008	4.058	1.520	1.059	7.057
	Equal variances not assumed			2.573	110.730	.011	4.058	1.577	.933	7.183
Eosinophils	Equal variances assumed	1.118	.292	1.519	185	.131	.348	.229	-.104	.800
	Equal variances not assumed			1.325	87.703	.189	.348	.263	-.174	.870
Monocytes	Equal variances assumed	.054	.817	2.239	185	.026	.804	.359	.096	1.513
	Equal variances not assumed			2.244	122.483	.027	.804	.358	.095	1.514
Platelet Count	Equal variances assumed	.477	.491	2.266	185	.025	46.34052	20.45247	5.99046	86.69057
	Equal variances not assumed			2.120	102.821	.036	46.34052	21.86033	2.98481	89.69622
Neutrophil-Lymphocyte ratio	Equal variances assumed	16.118	.000	-3.119	185	.002	-7.559329	2.423469	-12.340517	-2.778141

	Equal variances not assumed			-3.967	181.498	.000	-7.559329	1.905541	-11.319191	-3.799467
Platelet-Lymphocyte ratio	Equal variances assumed	16.172	.000	-2.335	185	.021	-14.62946	6.26456	-26.98862	-2.27030
	Equal variances not assumed			-2.981	180.656	.000	-14.62946	4.90815	-24.31414	-4.94479
ESR	Equal variances assumed	.094	.759	-.818	185	.005	-3.827	4.680	-13.060	5.406
	Equal variances not assumed			-.833	127.839	.000	-3.827	4.595	-12.919	5.266
Blood Glucose	Equal variances assumed	.575	.449	-1.670	185	.097	-22.616	13.539	-49.327	4.095
	Equal variances not assumed			-1.747	137.139	.000	-22.616	12.949	-48.222	2.990
Total protein	Equal variances assumed	2.683	.103	.423	185	.673	.0622	.1472	-.2282	.3527
	Equal variances not assumed			.480	167.676	.632	.0622	.1298	-.1940	.3185
Albumin	Equal variances assumed	1.157	.284	1.964	185	.051	.1774	.0904	-.0008	.3557
	Equal variances not assumed			2.085	142.924	.039	.1774	.0851	.0092	.3456
Globulin	Equal variances assumed	3.991	.047	-1.538	185	.126	-.1821	.1184	-.4156	.0514
	Equal variances not assumed			-1.689	155.685	.093	-.1821	.1078	-.3950	.0308
Bilirubin	Equal variances assumed	11.467	.001	-2.046	185	.042	-.4730	.2312	-.9291	-.0168
	Equal variances not assumed			-2.888	128.717	.005	-.4730	.1638	-.7971	-.1489
Direct Conjugated bilirubin	Equal variances assumed	13.355	.000	-2.054	185	.041	-.3904	.1900	-.7653	-.0155
	Equal variances not assumed			-2.909	126.598	.004	-.3904	.1342	-.6559	-.1249
Indirect Unconjugated bilirubin	Equal variances assumed	9.729	.002	-2.109	185	.036	-.1907	.0904	-.3690	-.0123
	Equal variances not assumed			-2.930	139.099	.004	-.1907	.0651	-.3193	-.0620
SGOT/AST	Equal variances assumed	8.535	.004	-2.401	185	.017	-26.710	11.125	-48.659	-4.762
	Equal variances not assumed			-2.971	184.931	.003	-26.710	8.990	-44.446	-8.975
SGPT/ALT	Equal variances assumed	2.125	.147	-1.252	185	.212	-11.004	8.790	-28.345	6.336
	Equal variances not assumed			-1.510	183.588	.133	-11.004	7.288	-25.383	3.374
Alkaline Phosphatase	Equal variances assumed	3.727	.055	-1.653	185	.100	-42.156	25.510	-92.485	8.172
	Equal variances not assumed			-1.940	178.246	.054	-42.156	21.733	-85.043	.731
Blood Urea	Equal variances assumed	4.998	.027	-3.032	185	.003	-19.466	6.421	-32.135	-6.798
	Equal variances not assumed			-2.981	116.571	.003	-19.466	6.529	-32.398	-6.535

Serum Creatinine	Equal variances assumed	9.933	.002	-2.291	185	.023	-.6451	.2816	-1.2007	-.0895
	Equal variances not assumed			-2.751	182.973	.007	-.6451	.2345	-1.1078	-.1824
Sodium	Equal variances assumed	3.496	.063	.342	185	.733	.6074	1.7777	-2.8999	4.1146
	Equal variances not assumed			.461	157.050	.645	.6074	1.3174	-1.9949	3.2096
Potassium	Equal variances assumed	11.710	.001	-2.432	185	.016	-.2715	.1116	-.4917	-.0513
	Equal variances not assumed			-2.805	173.234	.006	-.2715	.0968	-.4624	-.0805

Table 3:-Haematological parameters with Mean, Standard Deviation (SD) and p-value representation among Alive and Dead group of patients admitted to ICU.

HAEMATOLOGICAL PARAMETERS			
Haematological parameters	Mean and Standard Deviation with respect to Discharge Status		p-value
	Alive (n = 62)	Dead(n = 125)	
HB	12.938(2.0172)	12.255(2.6594)	0.05
RBC	4.4346(0.58886)	4.1392(0.89397)	0.008
WBC	8898.387(565.24)	14830.4(1043.15)	0.000
DLC	75.66(12.151)	82.35(12.382)	0.001
Polymorph/Neutrophil	2.42(0.497)	2.62(0.505)	0.013
Lymphocytes	16.26(10.499)	12.20(9.418)	0.008
Eosinophils	2.52(1.880)	2.17(1.230)	0.131
Monocytes	4.55(2.302)	3.74(2.317)	0.026
Platelet Count	261.56(18.93177)	215.22(10.92988)	0.025
Neutrophil-Lymphocyte ratio	8.2298(7.715627)	15.7892(18.2719)	0.000
Platelet-Lymphocyte ratio	24.0879(2.48739)	36.5933(3.69248)	0.000
ESR	66.68(3.687902)	70.504(2.741453)	0.000

Table 4:- Biochemical parameters with Mean, Standard Deviation (SD) and p-value representation among Alive and Dead group of patients admitted to ICU.

BIOCHEMICAL PARAMETERS			
Biochemical parameters	Mean ± Std. Deviation with respect to Discharge Status		p-value
	Alive (n = 62)	Dead(n = 125)	
Blood Glucose	151.016(10.0925)	173.632(8.1131)	0.000
Total protein	6.68(0.7087)	6.62(1.0456)	0.673
Albumin	3.38(0.5123)	3.20(0.6129)	0.051
Globulin	3.34(0.6200)	3.52(0.8228)	0.093
Bilirubin	0.68(0.1771)	1.15(1.8138)	0.042
Direct Conjugated bilirubin	0.30(0.1079)	0.69(1.4923)	0.041
Indirect Unconjugated bilirubin	0.37(0.1252)	0.56(0.7054)	0.004
SGOT/AST	67.21(5.09036)	93.92(7.40944)	0.003
SGPT/ALT	45.45(4.4386456)	56.46(5.7799598)	0.133
Alk Phosphatase	184.48(14.10531)	226.64(16.53362)	0.054
Blood Urea	41.69(42.703)	61.16(40.650)	0.003
Serum Creatinine	1.16(1.1370)	1.81(2.0657)	0.007
Sodium	135.92(3.7604)	135.31(13.7277)	0.645
Potassium	4.07(0.5124)	4.34(0.8007)	0.006

Discussion:-

To race against COVID-19 disease, the correct analysis of biomarkers is essential in diagnosing the criticality of the disease, investigating the admission criteria of the patient, treatment standardization and patient care (Ketenci et al., 2022).In the fight against COVID-19 disease, the correct interpretation of biomarkers is very important in terms of diagnosing the severity of the disease, evaluating patient admission criteria, patient care, and standardization of treatment.In this study, the roles of haematological, immunological and biochemical parameters or markers were evaluated for improvement in the management of COVID-19 patients admitted to ICU irrespective of discharge outcome(Alive orDead). In the present retrospective study, the haematological and biochemical characteristics of COVID-19 ICU patients were compared between two distinct discharge status groups i.e. Alive and Dead.Various studies have revealed that males are at higher chance of developing complications of COVID-19 (Al-Bari et al., 2021). In this study, COVID-19 ICU patients were also more commonly observed to be males than females. This finding is consistent with other studies as reported by Usul and his coworkers and others (Usul et al., 2020, Al-Bari et al., 2021). This data can in turn be interpreted such that men maybe more susceptible to infection with COVID-19 than women due to genetic factors and biological variations in the immune system (Bwire 2020; Zhong et al., 2021).Early diagnosis of patients with a potential to cause severe COVID-19 helps to lower fatality rates (Qi et al., 2021).

With respect to age, elderly age group ranging from 65 years and above were found to be more susceptible to severity of the disease, thus eventually leading to mortality (Dead group). Our finding is in leu with several similar studies carried out in different where age is often a major contributing factor of disease outcome (Alive or Dead), wherein reports showed that severe COVID-19 patients were high aged group and had more comorbidities (Al-Bari et al., 2021, Bairwa et al., 2021). As can be understood, old age is commonly associated with a number of co-morbidities thus making the individual more susceptible to infections eventually leading to the severity of fairly new disease like COVID-19 which the body is not accustomed to. Thus, as supported by our study and other studies, elderly age should be considered as a crucial contributing factor for determining disease severity and outcome by clinicians (Bairwa et al., 2021. In addition, consistent with other studies, our findings implicate that vaccination seems to have an impact on disease outcome, with unvaccinated patients having higher mortality rate as compared to partially and fully vaccinated individuals, who have higher rate of survival (Cianci et al., 2023, Moghadas et al., 2020).

In this study, haematological findings showed that the Dead group had higher white blood cells (WBC) and neutrophil count. In contrast, the Dead group had lower lymphocyte count than Alive group. Our findings match earlier studies reported by Rachakonda and co-workers (Rachakonda et al., 2021). The present study also found a significant decrease in platelet count mean values in dead patients compared with alive patients. This result is further in agreement with previous studies (Ketenci et al., 2022). An elevated erythrocyte sedimentation rate (ESR) often indicates a negative impact on COVID-19 patients as it is associated with both renal and hepatic dysfunction, often leading to joint diseases such as osteoporosis (Stojan et al., 2013). Consistent with other findings, our study also showed elevated ESR readings in most ICU patients, with statistically higher mean value in Dead patients. A high neutrophil-lymphocyte ratio (NLR) at the admission time can be a good indicator for COVID-19 diagnosis (Ma et al., 2020). High levels of NLR and platelet-lymphocyte ratio (PLR) may serve as strong markers for worsening COVID-19 or each as independent markers of the disease severity (Lagunas-Rangel 2020; Huang et al., 2020, Yang et al., 2020). In our study, similar elevated findings of ESR, NLR and PLR in more severe patients (Dead group) was also found which is consistent with the study reported by Huang and his colleagues (Huang et al., 2020).However, in this study the mean values of eosinophils showed no statistical difference between the two groups.

In addition, CRP is known as an important infection biomarker of severe COVID-19 disease (Zhang et al., 2020). Significantly higher CRP values in ICU patients have been associated with severe and adverse progress of COVID-19 (Ketenci et al., 2022). Previous studies have published that CRP levels can be used in the initial diagnosis of pneumonia and therefore, higher CRP levels were related with severe pneumonia (Ling, 2020). CRP can be used as diagnostic criterion and also deliberate the prognosis and severity of COVID-19 (Luan et al., 2021).In our study, there was significant difference in CRP levels between the two groups i.e., alive and dead group. Our findings are consistent with the studies evaluated by Ketenci and co-workers (Ketenci et al., 2022), where elevated CRP levels were observed more commonly in dead groups compared to the alive discharged group. Higher levels of C-reactive protein (CRP), neutrophils and leukocytes, along with lower levels of platelets, albumin and lymphocyte counts were commonly identified, in lieu with our findings (Wu et al., 2020; Huang et al.,2020). Blood glucose was found

to be significantly higher in Dead group patients (20%) compared to Alive group (14.52%). In this study, it is interesting to note that patients with consistent elevated blood glucose levels did not necessarily have history of diabetes, have more severe prognosis which often resulted to mortality, similar to previous studies (Réa et al., 2023).

Among the biochemical parameters, kidney function tests such as blood urea, serum creatinine and potassium were found to be significantly higher among the dead/deceased group. Similar findings were shown in previous studies where COVID-19 infection had acute to severe adverse effects to the kidney (Wang et al., 2020, Swetha et al., 2022). However, there was no significant difference in sodium between the two groups. Liver function test such as SGOT/ AST were found to be significantly higher among the dead group, thus indicating more severe liver injury in the cohort. These findings are consistent with the earlier report on patients with COVID-19 (Bairwa et al., 2021). In the present study, other liver function tests including albumin, bilirubin, direct conjugated and indirect conjugated bilirubin also showed significant differences between alive and dead groups. Severe COVID-19 patients presenting with liver dysfunction have increased level of SGOT/ AST, SGPT/ ALT and bilirubin levels (Ciaccio and Agnello, 2020). There was no significant difference in total protein, SGPT/ ALT and alkaline phosphatase among the two groups. In summary, various biochemical parameters showed significant differences between alive and dead groups in the present study. The abnormalities or changes in these parameters suggests that COVID-19 disease may harm kidney, myocardial, liver/ hepatic and other human organs (Bairwa et al., 2021).

Limitations Of Study

Our study is carried out as a single-centre retrospective study with all the data obtained from the Medical Record department of ZMC/ SRHF, thus has to be interpreted with caution. It would be highly beneficial to conduct multicentric studies, especially with similar demographic and population centres like neighboring North Eastern States in India, to support our findings and provide deeper understanding to our interpretations.

Conclusion:-

This retrospective study analyzed the different laboratory parameters of COVID-19 ICU patients both in alive and dead groups, which may be useful in identifying critical factors for early provision of appropriate clinical interventions. Overall, this study presents that age, gender, diagnosis and interpretation of significant haematological data like HB, total RBC and WBC counts (polymorphs/ neutrophils, lymphocytes, monocytes, platelet count), DLC, ESR, NLR, PLR, and further biochemical and immunological data like blood urea, serum creatinine, potassium, bilirubin, albumin, direct and indirect conjugated bilirubin, SGOT/ AST, blood glucose and CRP are of immense value, and could be used to efficiently predict and guide clinical management of COVID-19 patients.The present research findings may potentially aid further as a referential scientific literature to serve the contemplative and prospective inquiry of COVID-19 in Mizoram.

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