Original Research Paper

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General Medicine

AUSTERITY OF COVID-19 BY CHEST COMPUTERIZED TOMOGRAPHY SCORES AND INFLAMMATORY BIOMARKERS

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ABSTRACT **INTRODUCTION:** Coronaviruses are important human and animal pathogens. At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in the Hubei Province of China. Accumulating evidence has suggested that inflammatory biomarkers and chest computerized tomography(CT) scores play a critical role in the progression of COVID-19. CT showing ground glass opacities (GGO) and consolidations serves as an important and effective method for the diagnosis and evaluation of severity of COVID-19. **AIM:** Analysis of chest computerized tomography scores with inflammatory biomarkers in COVID-19 patients. MATERIALS & METHODS:136 laboratory confirmed cases of COVID–19 subjected to nucleic acid amplification tests such as reverse transcriptase-quantitative polymerase chain reaction (RT-qPCR) were enrolled. They are divided into severe and non-severe groups. CT scanner (Toshiba Aquilion Prime 160; Toshiba medical systems, Japan) was used for examining all patients. Various semi quantitative and qualitative methods were used for biomarker assessment. RESULTS: Biomarker results mean ± SD were statistically significant between severe and non-severe for all biomarker parameters. CT scores and biomarkers were statistically significant for severe group of COVID-19.CONCLUSION: Elevated levels of biomarkers like D dimer, CRP, LDH, ferritin and IL-6 along with total CT severity scores are independent risk factors for poor prognosis in patients with COVID-19, which may be a core tool for early identification of severe cases and eventually reducing the morbidity and mortality of COVID-19.

KEYWORDS : COVID-19, CT scores, RTPCR.

INTRODUCTION:

Novel coronavirus infection first occurred in Wuhan, Hubei Province, China in December 2019[1] named as COVID-19 by World Health Organization (WHO) standing for coronavirus disease 20192 has spread rapidly throughout world. First case was reported outside Mainland China in Thailand on 11 January 2020[2].

Inflammatory responses play a critical role in the progression of COVID-19. Inflammatory responses triggered by rapid viral replication of SARS-CoV-2 with cellular destruction recruit macrophages and monocytes. They induce release of cytokines and chemokines which then attract immune cells and activate immune responses leading to cytokine storms and aggravations. Computerised Tomography (CT) is an important method of diagnosis and evaluation of severity of COVID-19. Most common patterns include ground glass opacities (GGO) followed by crazy-paving pattern and parenchymal consolidations. CT findings in patients with COVID-19 are associated with the course and severity of the disease. Assessment of laboratory and chest CT imaging features for the prognostic prediction in patients with COVID-19 will be helpful for a better understanding of disease pathophysiology, risk stratification and for early interventional plan-making which eventually reduce mortality. With this perspective present study was undertaken with an objective to investigate association between level of biomarkers, CT chest finding and COVID–19 disease severity to identify patients at risk of fatal complications.

MATERIALS & METHODS:

Total 136 COVID–19 patients admitted during period from November 2020 up to November 2022 in a tertiary care centre were included in present study as per inclusion & exclusion criteria irrespective of gender, ethnicity or duration of symptoms of underlying illness. Approval of Institutional Ethics Committee was taken prior to commencement of present study. Patients' information were collected from electronic and laboratory record on demography, clinical data with symptoms, comorbidity, disease severity, laboratory measurements and radiology imaging. Clinical disease severity scoring based on the criteria provided by Chinese Centre of Disease Control (CDC)[3] was applied to all cases and they were divided into two groups as

A) Group A (Severe) N=68: Disease presenting with dyspnoea, respiratory rate ≥ 30/min and SpO2 ≤ 93% on room air
B) Group B (Non-severe) N=68: Disease presenting with mild symptoms without dyspnoea, respiratory rate < 30/ min and SpO2 > 93 % on room air.

INCLUSION CRITERIA:

1. COVID 19 patients of age > 18 years of both gender with swab positive RTPCR result
2. Patients assessed by inflammatory biomarkers and chest CT scores

EXCLUSION CRITERIA:

1. Patients less than 18 years old.
2. Patients with significant artefacts on CT images

STATISTICALANALYISIS:

Data collected compiled in MS EXCEL Sheet 2019. Analysis of Data is done by SPSS Software Version 2.0. Qualitative data tabulated in the frequency and percentage form. Quantitative data tabulated in the form of Mean and Standard deviation.

OBSERVATION & RESULTS:

Table 1: Distribution of Cases according to Age

Sr. No.	Age group (Years)	Group A N (%)	Group B N (%)	Total N (%)
1	19 to 30	11 (8 %)	16 (12 %)	27 (20 %)
2	31 to 50	32 (24 %)	34 (24.5 %)	66 (48.5 %)
3	51 to 70	21 (15 %)	16 (12 %)	37 (27 %)

4	> 70	4 (3 %)	2 (1.5 %)	6 (4.5 %)
Total		68 (50 %)	68 (50 %)	136 (100 %)

Table 1 shows distribution of cases according to Age. Maximum patients in clinically severe group (Group A) were between the age group 31 to 50 years i.e. 32 (24 %) followed by 21 (15 %) patients in 51 to 70 years group. In clinically non severe group (Group B) also maximum patients i.e. 34 (24.5 %) were from age group 31 to 50 years

Table 2: Distribution of Cases according to Lobe involved

Sr. No.	Lobe	Group A Involved N (%)	Group B Involved N (%)	Total Involved N (%)
1	Right Upper Lobe(RUL)	25 (18 %)	16 (12 %)	41 (30 %)
2	Middle Lobe (ML)	39 (29 %)	20 (15 %)	59 (44 %)
3	Right Lower Lobe(RLL)	56 (41 %)	51 (38 %)	107 (79 %)
4	Left Upper Lobe(LUL)	28 (21 %)	19 (14 %)	47 (35 %)
5	Left Lower Lobe (LLL)	61 (45 %)	52 (38 %)	113 (83 %)

Table 2 shows distribution of Cases according to Lobe involved. In 113 (83 %) cases left lower lobe, in 107 (79 %) cases right lower lobe, in 47 (35 %) cases left upper lobe, in 59 (44 %) cases middle lobe and in 41 (30 %) cases right upper lobe was involved out of total. Proportion of involvement of lobes amongst Group A and B was almost similar

Graph 1: Distribution of Cases according to Lobe involved

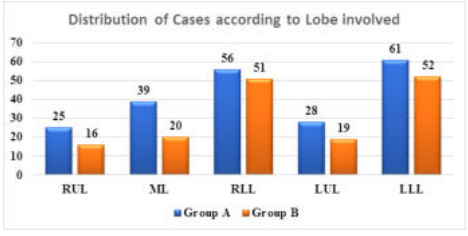
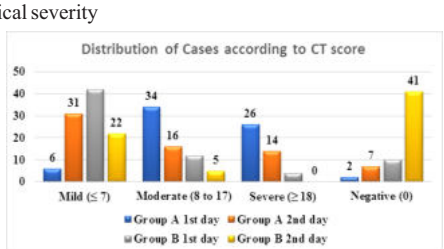


Table 3: Distribution of Cases according to CT score

Sr. No.	CT score	Group A		Group B		Chi square	P Value
		1st Day N (%)	7th day N (%)	1st Day N (%)	7th day N (%)		
1	Mild (≤ 7)	6 (4 %)	31 (23 %)	42 (31 %)	22 (17 %)	1st Day 58.9884 7th day 13.87	1st Day < 0.00001 7th day 0.00307
2	Moderate (8 to 17)	34 (25.5 %)	16 (12 %)	12 (9 %)	5 (3 %)		
3	Severe (≥ 18)	26 (19 %)	14 (10 %)	4 (3 %)	0 (0 %)		
4	Negative (0)	2 (1.5 %)	7 (5 %)	10 (7 %)	41 (30 %)		
Total		68 (50 %)	68 (50 %)	68 (50 %)	68 (50 %)	-	-

Table 3 shows distribution of cases according to CT score. In Group A on day 1 maximum patients i.e. 34 (25.5 %) CT score was Moderate (8 to 17) whereas in Group B on day 1 maximum patients i.e. 42 (31 %) CT score was Mild (≤ 7). In Group A on day 7 maximum patients i.e. 31 (23%) CT score was Mild (≤7). In Group B on day 7 maximum patients i.e. 41 (30%) CT score was negative (0). Result showed statistically significant (P< 0.00001) association between CT scoring and clinical severity



Graph 2: Distribution of Cases according to CT score

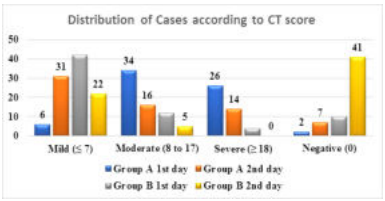


Table 4: Distribution of Cases according to Biomarkers result

Sr. No.	Biomarkers	Group A		Group B		Total Raised N (%)	t value	P value
		Raised N (%)	Mean ± SD	Raised N (%)	Mean ± SD			
1	D-dimer (mg/L)	59 (43 %)	2.02 ± 0.99	22 (16 %)	0.51 ± 0.38	81 (59 %)	-11.742	P < 0.0001
2	CRP (mg/L)	60 (44 %)	20.08 ± 6.97	21 (15 %)	6.37 ± 5.02	81 (59 %)	-13.162	P < 0.0001
3	LDH (U/L)	7 (5 %)	185.98	5 (4 %)	155.26 ± 33.5	12 (9 %)	-3 .573	P = 0.0005
4	Ferritin (µg/l)	20 (15 %)	231.10 ± 94.5	16 (12 %)	147. 35 ± 124. 05	36 (27 %)	-4.429	P < 0.0001
5	IL-6 (pg/ml)	42 (31 %)	7.99 ± 6.39	22 (16 %)	2.05 ± 1.04	64 (47 %)	-7.566	P < 0.0001

Table 4 shows distribution of cases according to biomarkers result. In Group A mean ± SD for D-dimer was 2.02 ± 0.99, for CRP was 20.08 ± 6.97, for LDH was 185.98 ± 62.49, for Ferritin was 231.10 ± 94.5 and for IL-6 was 7.99 ± 6.39. In Group B mean ± SD for D-dimer was 0.51 ± 0.38, for CRP was 6.37 ± 5.02, for LDH was 155.26 ± 33.5, for Ferritin was 147.35 ± 124.05 and for IL-6 was 2.05 ± 1.04. Results were statistically significant between Group A and Group B for all biomarker parameters.

Graph3: Distribution of Cases according to Biomarkers result

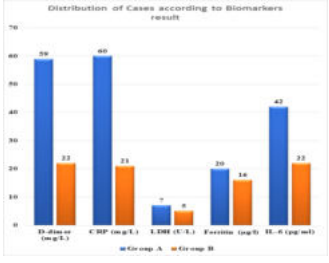


Table 5: Distribution of Cases according to correlation between Biomarkers result & CT severity

Sr. No.	Biomarkers	CT Severity				Total Raised N (%)	t value	P value
		Severe (N=30)		Non-Severe (N=106)				
		Raised N (%)	Mean ± SD	Raised N (%)	Mean ± SD			
1	D-dimer	29 (21 %)	1.96 ± 0.95	52 (38 %)	1.06 ± 1.014	81 (59 %)	-4.350	< 0.0001
2	CRP	28 (20 %)	20.40 ± 6.23	53 (39 %)	11.2 ± 8.85	81 (60 %)	-5.326	< 0.0001
3	LDH	7 (5 %)	207.43 ± 86.51	5 (4 %)	160.20 ± 30.84	12 (8.5 %)	-4.696	< 0.0001
4	Ferritin	4 (3 %)	223. 56 ± 110.82	32 (23 %)	179.50 ± 118.18	36 (27 %)	-1.827	0. 0700
5	IL-6	15 (11 %)	6.49 ± 6.39	49 (36 %)	4.60 ± 5.11	64 (47 %)	-1.688	0. 0937

Table 5 shows distribution of Cases according to correlation between Biomarkers result & CT severity. In CT severe group mean ± SD for D-dimer was 1.96 ± 0.95, for CRP was 20.40 ± 6.23, for LDH was 207.43 ± 86.51, for Ferritin was 223.56 ± 110.82 and for IL-6 was 6.49 ± 6.39. In CT non severe group mean ± SD for D-dimer was 1.06 ± 1.014, for CRP was 11.2 ± 8.85, for LDH was 160.20 ± 30.84, for Ferritin was 179.50 ± 118.18 and for IL-6 was 4.60 ± 5.11. Results were statistically significant between two groups for all biomarkers except for ferritin

Graph4: Distribution of Cases according to correlation between Biomarkers result & CT severity

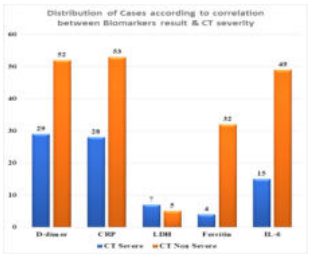


Table 6 : Distribution of Cases according to Mode of Oxygenation

Sr. No.	Mode of Oxygenation	Group A N (%)	Group B N (%)	Total N (%)
1	No supplemental O2	1 (1 %)	16 (12 %)	17 (13 %)
2	Nasal Prongs	38 (28 %)	35 (26 %)	73 (54 %)
3	NIV	18 (13 %)	10 (7 %)	28 (20 %)
4	Intubated	11 (8 %)	7 (5 %)	18 (13 %)
Total		68 (50 %)	68 (50 %)	136 (100 %)
Chi Square 16.53p-value0.0008				

Table 6 shows distribution of Cases according to mode of Oxygenation.73 (54 %) cases received O2 through nasal prongs and 28 (20 %) received through NIV whereas 17 (13 %) needed no O2 supplementation. 18 (13 %) cases were intubated. Result showed statistical significance (P=0.0008) which interprets that mode of O2 supplementation is dependent on clinical severity.

Graph5 : Distribution of Cases according to mode of Oxygenation

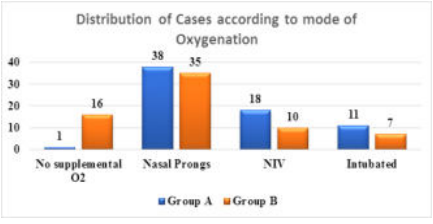
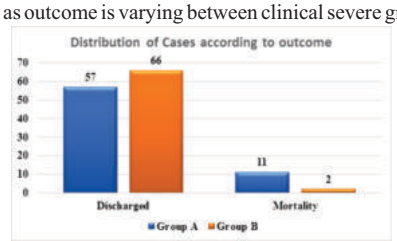


Table 7: Distribution of Cases according to outcome

Sr. No.	outcome	Group A N (%)	Group B N (%)	Total N (%)
1	Discharged	57 (42 %)	66 (49 %)	123 (91 %)
2	Mortality	11 (8 %)	2 (1 %)	13 (9 %)
Total		68 (50 %)	68 (50 %)	136 (100 %)
Chi Square 6.88p-value0.0086				

Table 7 shows distribution of Cases according to outcome. Majority of patients i.e. 123 (91 %) were discharged whereas mortality found in 13 (9 %) cases. Result showed statistical significance (P=0.0086) which is interpreted as outcome is varying between clinical severe groups.



Graph6: Distribution of Cases according to outcome

DISCUSSION:

COVID–19 caused by SARS-CoV2 progressed rapidly causing severe and fatal complications. Biomarkers profile containing D – Dimer, serum ferritin, CRP, IL-6, LDH found helpful in screening, categorization of patients, clinical management and prevention of serious complications. CT Chest and inflammatory biomarker was sent in every patient at the time of admission.

In present study maximum patients in clinically severe group (Group A) were between the age group 31 to 50 years i.e. 32 (24 %) followed by 21 (15 %) patients in 51 to 70 years group. In clinically non severe group (Group B) also maximum patients i.e. 34 (24.5 %) were from age group 31 to 50 years. In Group A maximum patients were male i.e. 49 (36 %) and in Group B males & female were in fairly same proportion i.e. 38 (28 %) & 30 (22 %) respectively.

Ahmed M. Magdy et al (2021)[4] in their study population included 266 patients (176 males, 90 females). Mean age was 34.75 ± 10.7 years. Average age of severe and critical cases was 41.23 ± 14.38 years which was significantly higher than that of non-severe cases 32.11 ± 10.51 years (P value 0.009).

Ghufran Aref Saeed et al (2021)[5] in their study found mean age as 44.2 ± 11.9 years (range 19–87 years). 769 were males (85.3%) and 133 were females (14.7%).

In present study in 128 (94 %) cases left lower lobe, in 124 (91 %) cases right lower lobe, in 112 (83 %) cases left upper lobe, in 105 (77 %) cases middle lobe and in 110 (80 %) cases right upper lobe was involved out of total. Proportion of involvement of lobes amongst Group A and B was almost similar. In present study in Group A in maximum patients i.e. 34 (25.5 %) CT score was Moderate (8 to 17) whereas in Group B in maximum patients i.e. 42 (31 %) CT score was Mild (≤ 7). Result showed statistically significant (P< 0.00001) association between CT scoring and clinical severity.

In similar study by Shuchang Zhou et al (2020)[6] found when selecting the chest CT images with peak severity from both groups, the total CT score of lung involvement was significantly greater in the deceased patients than that in the recovered patients as well as the CT scores for each of the five lung lobes (all P<0.001). The crazy-paving pattern and vacuolar sign on chest CT images were significantly more commonly observed in the deceased patients than those in the recovered patients (all P<0.05, except for the right lower lobe). By contrast, GGO and linear opacities were more commonly observed in the lower lobe of the bilateral lungs in the recovered patients. When comparing CT scores and imaging features at different disease stages of the two groups, the total CT severity scores were significantly greater in the deceased patients as compared with the recovered patients for the corresponding disease stage 1 to 3 (all P<0.001).

In present study in Group A mean ± SD for D-dimer was 2.02 ± 0.99, for CRP was 20.08 ± 6.97, for LDH was 185.98 ± 62.49, for Ferritin was 231.10 ± 94.5 and for IL-6 was 7.99 ± 6.39. In Group B mean ± SD for D-dimer was 0.51 ± 0.38, for CRP was 6.37 ± 5.02, for LDH was 155.26 ± 33.5, for Ferritin was 147.35 ± 124.05 and for IL-6 was 2.05 ± 1.04. Results were statistically significant between Group A and Group B for all biomarker parameters. In CT severe group mean ± SD for D-dimer was 1.96 ± 0.95, for CRP was 20.40 ± 6.23, for LDH was 207.43 ± 86.51, for Ferritin was 223.56 ± 110.82 and for IL-6 was 6.49 ± 6.39. In CT non severe group mean ± SD for D-dimer was 1.06 ± 1.014, for CRP was 11.2 ± 8.85, for LDH was 160.20 ± 30.84, for Ferritin was 179.50 ± 118.18 and for IL-6 was 4.60 ± 5.11. In Group A mean ± SD for D-dimer was 1.58 ± 0.9, for CRP was 14.6±5.58, for LDH was 155.98±51.69, for Ferritin was 190.86±73.45and for IL-6 was 6.1±4.48. In Group B mean ± SD for D-dimer was 0.41±0.31, for CRP was 5.3±4.12, for LDH was 140.83±30.31, for Ferritin was 134.44±109.4and for IL-6 was 1.7±0.82. Results were statistically significant between two groups for all biomarkers except for ferritin.

In similar study by Prakhar Gupta et al (2021)[7] out of 200 patients included in study 5 patients had isolated raised D –Dimer. It showed weak association with severe lung involvement. There was a significant association seen between raised values of both D –Dimer and Ferritin with severity of lung involvement. They also found that 14 patients had raised values of both D –Dimer and LDH and 71 patients had raised values of both D –Dimer and CRP. Both showed significant association. Results suggested that raised D- Dimer with Ferritin

showed strongest association with severity of lung involvement (based on HRCT chest) of disease when compared to combination of D –Dimer with other inflammatory markers like LDH, CRP or isolated D - Dimer. There were 121 patients with raised CRP, out of which 31 were having severe lung involvement and 90 had non-severe lung involvement. In contrast, there were 79 patients with normal CRP levels, of which 10 had severe lung. There was significant association between levels of CRP and severity of lung involvement.

In present study73 (54 %) cases received O2 through nasal prongs and 28 (20 %) received through NIV whereas 17 (13 %) needed no O2 supplementation. 18 (13 %) cases were intubated. Result showed statistical significance (P=0.0008) which interprets that mode of O2 supplementation is dependent on clinical severity. Majority of patients i.e. 123 (91 %) were discharged whereas mortality found in 13 (9 %) cases. Result showed statistical significance (P=0.0086) which is interpreted as outcome is varying between clinical severe groups.

Zhang et al(2020)[8] reported that the chest CT score was a reliable indication of the severity of systemic inflammation and had a favourable connection with inflammation indicators.

Qin et al(2020)[9] reported that certain CT features such as the distribution of lesions in the periphery and the crazy-paving pattern can help differentiate between COVID-19 pneumonia and non-COVID-19 pneumonia more effectively. The predictive significance of CT scores on the severity of this disease has not yet been investigated which we have tentatively identified the severity scores and CT imaging features as independent risk factors for the poor prognosis in COVID-19 patients.

CONCLUSION:

Our study shows elevated inflammatory biomarkers and moderate to severe CT scores are directly correlating with the clinical severity of COVID-19 infection hence providing valuable initial investigatory tool for early risk stratification, medical management and identification of morbidity and mortality in COVID-19 infection.

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