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COMPARISON OF INFLAMMATORY MARKERS WITH GLYCEMIC CONTROL AMONG COVID-19 PATIENTS

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ABSTRACT

SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2), is the virus that cause COVID-19 (coronavirus disease 2019), has become a major threat to the human society globally and has spread quickly became a pandemic. Several studies had been conducted about the inflammatory markers of covid-19. But strong evidence about the primary inflammation is yet to be understood. This study is aimed to compare the inflammatory markers with glycemic control among covid-19 patients. The cross sectional study was conducted with 130 participants in the age group 25-70 years. The participants were divided into 2 groups out of which, 62 COVID-19 positive individuals with HbA1C values less than 6.5 (< 6.5) were included in the group I and 68 COVID-19 positive patients with HbA1C ≥ 6.5 were included in the group II. The mean values of Ferritin, CRP, ESR, urea and uric acid were found to be elevated in the COVID-19 patients with HbA1c ≥ 6.5 (group II) when compared to the group I with HbA1c values < 6.5, but creatinine did not vary significantly among both groups. It is seen that the inflammatory marks like ferritin, CRP and ESR were found to be increased than normal in group I patients who are non-diabetic. This shows that the inflammatory marks may rise in COVID-19 patients. The renal function test which includes urea, creatinine and uric acid were under normal range in non-diabetics, but in diabetic individuals the levels were increased. Diabetic patients with higher

HbA1C levels are more prone to develop severe COVID-19, as a result of significant relationship of HbA1C with inflammatory markers like ferritin, CRP and ESR. Hence, additional care must be taken to treat COVID-19 positive diabetic patients with increased HbA1C values who are at greater risk to develop severe conditions.

Keywords: covid-19, HbA1c, Inflammatory markers, Diabetes mellitus

INTRODUCTION:

SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2), is the virus that causeCOVID-19 (coronavirus disease 2019), has spread quickly became pandemic **[1]**. In India the first wave started in September 2020, which decreased after many months. Later, in mid-March 2021 the second wave started and increased rapidly from April. 300 000 new infections were recorded after 10 consecutive days, then India reported just above 400 000 new COVID-19 cases on 1May, 2021 **[2]**. Several risk factors that can cause increased severity of COVID-19. Various data propose that COVID-19 is corporate in patients with cardiovascular diseases (CVD), diabetes, and hypertension with change in the prevalence rate in various studies, in which diabetes mellitus is found to be severe among them **[3]**. Persisted hyperglycemia might diminish immune responses, thus prompting patients to a condition of severe COVID-19and probable fatal outcomes **[4]**. Severe state of Covid-19 is assumed to be initiated by the release of cytokine that lead to organ failure by the respond of immune system mediated by inflammatory response. The liver to produce C-reactive protein (CRP) by the stimulation of interleukin (IL)-6 that is associated with the severe Covid-19 with the release of cytokine. In addition,ferritin also correlates with plasma IL-6 levels. Though injury to multiple organs can occur as a result of Covid-19, the lungs are the common site of injury, where the positive individuals with hypercoagulability have a chance to become micro thrombi or pulmonary emboli that leads to acute respiratory distress syndrome (ARDS) **[5]**. Hence, this study intended to find any relationship with HbA1c with inflammatory markers like ferritin, CRP, and ESR among COVID-19 positive individuals.

Aim:

To compare the inflammatory markers with glycemic control among covid-19 patients.

MATERIALS AND METHODS

The cross sectional study was conducted with 130 participants in the age group 25-70 years. The participants were divided into 2 groups out of which, 62 COVID-19 positive

individuals with HbA1C values less than 6.5 (< 6.5) were included in the group I and 68 COVID-19 positive patients with HbA1C≥ 6.5 were included in the group II.

Inclusion Criteria: Diabetic COVID-19 patients under the age group of 25-70 years.

Exclusion Criteria: Diseases that alter the inflammatory markers

All patients registered in the study were explained about the study. Under aseptic precautions, 3 ml venous blood sample was collected from antecubital vein after overnight fasting of 10-12 hours from all the subjects in a plain vaccutainer tube and EDTA tube. Analyses of inflammatory markers like ferritin by chemiluminesent immune assay method by siemens centaur CP adventitia, CRP by turbidometry method in AGAPPE, ESR by westerngren method using Sysmax ERBA, urea by urease method, creatinine by enzymatic method and uric acid by uricase method using BS 480 Mindray auto analyzes were carried out. HbA1C was estimated in BS 390 Mindrayauto analyzes by immunoturbidimetry method.

Data were analyzed using Statistical Package of Social Service (SPSS 22.0). Normally distributed datawith continuous variables were presented as Mean ± SD and the categorical variables were expressed as percentages. To compare the difference between the mean levels of parameters between the two groups Student's t- test was used. Pearson's correlation was done using statistical software. To indicate a significant difference a p value <0.05 was taken, for all statistical tests.

RESULTS

A total of 130 COVID-19 positive individuals were studied in which 62 subjects with HbA1c values < 6.5 (non-diabetic patients) were taken as group I and 68 subjects with HbA1c values ≥ 6.5 (diabetic patients) were taken as group II. The mean ages of group I and II were 47.9 ± 13.0 years and 56.0 ± 11.8years respectively with age range from 25-70 years.Among 130 subjects about73% group I and 52% group II were male and 27% group I and 48% group II were female, which shows that male are more prone to the COVID-19 diseases than female even if they are non-diabetic **(Table I)**.

The mean values of Ferritin, CRP, ESR, urea and uric acid were found to be elevated in the COVID-19 patients with HbA1c ≥ 6.5 (group II)when compared to the group I with HbA1c values < 6.5, but creatinine did not vary significantly among both groups **(Table II)**. It is seen that the inflammatory marks like ferritin, CRP and ESR were found to be increased than normal in group I patients

who are non-diabetic. This shows that the inflammatory marks may rise in COVID-19 patients. The renal function test which includes urea, creatinine and uric acid were under normal range in non-diabetics, but in diabetic individuals the levels were increased.

Pearson correlation analysis ofHbA1C (≥ 6.5) with serum Ferritin and ESR shows a strong positive correlation, and a weak positive correlation with CRP.(Table III)Though the inflammatory marks were raised in control the raise was more pronounce in case group, with significant relationship with the HbA1C.

Table I: Demographic features of the study group

Parameters	GROUP I (n= 62)	GROUP II (n= 68)
Mean age (MEAN ± SD)	47.9 ± 13.0	56.0 ± 11.8
Male %	73 %	52%
Female%	27 %	48%

Table II:Comparison of Mean ± SD of the Measured Biochemical Parameters between GROUP I AND GROUP II

PARAMETERS	GROUP I (n= 62)	GROUP II	p VALUE
HbA1c (%)	5.9 ± 0.3	8.0 ± 1.7	< 0.0001***
FERRITIN (ng/dl)	286.07 ± 151.7	782.3 ± 254.2	<0.0001***
CRP	2.8 ± 2.4	4.6 ± 2.8	<0.0001***
ESR	45.9 ± 23.9	51.2 ± 19.0	0.017**
UREA (mg/dl)	30.66 ± 13.03	36.65 ± 17.36	0.02*
CREATININE (mg/dl)	0.75 ± 0.63	1.13 ± 1.07	0.07
URIC ACID (mg/dl)	3.25 ± 1.54	4.14 ± 1.46	0.02*

Values are expressed in mean ± standard deviation.The values are statistically significant based on the p value.p value <0.05*, p value <0.01, p value <.001***, NS-Not Significant.**

Table III: Pearson correlation analysis between HbA1c (≥ 6.5) with inflammatory markers in subjects with COVID-19 positive individuals.

Parameters	HbA1c ≥ 6.5	p value
FERRITIN	0.686[a]	<0.0001***
CRP	0.453[a]	<0.0001***
ESR	0.680[a]	<0.0001***

The values are statistically significant based on the p value.p value < 0.05*, p value < 0.01, p value <.001***, NS-Not Significant**

[a]Positive Correlation; [b]Negative Correlation

DISCUSSION:

India stayed lucky by not being the first countries to be hit by COVID-19 but found to be one among the high-risk country for COVID-19. Though the number of case burden was small, India was expected to be at an increasedthreat for COVID-19 for severalcauses. A huge population,

particularly in urban locations, might intensify the extent of SARS-CoV-2. On other hand, the Indian population with increase in the amount of hypertension and diabetes mellitus (DM) especially when uncontrolled, found to have a raised chance of getting severe COVID-19 with increase death rates **[6]**. DM is the most common cause of COVID-19, with clinical manifestations of wide range from non-symptomatic infection condition to severe respiratory syndrome and even death **[7]**.

In the present study, the mean age in the group II was 56.0 ± 11.8 years as compared to 47.9 ± 13.0 years among the group I, in which the majority of the patients in both the groups were males (73 % group I and 52 %group II) compared with females (27 %group I and 48 % group II). This shows that males are more prone to develop COVID-19 compare to female independent to any age group. A study by Farhaan S. Vahidy *et al*, concludes that males are more likely to test COVID-19 positive and develop severe complications with increase hospital administration **[8]**.

In the present studyof Ferritin, CRP, ESR, urea and uric acid were found to be elevated in the COVID-19 patients with HbA1c ≥ 6.5 (group II) when compared to the group I with HbA1c values < 6.5, but creatinine did not vary significantly among both groups as per the Student's t-test (p value <0.05). However, in patients with < HbA1C in a group I group of COVID-19 patients the inflammatory markers were elevated. Another study by Michal Shauly-Aharonov *et al*, showed that pre and post blood glucose raise in COVID-19 positive individuals the complications severs **[9]**. A study by Rohit *et al*, showed that the inflammatory markers like CRP and ESR were significantly elevated in COVID-19 patients with HbA1C values > 6.5, in which the mortality rates were higher among these individuals **[10]**.

Another study by Furong Zeng *et al*, found that severity of COVID-19 is associated with increase in the rate of inflammatory markers. Where assessment of the inflammatory markers can be used to observe the condition of COVID-19 **[11]**.

Earlier studies states thatdiabetes results inpulmonary epithelial dysfunction, with increased permeability causing alveolar damage, and lung collapse. This condition result in abnormal immune function by damaging the tissues of spleen, lungs, and lymph node with reduced lymphocyte counts **[12]**. Hence, diabetes and COVID-19 together result in the increase injury to the respiratory and immune systems. Further, DM individuals have additional comorbidity

which may result in various organelle damage along with COVID-19 leading to hypercoagulability, severe inflammation and ultimately greater mortality rate **[13]**.

In the present study, showed that HbA1C (≥ 6.5) with serum Ferritin (r = 0.68) and ESR (r = 0.68) shows a strong positive correlation, but a positively weak correlation with CRP (r= 0.45), this was similar to the study by Zhenzhou Wang *et al*, first time reported that HbA1C positively correlated with ferritin , CRP and ESR **[14]**.

Therefore, there is a significant relationship between HbA1C and inflammatory markers like ferritin, CRP and ESR. Hence testing HbA1C in positive COVID-19 after admission is use full for assessing inflammatory markers in the patients.

CONCLUSION:

Diabetic patients with higher HbA1C levels are more prone to develop severe COVID-19, as a result of significant relationship of HbA1C with inflammatory markers like ferritin, CRP and ESR. Hence, additional care must be taken to treat COVID-19 positive diabetic patients with increased HbA1C values who are at greater risk to develop severe conditions. Testing of HbA1C in positive COVID-19 after admission is use full for assessing inflammatory markers in the patients.

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