



Correlation Of Pro-Inflammatory Markers With Renal Function Tests In Covid Positive Diabetic Patients.

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Abstract

Introduction: The pro inflammatory markers have a role to play in the prognosis of Diabetic patients along with that the role of several symptoms, comorbidities, inflammation and hypercoagulability markers are also related to the prognosis of disease and in morbidity of COVID-19 patients.

Materials and Methods: Basic biochemistry parameters were performed in fully automated biochemistry analyzer *ilab 650*. Whereas Parameters like IL-6 and ferritin were estimated in *cobas e411*. The selected subjects were divided into two groups. Group 1: Covid Positive patients admitted to hospital with known history of DM-II who didn't require ICU treatment. Group 2: Covid Positive patients with known history of DM-II admitted in ICU.

Results and Discussion: All parameters including basic biochemical and proinflammatory markers were significantly increased in covid positive diabetic patients with ICU admission when compared with Non ICU admitted diabetic covid positive patients. This is due to cytokine storm creating an environment in correlation with Diabetic metabolic alterations.

Keywords: Pro-inflammatory markers, cytokines, diabetes mellitus

Introduction

Corona virus disease 2019 a pandemic declared by WHO has been affecting lives of millions world wide. Though Initial studies found increased severity of coronavirus disease 2019 (COVID-19), caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in patients with diabetes mellitus. Furthermore, it has been reported that COVID-19 might also predispose the infected individuals to hyperglycaemia. Now simultaneously with other risk factors, hyperglycaemia might modulate immune and inflammatory responses, thus predisposing patients to severe COVID-19 and possible lethal outcomes (1).

Recently the Research evidences are growing towards the role of several symptoms, comorbidities, inflammation and hypercoagulability markers in relation to the prognosis of disease and in morbidity of COVID-19 patients. The incidence of diabetes mellitus, which is one of the leading causes of morbidity throughout the world has been shown to be high and is associated with disease progression in COVID-19 (2,3).

Patients who are at high risk of severe COVID-19 have several peculiar features which includes advanced age, sex, and have underlying health issues, such as cardiovascular disease, obesity and diabetes mellitus. Few reports have been seen that shows an underlying cardiovascular diseases (CVD) and Diabetes mellitus as predisposing factor common in

patients with COVID-19 who are admitted to ICU's (4-6).

Materials and Methods

This study was conducted in Department of Biochemistry, Pt.J.N.M. Medical College, Raipur and associated Dr.BhimRao Ambedkar Memorial Hospital, a dedicated covid center. A total of 60 Samples were estimated for different biochemical parameters. All covid 19 patients above 18 years of age were included in the study.

The blood samples were brought to department in vacutainers, where it was centrifuged and processed according to proper guidelines laid by departmental protocol committee for covid19 blood sample processing (based on WHO guidelines) .

Basic biochemistry parameters were performed in fully automated biochemistry analyzer *ilab 650*.

Whereas Parameters like IL-6 and ferritin were estimated in *cobas e411*.

Group 1: Covid Positive patients admitted to hospital with known history of DM-II who didn't require ICU treatment.

Group 2: Covid Positive patients with known history of DM-II admitted in ICU.

Results

Since both groups consist of diabetic patients random blood sugar followed by HbA1c becomes most important criteria to distinguish the severity. it has been seen in our study that group 1 subjects have slight low random blood sugar (RBS) value than group 2 but there is significant ($p > 0.005$) difference in HbA1c with respect to group1 and group 2.

Table 1. Data showing Blood Biochemistry Parameters in covid 19

Parameters	Normal Range	Group-1	Group-2
RBS (mg/dL)	70-110	142±34	205 ± 67
HbA1c (%)	<6.5	7.2 ± 0.4	8.5 ± 1.1
Urea (mg/dL)	10-40	45 ± 12	116 ± 19
Creatinine (mg/dL)	0.5-1.2	1.3 ± 0.2	5.6 ± 0.8
Na ⁺ (mmoles/L)	135-145	133 ± 2	124 ± 4
K ⁺ (mmoles/L)	3.5-5.5	4.2 ± 0.9	5.9 ± 1.5
Total Proteins (g/dL)	6-8	7.0 ± 1	5.6 ± 0.9
Albumin (g/dL)	3.5-5.5	3.6 ± 0.6	3.0 ± 0.4

Table 2. Data showing inflammatory markers in covid 19

S.No	Parameters	Group 1 (mean)	Group 2 (mean)	Normal Range
1.	IL-6 (pg/ml)	131±88.6	1379.55± 230.2	0-9
2.	Ferritin (ng/ml)	328 ± 51	783.31± 96.7	20-400

We have assayed IL-6 and ferritin in our lab and found following results (Table 2) :- Interleukin 6 is significantly ($p < 0.05$) increased in group 2 samples (1379.55± 230.2) when compared group 1 patients (131±88.6).

Ferritin was also increased significantly ($p < 0.05$) in group 2 (783.31± 96.7) with respect to group 1 (328 ± 51).

The other biochemical parameters (Table. 1) most prevalent laboratory findings were increased renal markers urea and creatinine in group2 (urea 116 ± 19 ; Creatinine 5.6 ± 0.8) with respect to group1 cases (urea 45 ± 12 ; Creatinine 1.3 ± 0.2)

For electrolytes, There were also significant increase in Sodium (133 ± 2) and potassium (4.2 ± 0.9) in group1 cases than in group 2 (sodium 124 ± 4 ; potassium 5.9 ± 1.5)

Discussion

Diabetic patients with COVID-19 are at high risk of severe pneumonia and present a marked pro-inflammatory and pro-thrombotic state compared to infected non-diabetic patients. Inflammation markers such as CRP, interleukin-6, ferritin and D-dimers are increased compared to non-diabetic patients while a marked inflammatory or cytokine storm is thought to be associated with a more pejorative prognosis (7).

The significant rise in ferritin, CRP and IL-6 levels reflect monocyte-macrophage activation resulting in inflammatory storm and cytokine storm. With its expression time longer than others, the cytokine IL-6 levels have been reported to be better predictors of disease progression (8).

IL-6 mediates monocyte differentiation to macrophages and enhances mononuclear cell infiltration to the inflammation loci (8). Moreover, synergistically IL-6 and TGF- β induces maturation of naive helper T cells (CD4+) to T Helper 17 (TH17) cells which are potential effectors against pathogens. Interestingly, IL-6 also hinders the Treg expansion by TGF- β (9,10).

Malaise, coughing, high fever, myalgia and goes to developing acute respiratory distress syndrome (ARDS), with underlying lymphopenia, coagulation disorders, haemophagocytic lymphohistiocytosis and mild to severe pneumonia were noted as co-morbid and in each and every clinical state, there was a decline in circulating iron and elevation in Ferritin, thus manifesting consequence disease severity and cytokine storm. Some of the condition that manifest very high ferritin levels are macrophage activation syndrome (MAS), adult-onset still disease (AOSD), catastrophic anti-phospholipid syndrome (cAPS) and sepsis; conditions that were identified as 'hyperferritinemic syndrome'. Both MAS and haemophagocytic lymphohistiocytosis (HLH) can

trigger mass cytokine release, known as cytokine storm, corollary of marked systemic infection such as Covid 19 SARS (11-14). In present study, similar pathway might have been instigated which leads to elevated ferritin levels along with other proinflammatory markers with respect to diabetes mellitus.

Conclusion

Diabetes mellitus is one of the most important metabolic disorder which has affected worldwide this along with Covid-19 has affected the world like none before, the role of biochemistry in diagnosis and prognosis has given a ray of hope in managing the Covid-19 patients with diabetes mellitus. The role of biochemical monitoring in the screening of COVID-19 cases has not been established. Severely affected patients are characterised by cytokine release syndrome. Laboratory parameters such as IL-6 and other markers of inflammation such as CRP, PCT, Ferritin, LDH, FDP and D-dimer can be used in monitoring severity of disease in Covid-19 patients all this also leads to further complicated situation in diabetic patients. Targeting proinflammatory markers may be useful in treating the cytokine storm in severely affected individuals.

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