



## IS COVID 19 PANDEMIC ADDING MORE OF DIABETIC POPULATION: A STUDY IN CENTRAL INDIA

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**ABSTRACT** **Background**– COVID 19 is associated with high prevalence of diabetes along with other comorbidities which also increase the severity and mortality risk in COVID 19 disease. Recently many studies have shown the association between COVID 19 and new onset diabetes. This study was done with objectives 1. To find out the incidence of new onset of hyperglycemia/diabetes in COVID 19 patients and 2. To develop screening policy for detection of new onset hyperglycemia in COVID-19 patients. **Materials And Methods**- This study is a hospital based observational cross sectional and prospective, cohort study conducted in the COVID ICU of Dedicated COVID Hospital, Bundelkhand Government Medical College, Sagar (M.P.) India, a teaching tertiary care centre. Out of 1562 COVID 19 positive patients admitted with moderate to severe pneumonia from JULY 2020 to JANUARY 2021, 487 patients were hyperglycemic at the time of admission. Patients were categorized into two subgroups: 1. Patients with previously confirmed diabetes or Prediabetes and 2. Hyperglycemia with no existing diabetes. Patients in this later subgroup were our follow up subjects for this study; their blood sugar level was monitored regularly during their stay in hospital & a correlation of COVID 19 and hyperglycemia was observed. **Results**- In present study Incidence of new onset hyperglycemia was 16.8%; 262 out of 1562. Of all 1562 patients admitted in hospital, 660 (44.7%) were found to be hyperglycemic. Among 660 patients, 436 (66.06%) patients were already known diabetic or pre-diabetic and 262 (16.8) were with newly onset hyperglycemia. 15 out of 262 (5.7%) patients were expired during their disease course, 157(60%) remained hyperglycemic while 90 (34.3) had attained normoglycemia without anti-diabetic drugs. **Conclusion**- COVID 19 disease is causative factor for new onset hyperglycemia /new onset diabetes.

**KEYWORDS :** Covid 19 Disease, Diabetes, New Onset Hyperglycemia, Moderate To Severe Pneumonia

### INTRODUCTION

Novel Corona virus disease (COVID -19 disease) was declared pandemic by WHO on 11<sup>th</sup> march 2020 after initial outbreak in Wuhan city of China. COVID 19 disease has very wide spectrum and ranges from asymptomatic to mild acute respiratory illness to severe pneumonia, ARDS, septic shock. Severity and prognosis of the disease is worse in elderly people, in those with any co-morbidity such as diabetes, hypertension, severe obesity, CKD, immunocompromised status etc. Francesco Rubino and colleagues described the bidirectional relationship between SARS CoV2 outbreak and diabetes [1-2]. It is well known now that diabetes is an independent risk factor for COVID infection and also associated with increased severity and poor prognosis in COVID patients [3-8]. On the other hand, recently many studies have shown that COVID 19 infection is associated with new onset hyperglycemia/diabetes, severe metabolic complications of preexisting diabetes [9-11].

The pathophysiology of new onset diabetes is not known precisely and is multifactorial but is centered on Angiotensin Converting Enzyme-2 (ACE-2) receptor. Corona viruses are enveloped virus with SS positive sense RNA glucose known to cause SARS CoV is made up of 4 structural proteins: spike(S), membrane(M), nucleocapsid(N) and envelope(E) protein. ACE-2 is main entry receptor for SARS CoV into the cell and is expressed in upper respiratory system, type I, type II alveolar epithelial cells in the lungs, the heart, endothelial cells, kidney tubular epithelium, enterocytes and the pancreas [12-16]. The localization of ACE-2 expression in the endocrine part of the pancreas suggest that SARS corona virus enters in pancreatic islets and cause their destruction leading to impaired Insulin secretion triggering acute onset hyperglycemia /diabetes [17-18]. High level of IL-6 and TNF- $\alpha$  in the patients with severe COVID-19 disease cause Insulin resistance, thus also contribute to glycemic impairment [19-21]. Acute damage to pancreatic  $\beta$ - cells by coronavirus may occur during systemic illness so we need to confirm that if the insult to islet cells during COVID infection is transient or has long term effect. Study by Jin kui yang in 2008 showed that immune-staining for ACE-2 protein was strong in pancreatic islets but weak in the exocrine tissue [18]. Steroids use & stress were well recognized for hyperglycemia but observations of

corona virus entry via ACE-2 receptor support the diabetogenic effect of COVID-19 [1].

**Rationale of this study** is that many research studies have observed the diabetogenic effect of COVID-19 infection. In our study we want to estimate the number of new onset diabetic people adding to already exponentially increasing diabetic population. Thus we can identify the affected individuals by screening of patients at risk for hyperglycemia at primary contact health centre.

### Hence The Objectives Of This Study Were:

- To find out the incidence of new onset of hyperglycemia/diabetes in COVID 19 patients.
- To develop screening policy for detection of new onset hyperglycemia in COVID-19 patients and their follow up to confirm the diagnosis of new onset diabetes.

### MATERIAL AND METHODS-

This study was a hospital based observational cross sectional and prospective, cohort study conducted in the COVID ICU of Dedicated COVID Hospital, Bundelkhand Medical College, Sagar (M.P.) India, a teaching tertiary care centre. The ethical permission was obtained from institutional IEC.

### Inclusion Criteria:

- Lab confirmed COVID 19 patients admitted to the hospital
- Patients with moderate to severe respiratory illness admitted in COVID hospital
- Those giving consent to participate in study.

### Exclusion Criteria:

- Lab confirmed COVID 19 patients not admitted to the hospital or who opt for home isolation
- Asymptomatic and mildly symptomatic COVID 19 positive patients admitted in HDU
- Those who were on long term steroids
- Those who did not gave consent

We analyzed all the COVID 19 positive patients 1562 admitted in

COVID hospital of DCH, Bundelkhand medical college, Sagar, a teaching Institute and tertiary care centre in Madhya Pradesh, India from JULY 2020 to JANUARY 2021. These patients were suffering from moderate to severe pneumonia. According to ICMR, definition of MODERATE disease is PNEUMONIA with no signs of severe disease; Adolescent or adult with presence of clinical features of dyspnoea and /or hypoxia, fever, cough, including SpO<sub>2</sub><94%(range 90-94%) on room air, respiratory rate ≥24 per minute. SEVERE PNEUMONIA is Adolescent or adult with clinical signs of Pneumonia plus one of the following: respiratory rate >30 breaths/min, severe respiratory distress, SpO<sub>2</sub> <90% on room air.

After admission in ICU, detailed clinical history was taken, general and systemic examination was done and each patient was subjected to measure **baseline RBS at the time of admission** (this is the key step of our study) and FBS next morning. Other blood investigations were sent as per hospital standard protocol including CBC, fasting plasma glucose, postprandial plasma glucose, HbA1c, LFT, RFT, serum inflammatory markers (LDH, CRP, ESR, Serum ferritin), Fasting lipid profile, d-Dimer, PT, INR. Chest x-ray was taken at admission and HRCT chest in selective cases. Patients were categorized on the basis of past history, RBS at the time of admission, next morning FBS & HbA1c into two subgroups: 1. Patients with previously confirmed diabetes (HbA1c ≥6.5%) or Prediabetes (HbA1c <6.5% but ≥5.6%) with hyperglycemia or normoglycemia 2. Hyperglycemia (RBS ≥140 mg/dl and/or FBS ≥110 mg/dl) with no existing diabetes (HbA1c ≤5.6%); patients in this later subgroup were our follow up subjects for this study. Of all 1562 patients admitted in hospital, 698 were found to be hyperglycemic. 38 patients were excluded from study as they were on long term steroids therapy. Among 660 patients, 436 (66.06%) patients were already known diabetic or pre-diabetic and 262 (16.8%) were with newly onset hyperglycemia that had impaired Random Blood Glucose but HbA1c <5.6% and these patients are our study group for follow up. Hyperglycemia was managed with intravenous Insulin infusion, subcutaneous pre-prandial and basal insulin as per individual patient's glycemic level. Of these 262 patients with hyperglycemia with no diabetes, 15(5.7%) patients were expired during their disease course. 247 (94.3%) patients were discharged from ICU and shifted to general ward for maintenance after clinical stabilization including optimum glycemic control where regular blood glucose monitoring and titration of insulin /OHA was done. After 10 days follow up of these discharged patients, 157 remained hyperglycemic while 90 had attained normoglycemia with no further need of anti diabetic treatment.

**RESULTS-**

Of all 1562 patients admitted in hospital, 660 were found to be hyperglycemic. Among 660 patients, 436 (66.06%) patients were found to be known diabetic or pre-diabetic and 262 (16.8%) were newly found hyperglycemic who has impaired RBS and/or FBS but HbA1c <5.6% and these patients are our study group. 15(5.7%) patients were expired during their disease course. 247 (94.3%) patients were discharged from ICU to general ward after clinical stabilization where regular blood glucose monitoring and titration of insulin /OHA was done. At discharge, 157 out of 66 remained hyperglycemic while 90 had attained normoglycemia without anti-diabetic drugs.

**DISCUSSION**

According to International Diabetes Federation (IDF), 425 million in the world live with diabetes as of 2017 and the number is only increasing. According to INDIAB study 10<sup>th</sup> October 2019, 72.96 million cases of diabetes in adult population of India. Most recent studies suggest prevalence rate of diabetes in India between 15-20% in urban area and half of it in rural areas with an average prevalence of ~9%. There is explosive increase in prevalence of T2DM in developing countries and India is next only to China. The prevalence of hyperglycemia in previous studies was 70.86% (321 out of 453 patients) in study by Li H et al [22-24], 40.19% (451 out of 1122 patients) in study by Bode et al [25] and was 49.4% (82 out of 166 patients) in study by Zhang et al [26]. In present study the prevalence of hyperglycemia in COVID infected patients at the time of admission was 44.69%; 698 out of 1562 cases were hyperglycemic at the time of admission. (Chart 1). COVID 19 is also proved to have independently diabetogenic effect on previously normo-glycemic people the result of which is increasing incidence of new onset hyperglycemia and in long term new onset diabetes. This is very serious issue of concern as COVID 19 is a communicable disease, if it will be proved to be a causative factor of new onset diabetes in long term then the burden of diabetes will be multifold as compared to present. In previous studies

the incidence of new onset hyperglycemia was 28.48% (129 out of 453 patients) in study by Li H et al [3], 22.90% (257 out of 1122 patients) in study by Bode et al [25] and was 12.6% (21 out of 166 patients) in study by Zhang et al [26]. In present study the incidence of hyperglycemia in COVID infected patients at the time of admission was 16.8%; 262 out of 1562 cases were found to be hyperglycemic without any prior history of Diabetes or prediabetes at the time of admission (Table 1). In a study by J K Yang et al [18] in 2008, out of 39 study cases of Severe Acute Respiratory Syndrome (SARS) 20 patients developed diabetes during hospitalization and after 3 year follow up only 2 of these patients had diabetes. In present study the long term fate of new onset hyperglycemic patient is yet to be studied.

**Limitations Of The Study**

This study was focused on patients admitted in ICU with moderate to severe pneumonia so we did not know about diabetogenic burden of COVID-19 in asymptomatic and mildly symptomatic population which accounts for about 80% of total COVID cases.

Long term follow up is needed to assess the course of new onset hyperglycemia in COVID 19 disease that if hyperglycemia is transient due to acute illness or leading to confirm diagnosis of Diabetes.

**CONCLUSION**

COVID 19 disease is causative factor for new onset hyperglycemia/new onset diabetes; therefore is adding on very significant number of diabetic patients to already increasing diabetic population all around the world. Early detection and optimum glycemic control of hyperglycemia in COVID patients will reduce the avoidable complications and improve the prognosis.

**Declarations**

**Ethics Approval And Consent To Participate**

All consents have been taken

**Consent For Publication**

Informed consent has been taken

**Availability Of Data And Materials**

Not applicable

**Competing Interests**

The authors declare that they have no competing interests

**Source Of Funding**

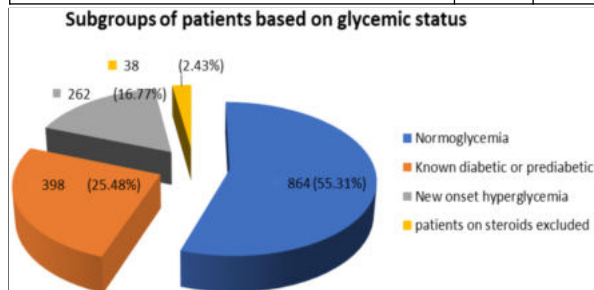
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**Table 1: Categorization Of Patients With Hyperglycemia In COVID 19 Positive With Moderate To Severe Pneumonia Admitted In ICU (n=1562)**

Hyperglycemia +/-	No.of patients	Perce ntage
Normoglycemia (RBS <140 mg/dl, FBS < 110 mg/dl, HbA1c ≤5.6%)	864	55.3%
Pre-existing Diabetes with or without hyperglycemia (HbA1c ≥6.5%)	436	27.9%
Hyperglycemia (RBS ≥200 mg/dl and/or FBS ≥126 mg/dl) without pre-existing Diabetes (HbA1c ≤5.6%)	262	16.8%
Total	1562	



**Chart 1: Categorization Of Admitted COVID 19 Positive Patients According To Glycemic Status (n=1562)**

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