Original Article

Impact of COVID-19 Pandemic on the Glycemic Status of a Large Cohort in Patients with Diabetes

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There is a general notion that glycemic control has deteriorated since the onset of COVID-19 pandemic. This study aimed to compare the glycemic status of a very large cohort of Persons with diabetes (PWD) prior to COVID-19 outbreak with that of a similar cohort post onset of the outbreak.

Materials and methods : In this retrospective study, entire data of glycated hemoglobin (HbA1c)% available in the hospital database from 3rd October, 2017 till 31st May, 2020 were collected and segregated into two cohorts namely on or prior to (ie, pre COVID-19) and after (ie, post COVID-19) 15th March, 2020 respectively.

Results : Total 20575 HbA1c values (12081 in the pre COVID-19 arm and 8494 in the post COVID-19 arm) were available for analysis. Mean (±SD) and Median HbA1c% in the pre COVID-19 arm (7.74±1.33, 7.5) was significantly (P<0.05) lower compared to those of the post COVID-19 arm (8.28± 1.9, 7.8). Such a difference was mainly driven by significantly higher numbers in the subgroup of HbA1c ≥10% (P<0.05). The Mean (±SD) and Median HbA1c% of the subgroups namely; males, females, age <65 years and age ≥65 years in the post COVID-19 arm (8.33±1.9, 7.8; 8.21±1.9, 7.7; 8.23±1.9, 7.7 and 8.13±1.8, 7.4 respectively) were significantly higher than the pre COVID-19 arm (7.73±1.3, 7.4; 7.75±1.2, 7.5; 7.72±1.2, 7.5 and 7.9±1.5, 7.6 respectively).

Conclusion : Onset of COVID-19 pandemic has adversely impacted glycemic control amongst PWD in general.

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***Key words* : COVID-19, Diabetes mellitus, HbA1c, Glycemic status, Hyperglycemia.**

The first cases of COVID-19 in India were reported on 30 January, 2020 in three towns of Kerala[1]. By March 11, 2020 the disease had spread in most countries and therefore was declared as a pandemic by the World Health Organization (WHO)[2]. Lockdowns started in different countries; in India it was announced in Kerala on 23 March and in the rest of the country on 25 March. The Ministry of Health and Family Welfare reported that due to scaling up of tests, which led to prompt identification and treatment, India's positivity rate had fallen to 8% by October, 2020[3]. The first case of COVID-19 in the state of Assam was registered on 31st March, 2020; a 52 year old person detected in Silchar Medical College[4].

The COVID-19 scenerio led to discontinuation in routine follow-up, treatment delays with treating physicians which were replaced by virtual consultations, except for emergencies. This situation mostly affected the people with chronic illnesses like diabetes, chronic kidney disease, hypertension etc[5-7]. Thus, the aforementioned lockdown situation brought restrictions to people's normal activities as only essential activities were allowed during the period[7,8]. Even outdoor exercise was restricted[9].

Editor's Comment :

- There are few indispensable factors like diet, exercise, stress management and treatment adherence for maintenance of glycemic status in patients with diabetes.
- The COVID-19 pandemic has posed a global threat, with collateral impact going beyond the direct outcome of infection, supposedly worsening the glycemic status of patients with diabetes in general.
- This study provides concrete evidence from a very large cohort of almost 20,000 patients' data. The findings of this study will serve as an important 'reference point' for impact of the COVID-19 epidemic on diabetes- both for our country and the whole world as well.

Diabetes is a metabolic condition which is in the increasing trend globally[10]. The predominant factors for management of chronic disease like diabetes includes life style modifications with proper diet and exercise and routine follow up visits with treating doctors. After the outburst of COVID-19 pandemic and social restrictions associated with it proper life style management was hindered, which is an important aspect to maintenance of glycemic status[11]. A report by the WHO, based on a survey in May, 2020 demostrated an interference in diabetes treatment in 155 Countries[6]. An earlier study in India reported that

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glycemic status worsened in diabetic patients after 3 weeks of lockdown[12]. Another study in Japan demonstrated a worsened glycemic status in terms of HbA1c values after declaration of state of emergency by the Government[13]. However, we have contrasting reports from different countries[14-16].

Hence aim of this study was to compare and analyze the values of HbA1c in a large cohort available in the hospital database during two specified periods; one prior to COVID-19 pandemic and another after the onset of COVID-19 pandemic.

Materials and Methods

In this registry based retrospective study, entire data of HbA1c since the day of commission of our hospital ie, from 3rd October, 2017 till 31st May, 2020 were included in the pre COVID-19 arm and HbA1c data from 1st June till 14th December 2021, were included in the post COVID-19 arm. Our institution became a Government registered COVID-19 care centre from 1st June onwards. Due to Government restrictions our hospital did not deal with any COVID-19 infected patient till 31st May, 2020. Hence, we took 31st May as our cut off for pre COVID-19 arm. The lowest cut -off for including an HbA1c value in either arm was kept at 6% so as to avoid biases like haemoglobinopathy, pre diabetic or non- diabetic status etc. Each arm was divided into 5 subgroups based on HbA1c categories such as (6 6 6.9) %, (7 6 7.9)%, (8 6 8.9)%, 9 6 9.9)% and ≥10%, and head to head comparison with regard to distribution of patients was performed between identical sub-groups from each arm. Additionally baseline characteristics and certain other attributes like sex and age (above and below 65 years) of the pre COVID-19 arm were compared with those of the post COVID-19 arm.

Microsoft Office Excel 2007[17,18] was used to perform descriptive statistical analysis, and to generate graphs and tables. Continuous measurements are expressed as Mean (±SD) and categorical measurements are expressed as percentages. Variance and mean difference were calculated to perform z- test for p value analysis using Microsoft Office Excel 2007.

Data of subjects were collected and used for the study after necessary permission from the hospital authority.

Results

HbA1c reports of 20575 subjects were included for final analysis; with 12081 in the pre COVID-19 arm and 8494 in the post COVID-19 arm. Mean age of the subjects in the pre and post COVID-19 arms were 53.7 and 54 respectively. Majority of subjects in the both the pre and post COVID-19-arms were males (58.45 and 61.43) % respectively.

Characterizations of Subjects based on Sex and Age of Pre and Post COVID-19 HbA1c status :

The Mean (±SD) and Median HbA1c (%) of male subjects, female subjects, subjects above and below 65 years of age and all subjects irrespective of age and sex in the post COVID-19 arm were significantly higher than the comparable categories of subjects in the post COVID-19 arm (Fig 1).

Sequential Hb1Ac Distribution of Pre and Post COVID-19 Subjects :

Analysis of the distribution of subjects into 5 sequential HbA1c subgroups such as (6 to 6.9)%, (7 to 7.9)%, (8to 8.9)%, 9 to 9.9)% and ≥10% revealed that there was a significantly higher proportion falling in HbA1c ≥10% sub group in the post COVID-19 arm (Fig 2). In the other sub-groups the difference between

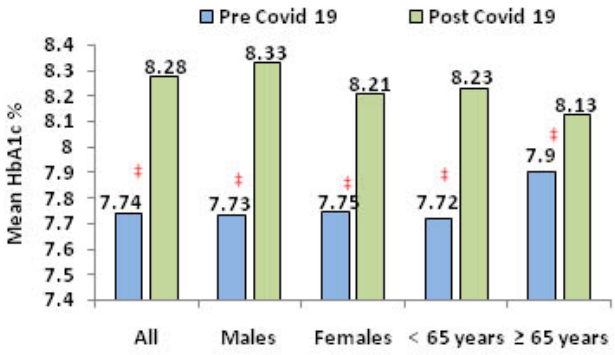

Fig 1 — Histogram showing the comparison of Mean HbA1c values in the pre and post COVID-19 sub-groups [all, males, females, subjects <65 years and ≥65 years. The difference of means in all the sub-groups was found to be statistically significant. (P<0.05). HbA1c, Glycated haemoglobin

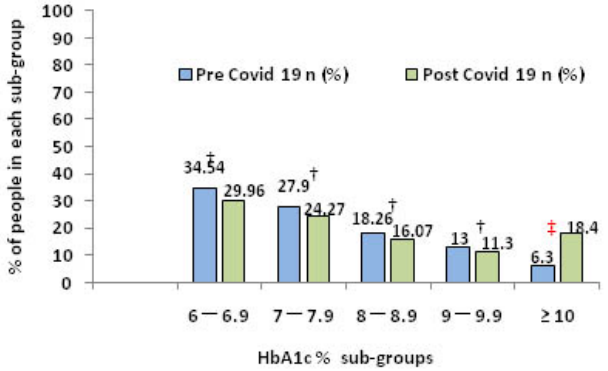

Fig 2 — Histogram showing the distribution of subjects in 5 different (6-6.9, 7-7.9, 8-8.9, 9-9.9 and ≥10) pre and post COVID-19 sub-groups based on HbA1c%. In the HbA1c ≥10 % sub-group, the distribution of subjects was statistically significant. P<0.05 is considered significant. ‡*p*=<0.05, †*p*=NS

pre and post COVID-19 arm were insignificant (Fig 2) After segregation of subjects based on sex and age (below and above 65years), or irrespective of age and sex, in both pre and post COVID-19 HbA1c >10% subgroup, we observed a statistically significant differential distributuion in all the groups ($p<0.05$) (Table 1, Fig 3).

Discussion

'Lockdown', an important decision taken globally to control and prevent the spread of COVID-19 disease, had an impact on glycemic control in diabetic patients as they weren't able to continue with their routine activities and follow up with physicians. Therefore, we conducted this study to evaluate the effect of COVID-19 pandemic related lockdown on glycemic status in PWD.

Our study used a huge data of subjects inclusive of pre (n=12084) and post COVID-19 (n=8490) diabetic patients. These subjects had HbA1c status of ≥6% segregated into 5 sub-groups who were attending a hospital in North East India from 3rd October, 2017 till 31st May, 2020. Higher Mean HbA1c values in the post COVID-19 subgroups suggested a correlation between poor glycemic status of subjects with COVID-19 pandemic (Fig 1). Possible reasons could be a discontinuity in the routine care of patients in the post COVID-19 period. Our study and others suggested that the lockdown situation worsened the glycemic status of PWD[12,13]. Most couldn't even continue with their daily exercise schedules as outdoor movement was restricted except for emergency situations[9]. It was also described by other researchers that the forced nationwide lockdowns could produce acute panic, anxiety and stress which may also lead to worsened glycemic status[19,20]. The pandemic situation became quite scary as there were deaths all over and most people preferred to stay at home rather than contract the disease.

Table 1 — *Total subjects in 5 different categories of HbA1c. Significance of each category is indicated in terms of p values*

HbA1c (%) category	Pre COVID-19 n (%)	Post COVID-19 n (%)	*P value*
6 - 6.9	4170 (34.54)	2542 (29.96)	0.3 (NS)
7 - 7.9	3368 (27.9)	2061 (24.27)	0.4 (NS)
8 - 8.9	2204 (18.26)	1365 (16.07)	0.2 (NS)
9 - 9.9	1565 (13)	959 (11.3)	0.4 (NS)
≥10	763 (6.3)	1562 (18.4)	< 0.05

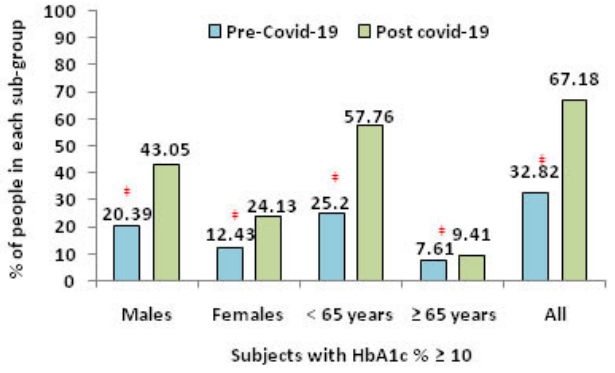

Fig 3 — Histogram showing the distribution of subjects with HbA1c >10% in the pre and post COVID-19 sub-groups based on sex [males, females, <65 years, ≥65 years and all irrespective of age and sex. ‡p=<0.05. HbA1c, Glycated haemoglobin

The segregation of subjects into 5 different subgroups based on HBA1c categories ie, (6 to 6.9)%, (7 to7.9)%, (8 to 8.9)%, (9 to 9.9)% and ≥10% gave us an opportunity to minutely look at influence of COVID-19 pandemic on trends of Hyperglycemia. Interestingly the trends in the lower HbA1c subgroups in the post COVID-19 cohort were not significantly different from the pre COVID-19 situation. In contrast, a clinically relevant and hugely impactful worsening trend was observed by way of significantly higher numbers in the HbA1c ≥10% sub group of post COVID-19 sub-group, irrespective of age and sex. (Table 1, Fig 2). Hence, it can be speculated that a COVID-19 pandemic had a global adverse impact on the glycemic control of diabetic patients. In other words, the above pattern of distribution of the subjects confirms that the glycemic status deteriorated during the COVID-19 pandemic leading to increased PWD in the highest HbA1c category in the post COVID-19 group. Thus, regular monitoring of HbA1c values, stringent treatment adherence with routine follow up visits with treating physicians and continued effort for lifestyle modifications with proper diet and exercise are important aspects for maintenance of glycemic status which was interrupted due to various factors during COVID-19 pandemic and associated lockdown.

Although we analyzed the pre and post COVID-19 glycemic status of PWD they were not exactly matched for age and sex distribution or presence or absence of comorbidities, ongoing treatments, socioe-conomic background, dietary and lifestyle factors etc. which may have significant bearing on the glycemic status. This remains a major limitation of our study. However, it would not have been possible to invite each and every patient who attended the hospital during pre COVID-19 period for evaluation during the pandemic. However the sheer number of available data for analysis represents two different situations namely; pre and post COVID-19 is definitely a strength of our study and justifies our effort to generate a hypothesis that COVID-

19 pandemic has adversely impacted the glycaemic status of diabetic patients in our country. This study provides some original data for reference with respect to COVID-19 pandemic situation in our country.

Conclusion

Onset of COVID-19 pandemic has adversely impacted glycemic control amongst PWD in general. Such an impact was seen in all sub categories irrespective of age and sex. Concerted effort with execution of alternative strategies for overall management of Diabetes Mellitus could possibly prevent such a worsening during the pandemic situation.

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