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Higher HbA1c was observed in young people with diabetes who fasted during COVID-19 pandemic lockdown of 2020 Ramadan in Bangladesh – A Post Ramadan survey

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ARTICLE INFO

Keywords:

COVID-19
Diabetes
Fasting
Ramadan
Pandemic lock down

ABSTRACT

Objective: Muslim people with T1DM should be actively discouraged from fasting during the COVID-19 pandemic, as diabetes has emerged as a significant risk factor for adverse outcomes of COVID-19 infection. We report the experience of young patients with type 1, type 2 and other types diabetes who fasted during Ramadan 2020 at the time of the COVID-19 pandemic time lockdown.

Research Design and Methods.

A Post- Ramadan survey was designed for young patients who fasted during Ramadan in 2020 during COVID pandemic time. The study was conducted to compared the basal characteristics and other parameters in children and adolescents (<18 years), with young adults (≥18 years) with diabetes at Paediatric Diabetes Center in BIRDEM in Bangladesh.

Results: Among the study participants, a significantly higher number of participants were in older age group who fasted for more than 15 days ($p = 0.045$). A considerable proportion (30.7%) of patients developed mild hypoglycaemia, and only eight patients (2.6%) developed moderate to severe hypoglycemia. There was significant reduction of post Ramadan basal insulin dose in both groups ($p = 0.001$). Although increased bolus insulin dose requirements were observed in older age group, but decreased requirement was observed in younger age group during Ramadan ($p = 0.001$). Post Ramadan median HbA1C in both groups was increased with marked increase in older age group compared to younger age group though it did not reach the statistical significance. ($p = 0.239$)

Conclusions: COVID-19 pandemic had minor impact on fasting during Ramadan in our cohort, they could fast safely with less complications during Ramadan. Our data supports Ramadan focused diabetes education with ample self-care, young people with diabetes can fast safely during Ramadan.

1. Introduction

COVID-19 was labeled a global pandemic by the World Health Organization on March 11, 2020 with a call to make crucial and timely changes to control global virus transmission and prevent overburdening of the healthcare system. [1] In Bangladesh, the lockdown started in March 26, 2020, aimed in preventing the spread of the virus through social distancing and isolation and as the number of cases was increasing day by day, a further extension of lockdown was done by the Government of Bangladesh. [2] Although Ramadan fasting is obligatory for all

healthy adult and adolescent Muslims from the time of completing puberty [3] but guidance has suggested that Muslim people with T1DM should be actively discouraged from fasting during the COVID-19 pandemic, as diabetes has emerged as a significant risk factor for adverse outcomes of COVID-19 infection. [4–7].

People with type 1 diabetes mellitus (T1DM) are considered at increased risk for complications during Ramadan, and advise against undertaking the fast in different guidelines. [8,9] Fasting affects the body's homeostasis, metabolic environment, fluid balance, and interaction of foods, drugs, and disease. Although exempt, adults and

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<https://doi.org/10.1016/j.diabres.2022.109812>

Received 18 September 2021; Received in revised form 30 December 2021; Accepted 28 February 2022

Available online 15 March 2022

0168-8227/© 2022 Published by Elsevier B.V.

children with diabetes refuse to take this concession as they feel psychologically and spiritually inclined to fast along with other Muslims. [10] Over the last two decades, there has been a significant increase in number of people with T1DM who are fasting during Ramadan. A population-based study, Epidemiology of Diabetes and Ramadan (EPIDAR), conducted among 13 countries, showed that 78.7% of patients with type 2 diabetes (T2DM) and 42.8% of T1DM could fast during Ramadan. [11] Although some experts consider fasting during Ramadan a high risk for metabolic deterioration, recent studies have demonstrated that individuals with T1DM can fast during Ramadan provided they comply with the Ramadan focused management plan and are under close professional supervision. In one prospective observational study done in 2012 in our center, we evaluated the safety of fasting in 33 children and adolescents with T1DM. [12] Safe fasting is possible during Ramadan through Ramadan focused diabetes education and monitoring under supervision of Diabetes Team. In our recent experience During the COVID-19 crisis in Bangladesh, patients with type 1 diabetes using insulin pump could fast safely with the support of the telemedicine service by the diabetes team. [13].

We report the experience of young patients with type 1, type 2 and other types diabetes who fasted during Ramadan 2020 at the time of the COVID-19 pandemic time lockdown. This study was conducted to see the safety, number of fasting days, breaking the fasting days, episodes of hypoglycemia and hyperglycaemia and changes in insulin dose, Post Ramadan HemoglobinA1c, in patients who did fasting during pandemic time Ramadan in Bangladesh.

2. Methods

2.1. Study design

A Post- Ramadan survey was designed for young patients who fasted during Ramadan in 2020 during COVID pandemic time. The Ramadan in Bangladesh was between 24th April to 24th May 2020. Due to COVID 19, there was lock down in whole month of Ramadan and these patients could not come for their Pre Ramadan follow up. Some of them did contact the diabetes team over phone. All young people with diabetes aged 8 to 26 years who came for their routine follow up at the end of Ramadan (between June to August 2020) at Changing Diabetes in Children Program (CDiC) and Life for a Child (LFAC) Paediatric Diabetes Center in BIRDEM, Dhaka, Bangladesh were invited to participate in the survey. The criteria of inclusion were diagnosis of all types of diabetes (diagnosed was established by clinical parameters as T1DM, T2 DM, FCPD and other types) who fasted during Ramadan. [14–16]. They were surveyed to determine whether the COVID-19 pandemic affected their decision to fast or not, fasting days or breaking the fast days, incidence of hypoglycemia and hyperglycemia during Ramadan fasting, insulin dose or oral drugs. They were asked about adverse events, including severe hypoglycemia or hyperglycemia, DKA or admission to hospital, the records from the Hospital and SMBG books were also seen. During education sessions in previous year, patients were instructed to break the fast if their blood sugar level was < 4 mmol/L or if they experience symptoms of hypoglycemia and if their blood glucose level > 16.7 mmol/L. [17].

Patients who did self-monitoring blood glucose at PreIftar, PreSohur, mid-afternoon, and at any time during the day when they feel symptoms of hypoglycemia were recorded along with the insulin dose.

Other clinical information was retrieved from the patient's previous records. A routine HbA1c was done during post Ramadan follow up. We compared the basal characteristics and other parameters in children and adolescents (<18 years), with young adults (≥18 years) with diabetes.

2.2. Insulin dose adjustment

Majority of T1 D patients were on multiple daily insulin injections (MDI) with regular insulin and NPH. The changing dose was recorded.

Those who were Type 2D were on oral drugs only or with NPH. Other types were having insulin only.

2.3. Ethical considerations

The study was approved by the Ethical Review Committee of the Diabetic Association of Bangladesh. Informed consent was taken from patients and parents.

2.4. Statistical analysis

Data analysis was performed by Statistical Package for the Social Sciences program version 26. Descriptive statistics are presented as mean(±SD) scores for normally distributed data and median (interquartile range or range) for skewed data. Continuous data were compared using parametric test Anova and skewed data using the non-parametric test Kruskal-Wallis test. Differences in demographic characteristics and clinical outcomes between participants < 18 years and ≥ 18 years old were tested using chi-squared analysis. All applied statistical tests were two-sided, p-values < 0.05 were considered as statistically significant.

3. Results

3.1. Basic characteristics

During the study period, 832 patients came for follow up and 300 (36%) patients with different types of diabetes fasted and agreed to participate the survey. None of them said that COVID-19 pandemic had influenced their choice on whether or not to fast while asked the question. The median age was 20 [17–23] years, 134 (44.7%) were male; all were on multiple or twice daily injections or oral drug. While dividing into two groups, 198 (66.0%) were in older age group (≥18 years) and 102 (34.0%) were in younger age group(<18 years). Among 300 patients, 211(70.3%) were T1D, 63 (21.0%) were T2 D and 26 (8.7%) were other types. Among other types, 14 were FCPD, 6 MODY type, 3 Secondary type (Thalassaemia), 1 steroid induced, 1 Wolfram syndrome and 1 was severe resistance syndrome (who were clinically diagnosed). Majority patients 268 (89.3%) fasted in previous years. The median age was 22.0[20.0–24.0] years in ≥ 18 years group and 16.0[14.0–17.5] in < 18 years group (p = 0.0001).[Table 1] Duration of diabetes was significantly higher in older age group (p = 0.0001). [Table1].

A large number of patients (62.3%) patients did Self-monitoring blood glucose regularly during Ramadan, among them more were in older age group. [Table 1] Pre Ramadan median HbA1c was higher in

Table 1
Comparison of Basal characteristics between two groups.

Characteristics	Age group < 18 years (n = 102)	Age group ≥ 18 years (n = 198)	P value
Area			
Age at Diagnosis	12.0[9.7–14.0]	13.0[12.0–15.0]	0.0001
Current age (years)	16.0[14.0–17.5]	22.0[20.0–24.0]	0.0001
Gender			
Male (%)	44 (43.1%)	90 (45.5%)	
Female (%)	58 (56.9%)	108(54.5%)	0.702
Duration of diabetes	4.0[2.0–6.0]	9.0[7.0–11.0]	0.0001
Types of diabetes			
Type 1 (n = 211)	75	136	
Type 2 (n = 63)	23	40	
Other types (n = 26)	4	22	0.110
SMBG done			
Yes (n = 102)	54 (28.9%)	48 (42.5%)	
No (n = 198)	133 (71.1%)	65 (57.5%)	0.016
Basal dose	24.0[19.5–32.0]	30.0[21.5–38.0]	0.001
Bolus dose	28.0[15.5–36.0]	34.0[21.5–46.0]	0.004
TDD	53.0[34.0–68.0]	64.0[44.0–84.0]	0.002
Median HbA1c	8.4[7.2–9.8]	7.9[7.1–9.0]	0.135

younger age group compared to older age group. Basal clinical characteristics of the two groups were described in [Table 1](#).

3.2. Numbers of fasting days and breaking the fast

Among the study participants, 56 (18.7%) fasted all days, 139 (46.3%) fasted between 15 and 29 days and 105 (35.0%) fasted 1 to 15 days. There was a significantly higher number of participants in older age group who fasted for more than 15 days ($p = 0.045$). While 69.6% in ≥ 18 years managed to the full month whereas 30.4% in < 18 years; and 43.8%, 28.8%, and 56.2%, 71.2%, could fast 1–14 days, 15–29 days respectively in < 18 years and ≥ 18 years of age groups ($p = 0.039$).

Among the different types of diabetes, there was no significant difference on fasting days, median fasting days was higher in type 2 diabetes 25.0 [17.0–29.0] whereas in type 1 was 21.0 [10.0–28.0] and other types was 22.5 [14.0–25.5] days. ($p = 0.228$). While comparing the breaking the fasting days, majority in older age group broke the fast within 7 days only ($p = 0.031$). [[Fig. 1](#)].

3.3. Incidence of hypoglycemia

Hypoglycemia was a common acute complication during fasting. A considerable proportion (30.7%) of patients developed mild hypoglycaemia, and only eight patients (2.6%) developed moderate to severe hypoglycemia. None of them required hospital admission. Most of them had hypoglycemia in morning after sehri, mid-afternoon and pre iftar time, few of hypos are also during pre sehri or early morning. Forty-four (14.6%) patients broke the fast due to hypoglycaemia. Among them 33 (75%) were T1 D, 5 (11.4%) were T2D and 6 (13.6%) were other types. Those who developed hypos just before iftar, did not break the fast. While comparing between the two groups, there was no significant difference ($P = 0.162$). [[Fig. 2](#)].

3.4. Incidence of hyperglycaemia

Hyperglycaemia was not very common in fasting hours during the day time. Only 9 (3%) patients, all of them were T1 D developed hyperglycaemia, mostly Post iftar and sehri, few had also during pre sehri or mid-afternoon time. Only 2 patients did break the fast due to

hyperglycaemia. Normoglycaemia and hyperglycaemia were more in older age group ($p = 0.084$). [[Fig. 3](#)] None of the fasting patients developed DKA during Ramadan.

3.5. Changes in hemoglobin A1c, and insulin dose

Changes in hemoglobin A1c, and insulin dose, before and at the end of Ramadan between and two groups are shown in [Table 2](#). There was significant reduction of basal insulin dose in both groups ($p = 0.001$). Although increased bolus insulin dose requirements were observed in older age group, but decreased requirement was observed in younger age group during Ramadan ($p = 0.001$). [[Table 2](#)] Post Ramadan median HbA1c 8.9 [7.6–10.3] was increased in T2 D patients compared to T1 D 8.5 [7.7–9.4]. There was increased Post Ramadan median HbA1C in both groups with marked increase in older group compared to younger age group though it did not reach the statistical significance. [[Fig. 4](#)]

4. Discussion

Fasting during Ramadan is not only abstinence from eating or drinking but also involves a radical change in lifestyle and usual habits which is more challenging for people with T1DM. Over the last two decades there has been a significant increase in number of people with T1DM who are fasting. Even during COVID time, Muslims around the world intended to fast. Amidst the COVID-19 pandemic, large DaR Global survey, a population-based survey was conducted among 13 countries, most of them with a Muslim majority population, showed that 71.1% of participants with T1DM fasted during Ramadan. [[18](#)].

The Epidemiology of Diabetes and Ramadan (EPIDIAR) study, which was conducted in 2001, found that as many as 42.8% people with T1DM reported fasting for at least 15 days and 78.7% of patients with T2DM fasted during Ramadan. [[11](#)] In our study population, among 300 patients 70.3% were T1D, and 21.0% were T2 D. In a recent survey, 26.8% managed to fast the full month, 6.1%, and 5.9% could fast, 8–14 days, and 1–7 days respectively. And 59.9% and 59.1% of < 18 years and ≥ 18 years of age broke their fast. [[18](#)] In our study population, majority 69.2% people in older age group fasted for atleast 15 days. Several studies including our previous study have shown that people with T1DM, including many adolescents, with the Ramadan based

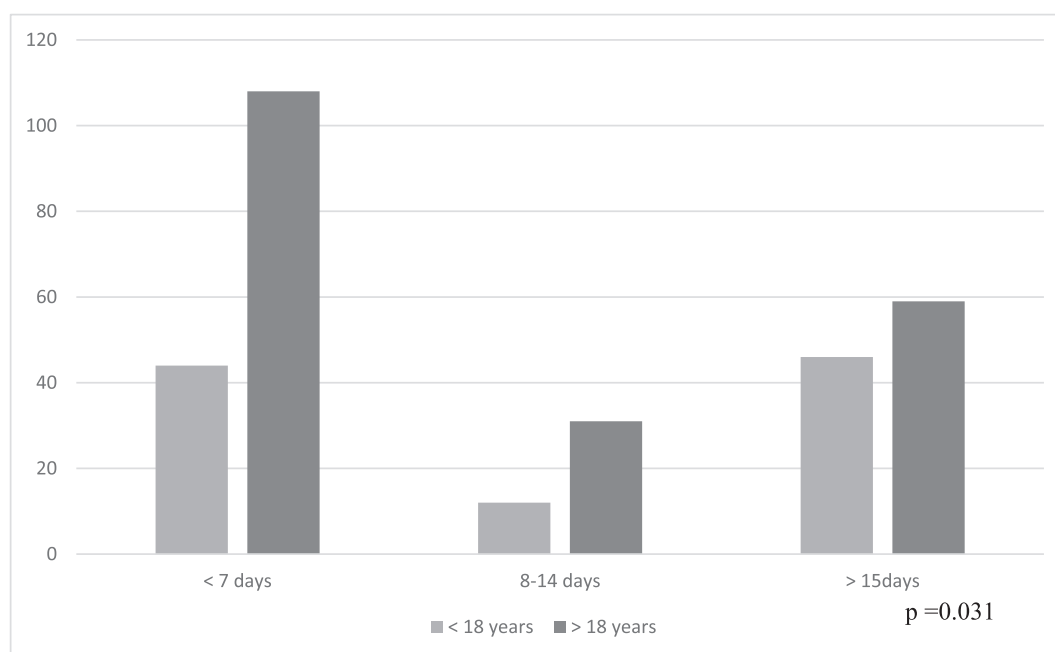


Fig 1. Comparison of fasting days between two groups.

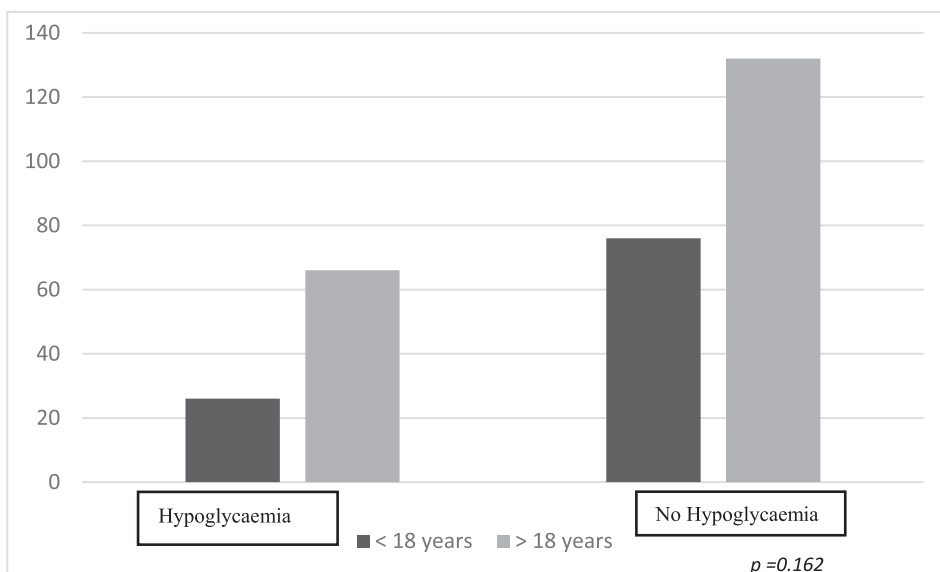


Fig 2. Incidence of hypoglycaemia between two groups.

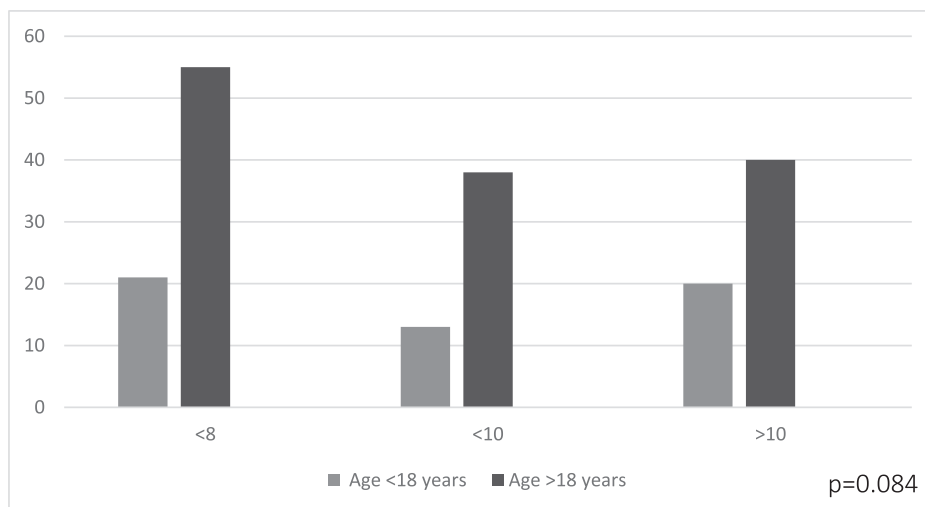


Fig 3. Incidence of hyperglycaemia and normoglycaemia between two groups.

Table 2

Comparison of Post Ramadan basal and bolus doses and HbA1c between two groups.

Parameters	<18 years	≥18 years	P value
Basal dose	20.0[4.0–26.0]	24.0[13.0–32.0]	0.001
Bolus dose	16.0[4.0–22.0]	53.0[37.5–70.0]	0.001
TDD	53.0[37.5–70.0]	62.0[43.0–84.0]	0.009
Median HbA1c	8.6[7.8–9.7]	8.5[7.7–9.4]	0.239

appropriate education, and supervision by Diabetes Team can fast safely during Ramadan. [19–29] A large number of our patients had fasted before and had the Ramadan based education in previous years which may made them confident enough to fast in this pandemic time where they cannot do their routine visit in the hospital.

The potential risks associated with fasting in patients withT1DM are a disruption in glycemic control revealing as hypoglycemia, hyperglycemia, and metabolic emergencies. [30] Hypoglycemia is a common acute complication during fasting. Monitoring blood glucose during fasting is essential to predict, prevent, and treat hypoglycemia. It is

usually advised that the fasting should be interrupted if significant hypoglycemia arises. [29] However, young people do not necessarily agree to break their fasting, particularly if hypoglycemia occurs close to sunset, which marks the end of fasting for the day. In our previous study, there was mostly incidence of mild hypoglycemia and only one patient had severe hypoglycaemia and none of them required admission. [20] In this study, majority developed mild hypoglycaemia only eight patients developed moderate to severe hypoglycaemia, 28.3 %of < 18 years and 71.7% of ≥ 18 years had experienced at least an episode of hypoglycemia. In a recent survey, the frequency, timing, and severity of hypoglycemia were elucidated where 55.6% of < 18 years and 62.6% of ≥ 18 years had experienced at least an episode of hypoglycemia. [18] Most of hypoglycemic episodes were encountered between 3 pm and Maghreb time before iftar (42.3%), followed by between 12 pm and 3 pm at noon (39.1%), then between Suhur and 11 am (17.3%) and only 1% developed after iftar at night. Whereas in a recent survey most of hypoglycemic episodes were encountered between 3 pm and Maghreb time (40%). [18] In our previous study we found that most of them had hypoglycemia in mid-afternoon and pre iftar time, few of hypos are also during pre sehri or early morning. [20] This implicates that

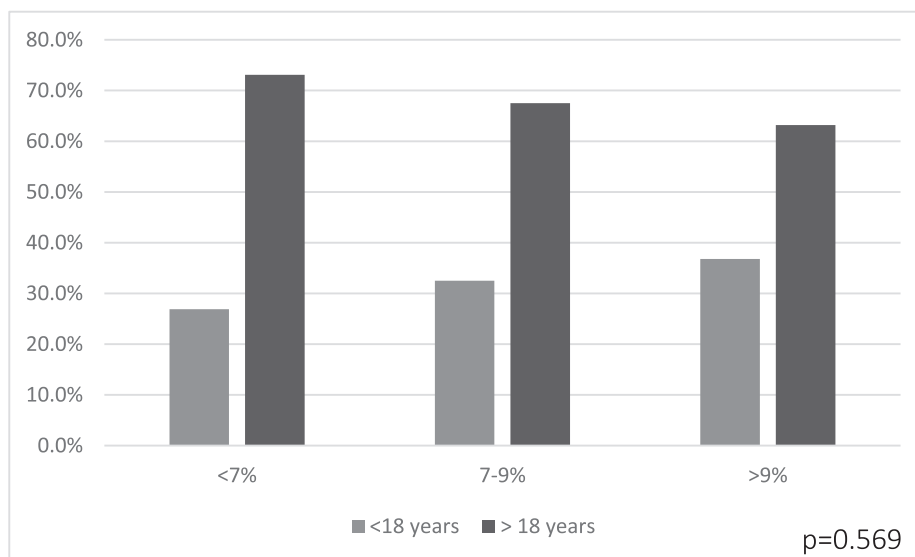


Fig. 4. Comparison of HbA1c at Post Ramadan time in between two groups p = 0.569.

hypoglycemia during Ramadan, occurs at all times of the day with the highest time during the period extending from mid-day to sunset time. Those who developed hypoglycaemia before iftar did not break the fast. though they had the intense education but may be they were unwilling to break the fast thinking spiritual aspect. Whereas a study done in young people with T1 D showed that the majority of fasting children and adolescents were willing to terminate their fast on the occurrence of hypoglycemia regardless of the timing of the day. [31].

Although mild hypoglycaemia is common but several studies showed that the incidence of severe hypoglycemia was negligible in people with T1DM during Ramadan fasting. [26,32–36] In our study population only 2.7% developed moderate to severe hypoglycaemia. The structured Ramadan focused diabetes education program can enable people with diabetes to reduce their risk of severity of hypoglycaemia during fasts. Our patients though could not come for follow up immediately before Ramadan but their previous knowledge could impact on management during fasting this year. The most concern part is even few participants fasted despite not doing any blood glucose monitoring but they did their insulin dose adjustment.

Although much of the focus during Ramadan is related to hypoglycemia, however, the studies have reported severe hyperglycemia with ketoacidosis. [37–39] None of our patients developed DKA during fasting and none of them required admission in the month of Ramadan. In DaR Global survey, 44.8% participants reported hyperglycemia and this occurred with no significant difference in the participants aged < 18 years and \geq 18 years whereas in our population, only 9(3%) patients developed hyperglycaemia and there was no significant difference between two groups. The reason may be the patients did little change in basal dose during sehri time according to their blood glucose level. The role of structured education in reducing the complications of diabetes is well established, and guidelines state that this structured education should be extended to Ramadan focused education programs so that people with diabetes can make informed decisions. Majority of our patients fasted in previous years and had structured Ramadan focused education before Ramadan each year.

The South Asian Guidelines for Management of Diabetes in Ramadan recommends reducing basal insulin by 10% to 20% during the fasting days. [40] Current recommendations for patients treated with multiple daily injection (MDI) include a reduction of the total daily dose (TDD) of insulin to 70% to 85% of the pre-fasting TDD or to 60% to 70% of the basal insulin. [9,36,41] In our study population there was significant reduction of basal insulin dose in both groups during Ramadan although there was episodes of mild hypoglycaemia. Though based on the

pharmacodynamic profile of NPH, there is a considerable risk of mid-day hypoglycemia and end of the day hyperglycemia, most of our patients were on NPH insulin and developed very few episodes of hyperglycaemia at the end of the day.

Pre Ramadan optimum glycaemic control is prerequisite for safe fasting in Ramadan. In our recent study we found that patients with poor control could fast safely without any severe acute complication with Post Ramadan reduction of HbA1c. [20] In our study, there was fair control in both groups and there was marked increase of Post Ramadan HbA1c in both groups with more in older age group. Gad et al assessment included a total of nine observational studies and showed that there was no difference in the change of HbA1c. [42] In pandemic time, fear of hypoglycaemia with reduction of insulin dose might cause post Ramadan hyperglycaemia in our patients. More over people here take lots of carbohydrates during iftar including simple carbohydrates and not adjusting the dose accordingly may cause worse glycemic control after Ramadan with higher HbA1c in both groups.

The recommendation to fast varies among different countries, depending on different cultural perspectives and religious views. In many diabetes centers with a Muslim population, health-care professionals agree that adolescents can fast if they have reasonable glycaemic control, good hypoglycemia awareness and are willing to frequently monitor their blood glucose levels during the fasting. [40] Over the past decade, several studies have evaluated fasting among adolescents with T1DM and its associated safety during the month of Ramadan. Kaplan et al used CGM to assess the impact of fasting on interstitial glucose concentrations in 14 adolescents with T1DM. There was no difference in the mean glucose readings or the duration of hypoglycemia, hyperglycemia, and severe hyperglycemia between the Ramadan and non-Ramadan period, respectively [21] Adolescents with T1DM continue to have wide glucose fluctuations during Ramadan and, when fasting, close glucose monitoring should be recommended.

The management of children with diabetes who choose to fast during Ramadan is a challenge for a pediatrician as the majority of guidelines and data on the safety and metabolic impact of fasting are based on practice and studies on the adult population. In pandemic time Ramadan, the lock down was going on and our patients could fast without any severe complications like severe hypoglycaemia or DKA. Our patients were more in older age, compared to our previous study probably have developed self-care, more attentive to the treatment regimen may have played a role in less complications though post Ramadan HbA1c was raised as the insulin adjustment was done by themselves. Moreover, we also assumed that parental supervision,

insulin adjustment by themselves, and receiving education in previous years are the main reasons for lower hypoglycemia episodes in our patients. It is also possible that high food intake and higher HbA1c in our patients provided them with protection against hypoglycemia and later developed high HbA1c after Ramadan.

This survey has some limitations as information were collected from recapitulating memory following Ramadan and based on documentation of self-reporting of some information - the incidence of hypoglycemia, hyperglycemia, insulin dose and the management of diabetes. Although recall bias may have affected the data, but hypoglycemia, hyperglycemia are recognized features, and especially fasting days and breaking of the fast cannot be forgotten as fasting has a religious impact and a person has to compromise on fasting days. Moreover, fasting is a spiritual and religious ritual and in our society, parents as well supervise their children vigilantly during fasting.

In conclusion, COVID-19 pandemic had minor impact on fasting during Ramadan in our cohort, who could fast safely without any severe complications like severe hypoglycaemia or DKA. Post Ramadan higher HbA1c was observed more in young adults compared to children and adolescents. Our patients were more in older age with longer diabetes duration who fasted in previous years which supports Ramadan focused diabetes education with ample self-care, young people with diabetes can fast safely during Ramadan.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

No funding was received in association with this manuscript

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