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Role of Professional Continuous Glucose Monitoring in the Management of Diabetes with High Glycemic Variability: A Cross-Sectional Study

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Abstract

Continuous Glucose Monitoring (CGM) systems, a promising technology for frequent blood glucose level monitoring and detection of hyperglycemic and hypoglycemic excursions, were evaluated in a cross-sectional study involving 30 diabetes patients with high glycemic variability. Using the iPro2 professional CGM system, baseline fasting and postprandial blood glucose levels were obtained and patients were monitored over 3-5 days. Post-CGM data analysis led to modifications in the patient's diet, physical activity, and insulin regimen, with follow-up assessments conducted after 2 months. The study, which eventually included 17 type 1, 8 type 2, and 5 gestational diabetes patients due to data recording issues, observed significant improvements in mean fasting blood glucose and HbA1C levels in all patients post-CGM-guided therapy modifications. However, the improvement in mean postprandial blood glucose was not statistically significant. The CGM also detected postprandial hyperglycemia and asymptomatic hypoglycemia, proving its value in managing diabetes with high glycemic variability and potentially preventing long-term complications.

Introduction

Diabetes is a major cause of mortality in the age group of 20-79 years. (Whiting et al., 2011) Based on its rapidly increasing incidence, it has been declared a global epidemic by the world health organization (WHO).China and India have the largest numbers of people with diabetes (109.6 million and 69.2 million, respectively). (Guariguataet al., 2011) (WHO, 2015) ('The mysteries of type 2 diabetes in developing countries', 2016)

The frequent monitoring of blood glucose is critical for diabetic management. The Diabetes Control and Complications Trial (Skyler, 2000) showed a ~60% decrease in the development of diabetic retinopathy and nephropathy in type 1 diabetics by intensive glycemic control. Similarly, the UK Prospective Diabetes Study (Skyler, 2000) showed a 25% decrease in overall microvascular complication rate in type 2 diabetics by intensive glycemic control.

Continuous glucose monitoring systems are an emerging technology that allow frequent glucose measurements every five minutes and the ability to monitor glucose trends.(Gross et al., 2000). Analysis of glucose levels, even in "well-controlled" patients with

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Type-1 or Type-2 diabetes, indicates that significant time is spent above and below desired target ranges. (Hay, Wilmshurst and Fulcher, 2003). These monitoring systems has the potential to improve detection of hyperglycemic excursions as well as asymptomatic hypoglycemia and the data to help maintain physiological glucose concentration in diabetes. (Bode et al., 2004)(Hoi-Hansen, Pedersen-Bjergaard and Thorsteinsson, 2005)

Our aim is to evaluate the role of professional continuous glucose monitoring in the management of type 1, type 2 and gestational diabetics who are on insulin with high glycemic variability.

Materials and Methods

This is a cross sectional, hospital based, study conducted in the OPD/IPD of Rajiv Gandhi Center of Diabetes and Endocrinology from January 2016 to September 2017. Study group comprised of patients of type I (n=17),type II (n=8) and gestational diabetes (n=5) on insulin with high glycemic variability.

High glycemic variability was defined as recurrent fluctuations in blood glucose levels including fasting and post prandial hyperglycemia, recurrent hypoglycemia or uncontrolled HbA1C. There diagnosis was based on the ADA criteria for type 1 and type 2 diabetes(American Diabetes Association, 2014) and IADPSG criteria for gestational Diabetes (International Association of Diabetes and Pregnancy Study Groups Consensus Panelet al., 2010)

We did not include the patients with recent surgery or any evidence of infection. Patients on drugs which cause hypo or hyperglycemia(except for OHA) were also excluded. We used **iPro2 professional CGM system**. Patients included in the study were motivated to wear the CGM device after explaining them the relation of uncontrolled diabetes and undetected glycemic excursions with the complications of diabetes and the benefits of CGM.

Baseline HbA1C values were obtained for the patients prior to being subjected to CGM. They were subjected to CGM for 3-5 days and were monitored for hyperglycemic and hypoglycemic excursions. For calibration of CGM data, patients were told to self-monitor their blood glucose values before meals using glucometer for all those days. Patients weretold to record their diet, physical activity, self-monitored blood glucose values and insulin administered with respect to correct timings on a log sheet.

After that, the CGM data was downloaded and analyzed. Average baseline fasting and postprandial blood sugar values were obtained from the data. Total time spent by the patient in normoglycemia, hyperglycemia and hypoglycemia as well as high and low excursions was obtained from the data.

According to the data obtained from CGM, patient's diet, physical activity and insulin was modified and they were told to strictly adhere to the regimen. After 2 months of follow up, patient's blood sugar fasting, post prandial and HbA1C values were again obtained and compared with the baseline values. The study was approved and passed by ethical committee of the institution

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Results and Discussion

A total of 40 patients participated in the study out of which there was no data recorded in 10 patients either due to some unexplained technical fault or due to poor patient profile, acceptability and compliance. No adverse effects of sensors were observed in the study.

Table 1: Baseline clinical and biochemical characteristics of study patients

		Type 1 Diabetes	Type 2 Diabetes	Gestational diabetes mellitus
Age	<30 years	16	0	2
	>30 years	1	8	3
Mean age ± SD (years)		19.40±6.61	51±9.65	30.8±5.89
Sex	Males	7	6	0
	Females	10	2	5
Duration of diabetes	<5 years	8	7	-
	5-10 yeas	7	1	-
	>10 years	2	0	-
Mean fasting blood glucose (mg/dl) (Mean± SD)		180.47±87.77	157.50±84.40	113.80±18.19
Mean PP blood glucose (mg/dl) (Mean± SD)		213.82±61.83	181.63±89.74	140±44.37
HbA1C (%) (Mean± SD)		8.99±1.53	9.55±3.03	6.16±0.21

Out of 30 patients in which data was recorded,17 patients were of type 1 diabetes, 8 were of type 2 diabetes and 5 of gestational diabetes. The mean age of total patients included in the study was 29.73±15.45 years. The oldest patient in the study group was 60 years and

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the youngest was 10 years. The mean age of type 1 diabetics included in the study was 19.40±6.61 years. The oldest patient in this group was 31 years and youngest was 10 years. The mean age of type 2 diabetics was 51±9.65 years. The oldest patient among this group was 60 years and youngest was 30 years. The mean age of gestational diabetics included was 30.8±5.89 years. The oldest patient among this group was 35 years and youngest was 23 years.

Out of total 30 patients included in the study 17 (56.66%) were females and 13 (43.33%) were males. Among the females,10 patients (58.82%) were of of type 1 diabetes,5(29.41%) were of gestational diabetes and only 2(11.76%) of type 2 diabetes. Among the males,7 patients (53.84%) were of type 1 diabetes and 6(46.15%) were of type 2 diabetes. Among the type 1 diabetic patients females (58.82%) outnumbered males (41.18%). Among the type 2 diabetics males (75%) outnumbered the females (25%).

Table 2: Comparison of mean fasting blood glucose, post prandial blood glucose and HbA1C of study patients

		Mean fasting blood glucose (mg/dl) (Mean± SD)	Mean PP blood glucose (mg/dl) (Mean± SD)	HbA1C (%) (Mean± SD)
Type 1 Diabetes	Baseline	180.47±87.77	213.82±61.83	8.99±1.53
	Follow up	150.06±46.44	192.76±56.62	8.24±1.02
Type 2 Diabetes	Baseline	157.50±84.40	181.63±89.74	9.55±3.03
	Follow	121.88±38.04	178.25±44.36	9.13±1.84

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	up			
Gestational diabetes mellitus	Baseline	113.80±18.19	140±44.37	6.16±0.21
	Follow up	91.40±4.10	118.2±16.25	5.62±0.13

Among the total patients included in the study the improvement in mean fasting blood glucose after 2 months of application of continuous glucose monitor was statistically significant (p-value <0.05). Among the type 1 diabetics the improvement in mean fasting blood glucose was statistically not significant (p-value > 0.05) Among the type 2 diabetics the improvement in mean fasting blood glucose was statistically not significant (p-value > 0.05). Among the gestational diabetics the improvement in mean fasting blood glucose was statistically significant (p-value<0.05)

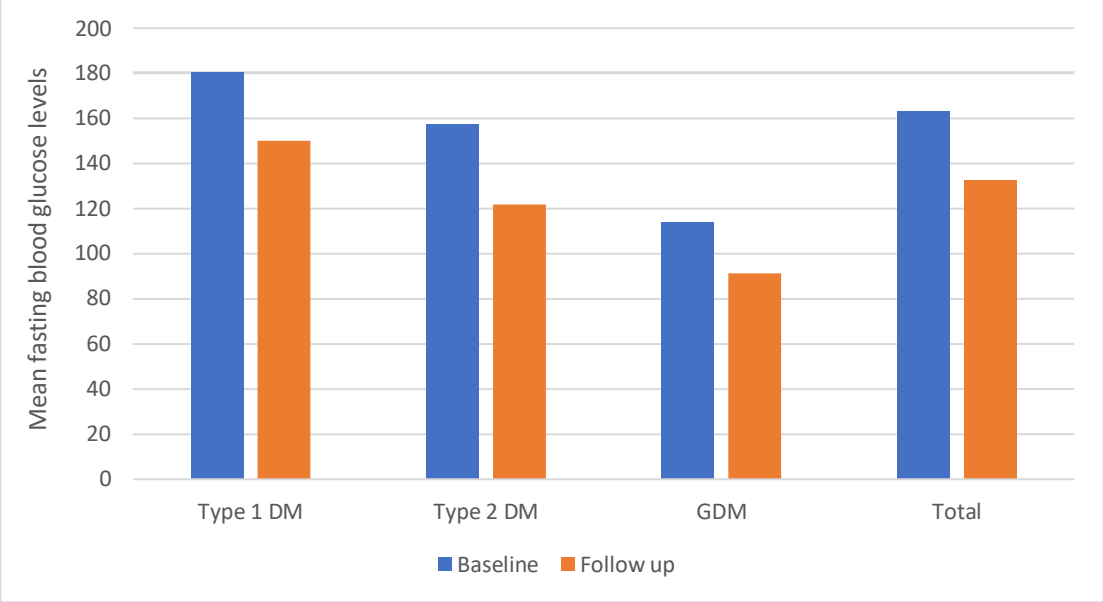

Figure 3: Showing mean baseline and follow up fasting blood glucose levels of all types of patients included in the study

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Among the total patients included in the study the improvement in mean postprandial blood glucose after 2 months of application of continuous glucose monitor was not statistically significant (p-value >0.05). Among the type 1 diabetics the improvement in mean post prandial blood glucose was statistically not significant (p-value > 0.05). Among the type 2 diabetics the improvement in mean post prandial blood glucose was statistically not significant (p-value > 0.05). Among the gestational diabetics the improvement in mean post prandial blood glucose level was statistically not significant (p-value>0.05)

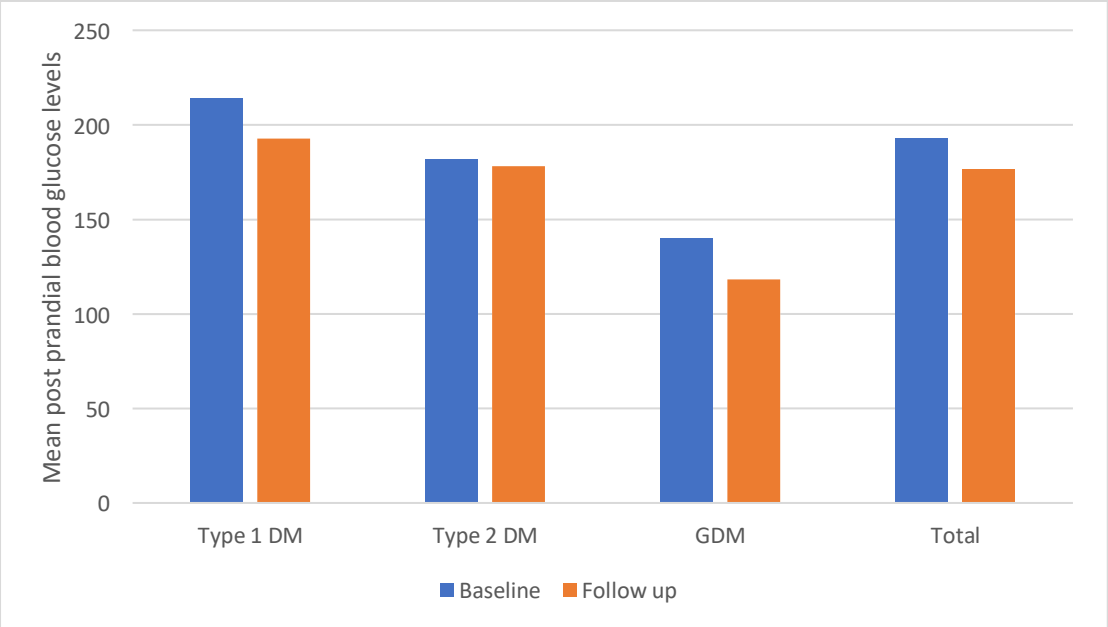

Figure 4: Showing mean baseline and follow up post prandial blood glucose levels of all types of patients included in the study

Among the total patients included in the study the improvement in mean HbA1C after 2 months of application of continuous glucose monitor was statistically significant (p-value<0.05). Among the type 1 diabetics the improvement in mean HbA1C was statistically significant (p-value < 0.05). Among the type 2 diabetics the improvement in mean HbA1C

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was statistically not significant (p-value > 0.05). Among the gestational diabetics the improvement in mean HbA1C was statistically significant (p-value<0.05).

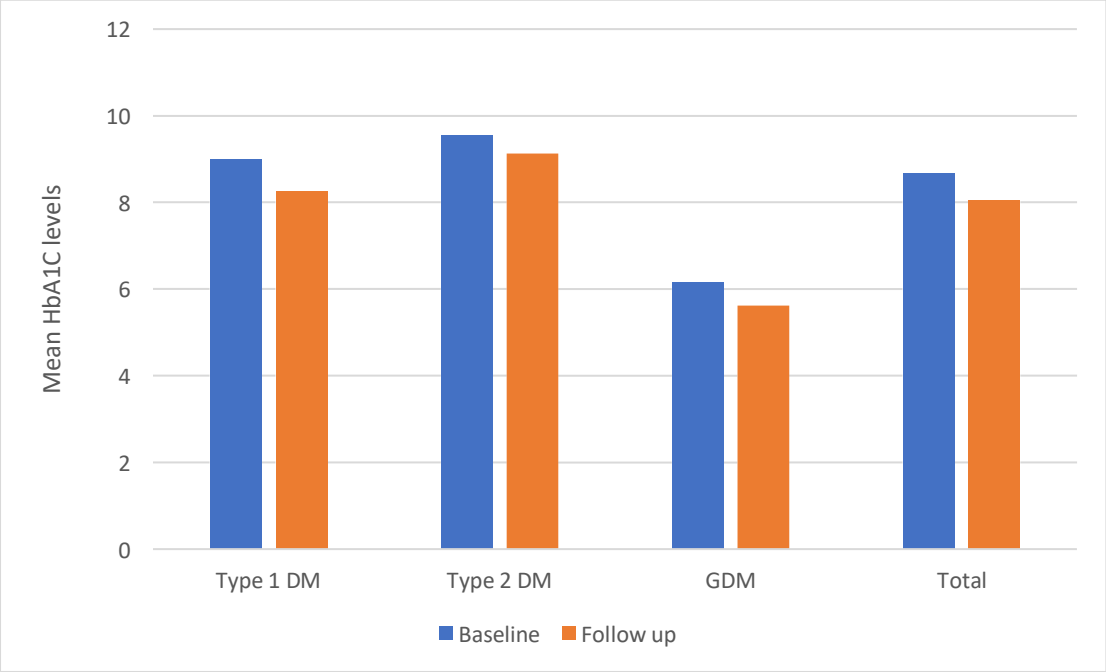

Figure 5: Showing mean baseline and follow up HbA1C levels of all types of patients included in the study

Table 4: Glycemic excursions observed in participants during continuous glucose monitoring

	Number of high glycemic excursions			Number of low glycemic excursions		
	<5	5-10	>10	<5	5-10	>10

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Number of Type 1 diabetic patients	2	9	6	12	3	2
Number of Type 2 diabetic patients	0	4	4	4	2	2
Number of GDM patients	2	3	0	4	1	0
All patients	4	16	10	20	6	4

Out of all 30 patients included in the study, in 16 patients, the number of high glycemic excursions observed during continuous glucose monitoring was between 5-10. The maximum number of high excursions (i.e., >10) was observed in 10 patients. The maximum number of low excursions (i.e., >10) was observed in 4 patients. In most of the patients (i.e., 20 patients) number of low glycemic excursions was <5.

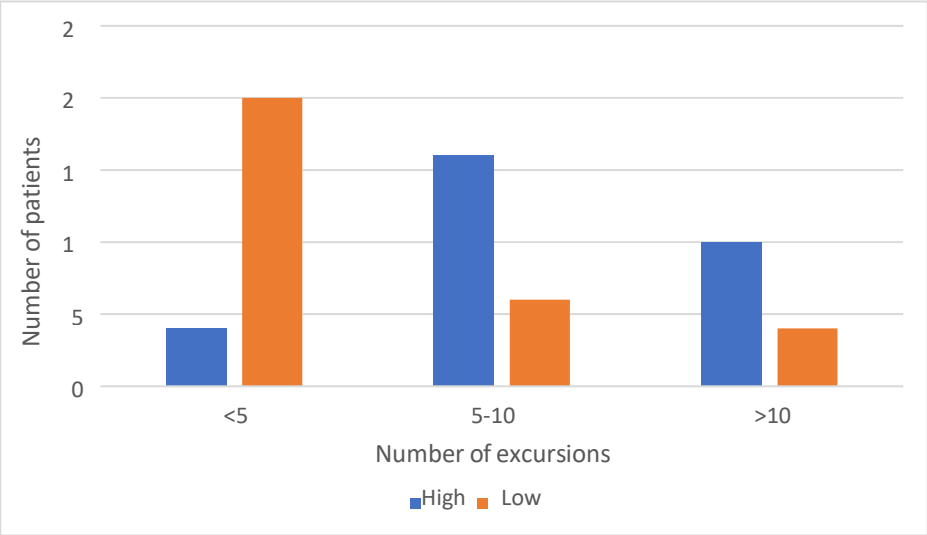

Figure 10: Showing high and low excursions observed in all the patients included in the study during continuous glucose monitoring

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Out of all 17 type 1 diabetic patients, in most of them (i.e., 9 patients) the number of high glycemic excursions observed during continuous glucose monitoring was between 5-10. The maximum number of high excursions (i.e., >10) was observed in 6 patients.The number of low glycemic excursions observed in most of these patients (i.e., 12 patients) was <5. The maximum number of low excursions (i.e., >10) was observed in 2 patients.

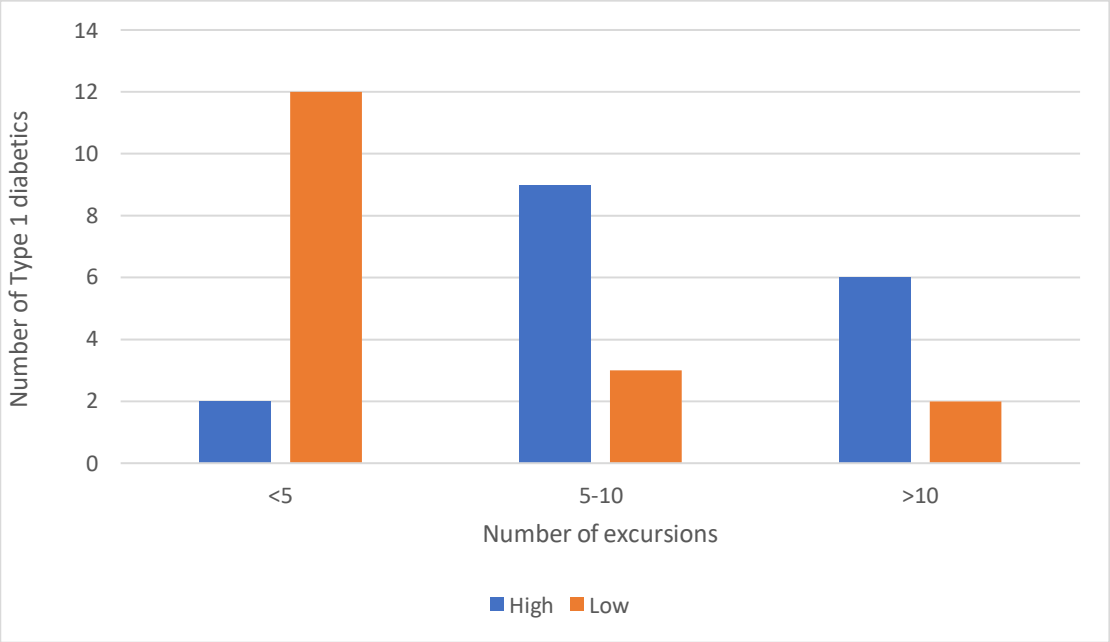

Figure 11: Showing high and low excursions observed in type 1 diabetics during continuous glucose monitoring

Out of all 8 type 2 diabetic patients, in 4 patients the number of high glycemic excursions observed during continuous glucose monitoring was between 5-10. The maximum number of high excursions (i.e., >10) was observed in 4 patients. The number of low glycemic

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excursions observed in most of these patients (i.e., 4 patients) was <5. The maximum number of low excursions (i.e., >10) was observed in 2 patients.

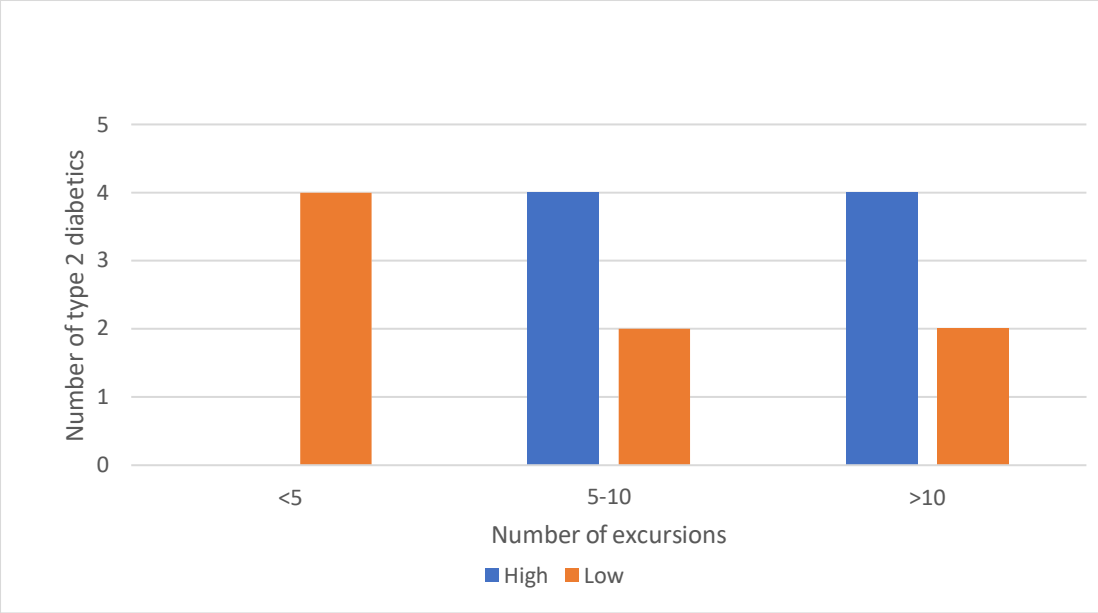

Figure 12: Showing high and low excursions observed in type 2 diabetics during continuous glucose monitoring

Out of all 5 gestational diabetes patients, in most of them (i.e., 3 patients) the number of high glycemic excursions observed during continuous glucose monitoring was between 5-10.The number of low excursions observed in most of these patients (i.e., 4 patients) was <5.

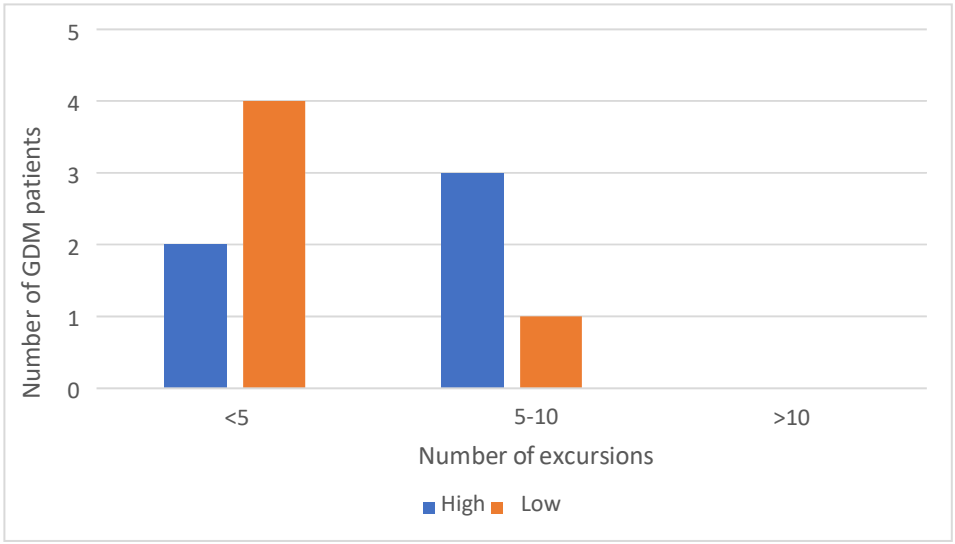

Figure 13: Showing high and low excursions observed in gestational diabetics during continous glucose monitoring

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Table 5: Glycemic status of all the patients included in the study as observed during continuous glucose monitoring (CGM)

Total time spent in (%)	All number of patients		
	Hyperglycemia	Hypoglycemia	Normoglycemia
<25	13	24	14
25-50	3	5	4
>50	14	1	12

Out of all the 30 patients included in the study, it was observed that >50% of the total time was spent in hyperglycemia in most of the patients i.e., in 14 patients. In 80% of the total patients (i.e., 24 patients) <25% of the total time was spent in hypoglycemia. Only 12 patients spent >50% of the total time in normoglycemia. Most of the patients (i.e., 14patients) spent only <25% of the total time in normoglycemia.

Table 7: Glycemic status different group of patients included in the study as observed during continuous glucose monitoring (CGM)

		Total time spent in (%)		
		<25	25-50	>50
Number of type 1 diabetics	Hyperglycemia	6	1	10
	Hypoglycemia	14	2	1
	Normoglycemia	10	2	5
Number of type 2 diabetics	Hyperglycemia	2	2	4
	Hypoglycemia	5	3	0
	Normoglycemia	4	2	2
Number of GDM patients	Hyperglycemia	5	0	0
	Hypoglycemia	5	0	0
	Normoglycemia	0	0	5

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Out of all the 17 type 1 diabetic patients included in the study, it was observed that >50% of the total time was spent in hyperglycemia in most of the patients, i.e., in 10 patients. In a significant number of patients (i.e., 14 patients) <25% of the total time was spent in hypoglycemia Only 5 patients spent >50% of the total time in normoglycemia. Most of the patients (i.e., 10 patients) spent only <25% of the total time in normoglycemia.
Out of all the 8 type 2 diabetic patients included in the study, it was observed that >50% of the total time was spent in hyperglycemia in most of the patients, i.e. in 4 patients.

In a significant number of patients (i.e., 5 patients) <25% of the total time was spent in hypoglycemia. Only 2 patients spent >50% of the total time in normoglycemia. Most of the patients (i.e., 4 patients) spent only <25% of the total time in normoglycemia.

In all the 5 gestational diabetes patients included in the study, it was observed that <25% of the total time was spent in hyperglycemia and hypoglycemia respectively. All the patients spent >50% of the total time in normoglycemia.

DISCUSSION

In this study we found that CGM helped to detect the baseline mean fasting and blood glucose levels on the basis of the average of a large number of variable glucose measurements over 3-5 days period which helped in better adjustment of diet, physical activity and insulin dose of the patients. This helped in improvement in fasting and post prandial blood glucose levels and HbA1C levels of the patients. It also helped to detect post prandial hyperglycemia and asymptomatic hypoglycemia in the patients. It also helped to detect high and low glycemic excursions in the patients which would have been missed otherwise.

The predominant postprandial hyperglycemia detected in type 1 diabetic patients by CGM in our study was similar to the study by Boland et al in 200 (Boland et al., 2001). The predominant postprandial hyperglycemia detected in type 2 diabetes by CGM was similar to the study by Kesavadev et al in 2017 (Kesavadev et al., 2017).The postprandial hyperglycemia detected in gestational diabetics by CGM was similar to the study by Jovanovic in 2000 (Jovanovic, 2000)

The improvement in blood glucose after 2 months of application of continuous glucose monitoring device was mainly assessed through the improvement in HbA1C in all the patients included in the study. This result was similar to the study conducted in type 1 diabetics by Chico et al.(Chico et al., 2003) but was partially in conflict with the study conducted by Al Hayek et al. which showed improvement in mean HbA1C but it was not statistically significant ($p>0.05$) (Al Hayek et al., 2015).

However, the improvement of mean HbA1C of type 2 diabetics was in partial conflict with the study conducted on professional CGM in type 2 diabetics on multiple therapies by Mohan et al. in 2016 which showed maximum improvement in mean HbA1C in those

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patients on insulin among all study groups and was statistically significant($p>0.05$).(Mohan et al., 2016) This was also partially in conflict with the studies conducted on professional CGM in type 2 diabetics on insulin by Jyothydev Kesavdev et al in 2017 (Kesavadev et al., 2017) and Leinung et al in 2013 (Leinung et al., 2013) both of which showed improvement in HbA1C and was statistically significant($p<0.05$). This was in complete conflict with the study conducted on professional CGM in type 2 diabetics on insulin by Pepper et al in 2012 (Pepper, Steinsapir and Reynolds, 2012) which showed no improvement in HbA1C. The mean baseline HbA1C of gestational diabetics was higher as compared to the studies conducted by Jovanovic et al. (Jovanovic, 2000) and Chen et al. (Chen et al., 2003)

Conclusions

The present study demonstrated the role of professional continuous glucose monitoring in the management of diabetes in high-risk groups such as type 1, type 2 and gestational diabetes on insulin with high glycemic variability including those with uncontrolled HbA1C, recurrent postprandial hyperglycemia or asymptomatic recurrent hypoglycemia. The therapy

modification done in these patients based on retrospective CGM reports lead to improvement in the mean fasting and post prandial blood glucose and mean HbA1C in these patients after a follow up of 2 months.

The improvement was statistically significant in mean fasting blood glucose and HbA1C and insignificant in mean post prandial blood glucose. Our study showed that CGM helps in better glycemic control with decreased glycemic variability which can prevent long term complications of diabetes in future as shown in previous studies such as Diabetes Control and Complications Trial (DCCT)and United Kingdom Prospective Diabetes Study (UKPDS).

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