Section: General Medicine

Original Research Article

IMPACT OF FLASH GLUCOSE MONITORING ON GLYCAEMIC CONTROL AMONG MEDICAL IN-PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract

Background: Abbott's investigational Flash Glucose Monitoring System offers an alternative to traditional capillary blood glucose monitoring, collecting continuous glucose data and generating an ambulatory glucose profile without the need for finger pricks. This study compares the effectiveness of flash glucose monitoring versus standard capillary glucose measurements among medical in-patients with type 2 diabetes mellitus. **Aims and Objectives:** • Primary Outcome: To compare blood glucose control in patients with type 2 diabetes mellitus managed using flash glucose monitoring versus standard capillary glucose measurements. • Secondary Outcomes: To compare in-hospital hypoglycemic episodes, total hospital days, and blood glucose control at first follow-up in both groups. **Materials and Methods:** This randomized controlled, open-label study was conducted in the Department of Medicine at Christian Medical College and Hospital, Ludhiana, from December 1, 2016, for eighteen months. Adult patients with type 2 diabetes mellitus admitted to non-intensive medical and medical specialty wards were included. One hundred patients were randomized into two groups: Group A (cases) and Group B (controls). Group A patients had their blood glucose monitored by the Flash Glucose Monitoring System, while Group B patients used standard capillary glucose measurements during the first 48 hours of admission. Insulin administration was at the treating physician's discretion in both groups. From day 3 to 5, both groups had 5-point blood glucose monitoring using capillary glucose measurements. Outcomes were assessed after recording blood glucose values. **Results: • Primary Outcome:** 29 (58%) cases and 26 (52%) controls had blood glucose values 50% of the time (5/10 readings) within the optimal range. In both groups, 5 (10%) patients had all blood glucose values within the optimal range **• Secondary Outcomes:** Hypoglycemia was reported once in the cases and four times in the controls, with all episodes being asymptomatic (p=0.171, not statistically significant). There were 31 (62%) cases and 27 (54%) controls whose blood glucose values were 50% of the time [5/10 readings] in the hyperglycemic range (p=0.7, not statistically significant). Three (6%) cases and one (2%) control had all blood glucose values in the hyperglycemic range. Twenty (40%) cases and ten (20%) controls were admitted for less than 6 days. The mean fasting blood glucose values at the outpatient visit were 178.82 mg/dL for cases and 170.42 mg/dL for controls (p=0.178, not statistically significant). The mean postprandial blood glucose values were 205.82 mg/dL for cases and 224.54 mg/dL for controls (p=0.123, not statistically significant). **Conclusion:** This study found no significant difference in glycaemic control using the flash glucose monitor compared to standard capillary glucose monitoring. However, flash glucose monitoring reduced hypoglycemic events. As hypoglycemia is a major challenge in achieving good glycemic targets in diabetic patients, the use of flash glucose monitoring can be beneficial in reducing the frequency of hypoglycemic episodes.

INTRODUCTION

About 350 million people living in the world have Diabetes mellitus, a number likely to be more than double in the next 20 years. Type 2 Diabetes mellitus accounts for roughly 90% of all the diabetic patients over the world and India has got the second largest diabetic population worldwide.[1]

The conventional method of blood glucose monitoring is the standard capillary blood glucose test performed by pricking the skin (typically on the finger) to draw the blood, then applying the blood to a chemically active disposable 'teststrip'. Capillary and venous blood glucose (BG) values are the mostly used as reference to assess the accuracy of glucose monitoring by glucometers.[2,3] Clinical laboratories use venous samples analyzed using a laboratory analyzer, whereas in hospital , capillary BG is measured using a glucometer.[4-6]

The 'glycaemic triad', which consists of fasting glucose, post prandial glucose, and HbA1C, highlights the need to include HbA1C as an important marker of diabetes control. HbA1C levels are reflective of blood glucose level over the past 6- 8 weeks and do not reflects daily ups and downs of blood glucose. This test is considered the gold standard for assessment of glycaemic status, as its correlation with long term outcomes is well established.[7] The concept of 'glycaemic triad' is now overtaken by the 'glycaemic pentad', which includes, in its range two more markers:(lack of) hypoglycaemia, and (lack of) glycaemic variability.[8]

Flash glucose monitoring system gives a more accurate assessment of blood glucose level and insulin adjustment is done accordingly which helps to reduce the number of hospital days. Patients on intensive glucose-lowering therapy, at risk for hypoglycemia(unawareness), with refractory disease and/or inconsistent blood glucose reports should consider Ambulatory glucose profile (AGP) as an integral part of their diabetes care. AGP combines inputs from multiple days of continuous glucose monitoring (CGM) data and collates them into a single 24 hour period. It is also useful for analysis of glycemic variability, allowing quick understanding of poor glycemic control and to change the treatment decisions. It graphically shows the amplitude and frequency of varying glycaemic values. Compared with knowing what happened in the past, the AGP gives the clinician current information about the accurate blood glucose values, to support clinical decisions and to change the treatment accordingly.[9]

The number of diabetic patients in India is increasing day by day due to poor diet control, lack of exercise and poor blood glucose monitoring. In this context, this study was planned to compare blood glucose values using flash glucose monitoring versus standard capillary blood glucose measurement.

MATERIALS AND METHODS

Study Design: This was a randomized controlled, open label study conducted in the Department of Medicine at Christian Medical College and Hospital, Ludhiana from 1st December, 2016 for a period of eighteen months.

Study Patients

Adult patients with pre-existing Type 2 Diabetes mellitus (using standard ADA criteria) and who were admitted to the non- intensive medical and medical specialty wards were considered for inclusion into the study.

Inclusion Criteria

1. Adult patients (age >18 years) diagnosed to have preexisting Type-2 diabetes mellitus. (Standard ADA criteria for diagnosis if details of testing available) or those already on anti-diabetic therapy who are admitted for medical illness to the hospital.
2. Willing to consent for study and study procedures on their own, with capacity to understand the study procedures

Exclusion Criteria

1. Critically unwell patients admitted to or likely to be transferred to High Dependency and Intensive care units
2. Patients with diabetic ketoacidosis or hyperosmolar non ketotic state.
3. Patients with Type -1 diabetes mellitus.
4. Patients on high dose steroid therapy (Prednisolone doses of 30 mg/day or equivalent)
5. Patients admitted for observation or those likely to be discharged early within 5 days of admission
6. Patients with skin disorders affecting both upper arms
7. Patients on hemodialysis or peritoneal dialysis

Methodology

Study Methods (summarized in Flow Chart-1)

Patients diagnosed with Type-2 Diabetes mellitus admitted to the medical wards from 01/11/2016 fulfilling the inclusion criteria and after written consent were block randomized in to two group, Group –A (study group) and Group-B (control group). Baseline data was collected after randomization and entered into the case record forms. In both group's blood sugars were monitored as follows for the first 48 hours of admission.

Patients in Group A had their blood glucose monitored by the Flash glucose monitoring system which was attached to the patient's upper arm by the investigators or the diabetic nurse within 12 hours of admission (description given later). Patients in Group B had their blood glucose monitored by the current capillary glucose measurements as regularly done by the ward nursing staff and entered into the diabetic sheet in the first 48 hours after admission. Insulin was

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given as per the discretion of the treating physician, in both groups.

Block randomization technique was followed

Computer generated random number tables was generated and created block allocation sequence. Numbered envelopes were created with a sequence number inside and sealed prior to start of study. During the study the seal of the numbered envelope was opened in sequence once the patient gives consent.

Flash Glucose monitoring system (Group A)

Patients randomized to Group A had flash glucose monitoring system attached within 12 hours of admission. Flash glucose monitoring is a new method of glucose testing that is seen as a hybrid between glucometers and continuous glucose monitoring (CGM). The Abbott free style libre is currently the only flash glucose monitoring system available. In flash glucose monitoring, patients will have a sensor (Figure- I) inserted on their upper arm by the investigator, diabetic nurse or any other trained personal. A separate touch screen reader device is available to the investigator and the treating physician. When the reader device is swiped close to the sensor, sensor transmits both an instantaneous glucose level and 24 hours trend graph to the reader. This allows the treating physician to get individual blood sugar reading (like a glucometer) and trend information (like CGM). The information from the sensor can be downloaded as often as required by the treating physician to make appropriate therapeutic decisions on the patients. The sensor works for 14 days but for the purposes of this study the information obtained in the first 48 hours was deemed to form the basis of the intervention. The treating physician may continue to use the information from the sensor after the first 48 hours to make subsequent therapeutic decisions and the patient may be discharged with the sensor in place if a follow up is planned within 15 days of having the sensor attached.

Figure 1: This cartoon shows the Sensor and the Reader and the information available on the screen on wiping the machine over the sensor

Standard Capillary measurements and Charting (Group B)

Patients randomized to Group B had standard 4-7-point capillary glucose measurements taken as per the treating physician's orders. Capillary glucose measurements were taken either pre meals or post meals or both by the ward nurses using (ACCU-CHEK Performa, Model NC) glucometers. The values were entered into the diabetic sheet maintained in the patient's records as is the current standard practice.

Therapeutic decision making in patients

Therapeutic decision making about in patient management of diabetes was at the discretion of the treating physician. A combination of oral agents with or without insulin were used. In group A, all decisions on therapy was made using information downloaded from the flash glucose monitoring sensor and in Group B decisions was made using capillary glucose values entered by the nurses in the diabetic chart. Achieving standard targets of blood glucose control which is to keep glucose values in hospital between 130-180 mg/dl (in non-critical patients) while avoiding hypoglycaemia was encouraged.

Outcome assessments

Primary Outcome- Blood glucose control

Outcomes were only assessed after 48 hours of admission. This was to allow sufficient time for therapeutic decisions to be made and for these decisions to have an impact on glucose control. Outcomes were assessed using capillary glucose measurements on day 3 to day 5 after admission. To standardize outcomes on both arms, patients in both Group A and Group B had a standard 5 point capillary glucose measurement done per day (Fasting, Pre-Lunch, Pre-dinner, Pre-bed and 2-3 am glucose) using (ACCU-CHEK, Performa, Model NC) glucometer for 48 hours. This was also done by the ward nurses but was entered into a special **outcome assessment sheet (OAS)** in addition to the standard diabetes sheet. The outcome assessment sheet was retained by the investigator while the diabetes sheet remained in the patient records.

Ten capillary glucose values was obtained in each patient over 48 hours. Optimal glucose values were between 71-199 mg/dl. Glucose control was expressed as percentage of capillary glucose values which are optimal. For e.g. if over 48 hours 4 out of 10 glucose values were between 71-199 mg/dl then glucose control would be expressed as 40%. Values of ≤ 70 were considered hypoglycemic and values ≥ 200 mg/dl were considered in hyperglycemic range.

Secondary outcomes

1. Hypoglycaemia assessments

All hypoglycemic episodes after 48 hours of admission till discharge were noted. Hypoglycemic episodes (blood glucose ≤ 70mg) were classified as symptomatic and asymptomatic. Symptomatic hypoglycaemia were further classified as mild (only autonomic symptoms),moderate (autonomic and neuroglycopenic symptoms) and severe (requiring/ assistance). Episodes occurring after completing dinner and before 7 am in the morning were classified as nocturnal hypoglycemic episodes. Hypoglycemic episodes were recorded by the nurses on the OAS and was treated with 15gms of simple quick acting

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carbohydrates followed by 15 gm of complex carbohydrates after recovery.

2. Duration of hospital stay was recorded from patient records and was noted in days
3. Blood glucose control on follow up was based on capillary sugar values obtained either a day before or on the day of first outpatient visit. Patients were encouraged to bring a fasting and post prandial glucose report. Fasting values of 70-130 and postprandial value less than 190 mg/dl were considered to be optimal.

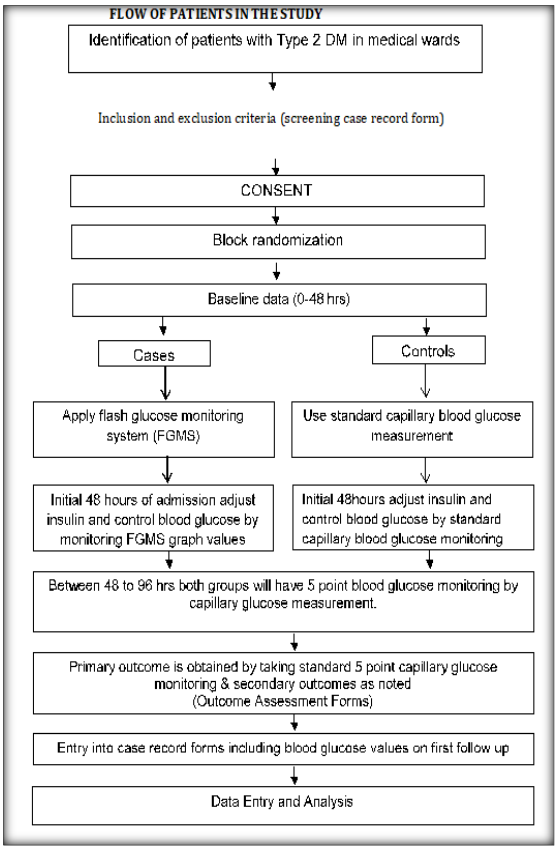
Sample Size Calculation

Assuming about a 60% improvement in glucose control, a sample size of 39 patients in each arm was calculated using Fleiss method ($\alpha = 5\%$, $\beta=80\%$).

To allow for drop-outs primarily because of unexpected early discharge it was planned to enroll 50 patients in each arm.

Statistical Analysis

The data was entered in Microsoft Excel and analyzed using SPSS (Statistical Package for Social Sciences) software version 22. T-test, chi-square and Pearson correlation test were used where appropriate, to assess the statistical difference of observed difference.



RESULTS

BASELINE CHARACTERISTICS (Table 1)

There were 23(46%) males and 22(44%) males in the case and control groups respectively. Majority of the patients were between the ages of 50 and 70 years.There were only 12(24%) cases and 9(18%) controls with BMI in the normal range of 23-24.9 kg/m^2.There were 6 patients in both the groups with BMI of more than 30 kg/m^2. Majority of the patients in both groups had a BMI ranging between 25-30kg/m^2. There were 40(80%) cases and 35(70%) controls with Diabetes mellitus of more than 5 years duration. Majority of the patients had a duration of diabetes of more than 10 years.

Hypertension was the commonest comorbidity present in 28(56%) patients in both groups followed by IHD in 22(44%) and 15(30%) cases and controls respectively. There were 10(20%) cases and 5(10%) controls on only insulin therapy for management of Diabetes mellitus. Majority of the patients in both groups were on OHA's. There were 27(54%) cases and 25(50%) controls with serum creatinine values of ≥1.2mg/dl.There were 8(16%) cases and 12(24%) controls with e GFR of less than 30ml/min/1.73m^2

Mean e GFR in Cases: 64.674 ml/min/1.73m^2

Mean e GFR in Controls: 63.44 ml/min/1.73m^2

There were 20(40%) cases and 21(42%) controls with RBS of less than 200mg/dl on admission. RBS of more than 400mg/dl on admission were present in 11(22%) and 14(28%) cases and controls respectively. There were only 3(6%) cases and 4(8%) controls with HbA1c of less than 6.5%. There were 29(58%) patients in both groups with HbA1c values of ≥9%. Urinary tract infection was the commonest infection diagnosed on admission, in 14(28%) cases and 18(36%) controls.

After 48 hours of blood sugar monitoring using either the Libre flash glucose monitor in the cases or atleast 3 glucometer readings per day in the controls, 5-point blood sugar monitoring using glucometer was continued in both groups for another 48 hours as follows

1) Fasting
2) Prelunch
3) Predinner
4) 2-hour post dinner
5) 2 AM

Insulin doses were administered accordingly and following were the results of the blood glucose values obtained.

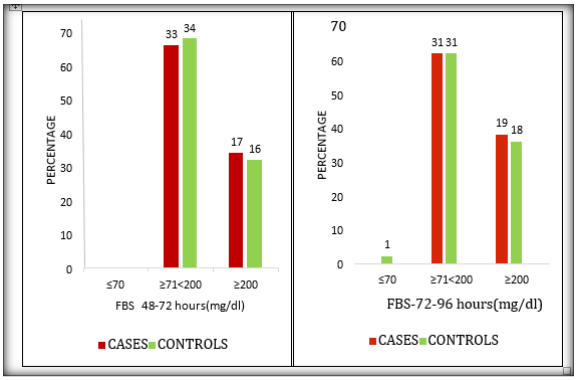


Table 2 and figures 2(A) and 2(B) show the distribution of FBS values between 48 to 96 hours after admission amongst the cases and controls.

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There was 1 patient in the control group who had hypoglycaemia between 72 to 96 hours. When the FBS of both groups were compared, at 48 to 72 hours (p= 0.877) and between 72 to 96 hours (p=0.333), there was no statistically significant difference found between them.(Table 2 and figures 2(A) and 2(B))

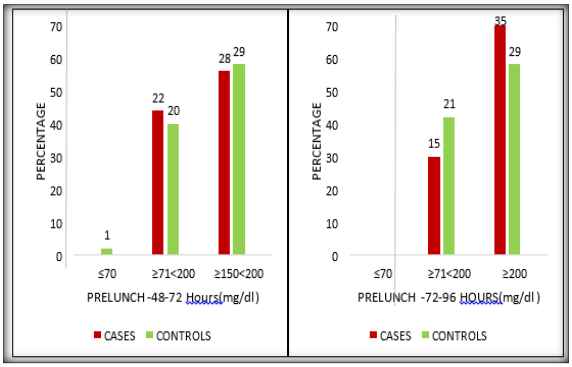

Table 3 and Figure 3(A) And (B): Pre-lunch Blood Glucose Values 48 to 96 Hours After Admission- Cases and Controls

There was 1(2%) patient in the control group who had hypoglycaemia between 48-72 hours.
However, there were 22(44%) cases compared to 20(40%) controls who had pre-lunch blood sugars within 71-200mg/dl at 48-72 hours.
However, at 72 to 96 hours, there were more cases i.e. 35 (70%) as compared to controls i.e. 29 (58%) with pre-lunch blood sugars ≥ 200mg/dl.
The p value at 48 to 72 hours was 0.62 and that at 72 to 96 hours was 0.898, which were not found to be statistically significant.(Table 3 and Figure 3(A) And (B))

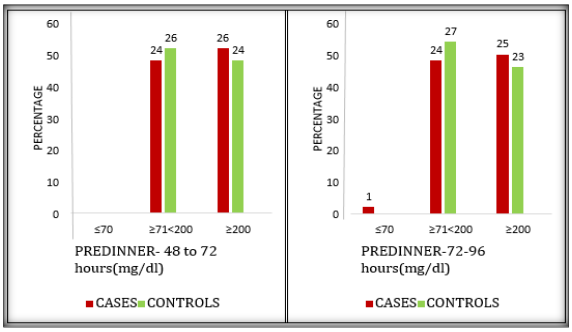

Table 4 and Figures 4(A) and (B): Predinner Blood Glucose values 48 to 96 hours After Admission-Cases and Controls

One of the cases had hypoglycaemia between 72 to 96 hours.
Pre-dinner blood glucose values of ≥200mg/dl between 48 to 72 hours were present in 24(48%) and 26(52%) cases and controls respectively.
At 72 to 96 hours, pre-dinner blood glucose values of ≥200mg/dl were present in 25(50%) and 23(46%) cases and controls respectively.
The p value at 48 to 72 hours was 0.873 and that at 72 to 96 hours was 0.941, which were not found to be statistically significant.(Table 4 and Figures 4(A) and (B))

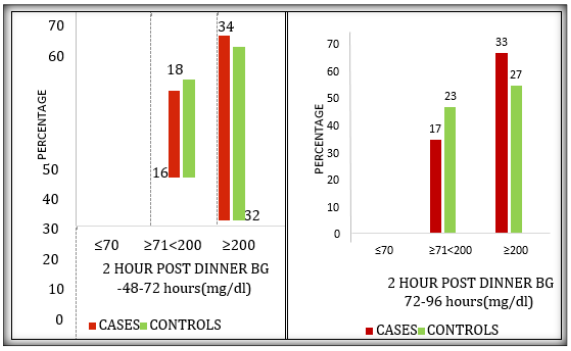

Table 5 and Figure 5 (A) and (B): 2 Hour Post Dinner Blood Glucose values 48 To 96 hours after Admission-Cases and Controls

The 2-hour post dinner blood glucose values of ≥200mg/dl were present in
34(68%) and 33(66%) cases as compared to 32(64%) and 27(54%) controls at 48 to 72 hours and 72 to 96 hours respectively.
The p value at 48 to 72 hours was 0.124 and that at 72 to 96 hours was 0.433, which were not found to be statistically significant.(Table 5 and Figure 5 (A) and (B))

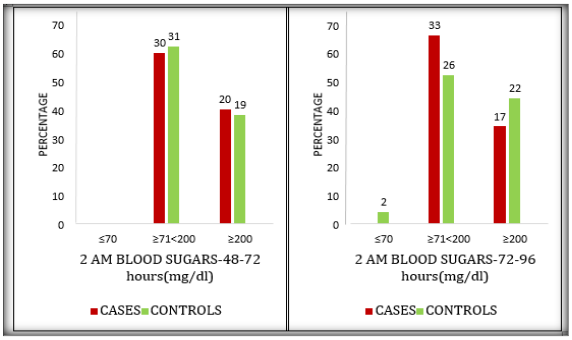

Table 6 and Figure 6(A) and (B): 2 Am Blood Glucose Values 48 To 96 Hours After Admission - Cases and Controls

The 2 AM blood glucose values of ≥200mg/dl were present in 20(40%) and 17(34%) of cases as compared to 19(38%) and 22(44%) of controls at 48 to 72 hours and 72 to 96 hours respectively.
There were 2(4%) patients in control group who had hypoglycaemia during72 to 96 hours after admission.
The p value at 48 to 72 hours was 0.694 and that at 72 to 96 hours was 0.586, which were not found to be statistically significant.(Table 6 and Figure 6(A) and (B))

Primary Outcome

Primary outcome was measured as the number of blood glucose values within the optimal range ie ≥71 to <200 mg/dl.

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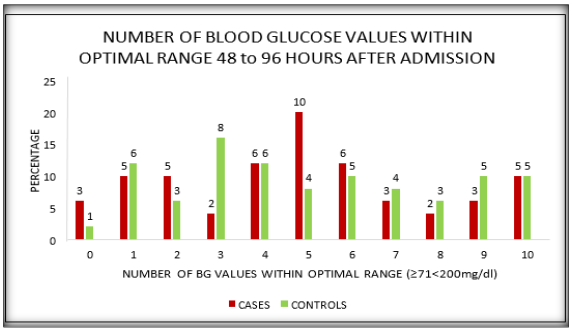

Figure 7: Number of Times Blood Glucose Values Within the Optimal Range Between 48-96 Hours After Admission

Table 7 and figure 7 shows the number of times the blood glucose values were within the optimal range (≥71<200 mg/dl), 48-96 hours after admission amongst cases and controls.

There were 29(58%) cases and 26(52%) controls whose blood glucose values were 50% of the time (5/10 readings) within the optimal range.

However, there were 5(10%) cases and controls who had all the blood glucose values (10/10 readings) within the optimal range.

The p value was 0.771 and not significant.

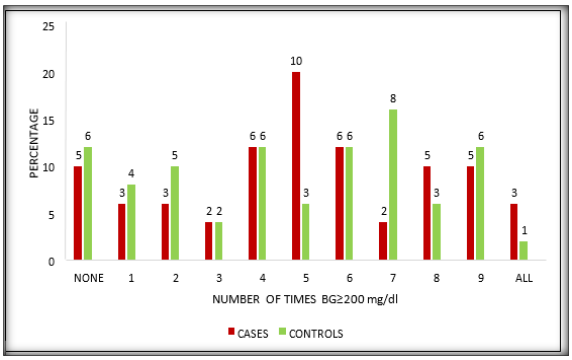

Figure 8: Number of Blood Glucose Values in The Hyperglycemic Range, 48 To 96 Hours After Admission

Table 8 and figure 8 shows the distribution of the number of times the blood glucose values were in the hyperglycaemic range (≥200 mg/dl), 48-96 hours after admission amongst cases and controls.

There were 31(62%) cases and 27(54%) controls whose blood glucose values were 50% of the time (5/10 readings) in the hyperglycaemic range.

There were 3(6%) cases and 1(2%) controls who had all the blood glucose values (10/10 readings) in the hyperglycaemic range.

The p value was 0.7 and not significant.

HYPOGLYCEMIA

Hypoglycaemia between 48 -96 hours was reported only once in the cases whereas it was reported 4 times in the control group and all these episodes were asymptomatic hypoglycaemia.

The p value was 0.171 and not significant.

NUMBER OF DAYS IN HOSPITAL

There were 20(40%) cases and 10(20%) controls who were admitted for less than 6 days in the hospital. p value: 0.992.

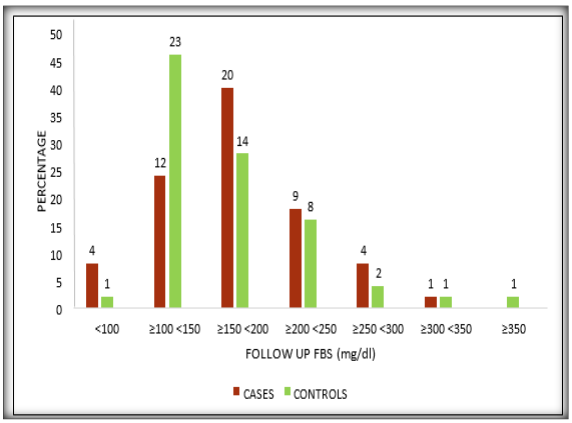

Figure 9: Follow Up Fasting Blood Glucose Values (OPD Visit) - Cases and Controls

Mean FBS: 178.82mg/dl (Cases)

Mean PPBS: 170.42mg/dl (Controls)

There were 34 (68%) cases and 26(52%) controls with FBS values ≥150 mg/dl during their OPD visit.

The correlation between the follow up FBS in both groups was not found to be statistically significant (p value was 0.178).(Figure 9)

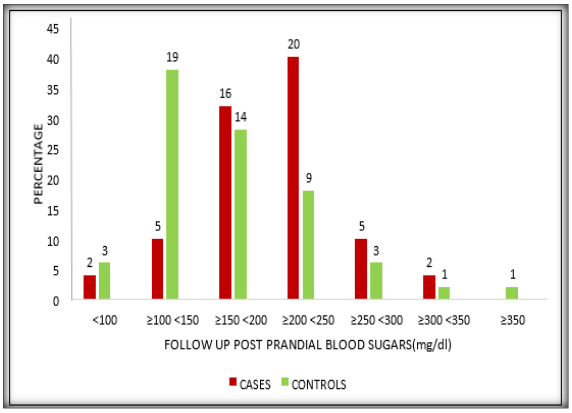

Figure 10: Follow Up Post Prandial Blood Sugars (OPD Visit) - Cases and Controls

Mean PPBS :205.82mg/dl(Cases)

Mean PPBS :224.54mg/dl (Controls)

There were 23 (46%) cases and 36(72%) controls with PPBS values less than 200mg/dl during their OPD visit. The correlation between the follow up PPBS in both groups was not found to be statistically significant (p value was 0.123).(Figure 10)

Table 1: Baseline Characteristics

	CASES (N=50)	CONTROLS (N=50)	p value
Gender	M(23) :F(27)	M(22):F(28)	0.841

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Age (years) Mean ± SD	61.5 ± 11.5	59.7 ± 11.6	0.43
BMI(kg/m2) Mean ± SD	25.6 ± 4.0	25.4 ± 5.41	0.835
Duration of Diabetes mellitus(years) Mean ± SD	12.6±9.43	8.8 ± 7.4	0.031
Serum creatinine(mg/dl) Mean ± SD	1.5±1.03	1.45±0.93	0.725
eGFR(ml/min/1.73m2) Mean ± SD	64.6±40.87	63.4±35.74	0.997
RBS on admission(mg/dl) Mean ± SD	266.5±126.5	264.6±141.4	0.94
HbA1c (%) Mean ± SD	10.21 ± 2.97	9.7 ± 2.85%	0.39

Table 2: FBS Values 48 To 96 Hours After Admission- Cases and Controls

FBS (mg/dl)	48-72 hours		P value	72-96 hours		P value
	Cases	Controls		Cases	Controls	
≤70	-	-		-	1(2%)	
≥71<200	33(66%)	34(68%)	0.832	31(62%)	31(62%)	0.598
≥200	17(34%)	16(32%)		19(38%)	18(36%)	

Table 3: Pre-lunch Blood Glucose Values 48 To 96 Hours After Admission- Cases and Controls

Pre-lunch BG (mg/dl)	48-72 hours		P value	72-96 hours		P value
	Cases	Controls		Cases	Controls	
≤70	-	1(2%)		-	-	
≥71<200	22(44%)	20(40%)	0.573	15(30%)	21(42%)	0.211
≥200	28(56%)	29(58%)		35(70%)	29(58%)	

Table 4: Pre-Dinner Blood Glucose Values 48 To 96 Hours after Admission-Cases and Controls

Predinner BG (mg/dl)	48-72 hours		P value	72-96 hours		P value
	Cases	Controls		Cases	Controls	
≤70	-	-		1(2%)	-	
≥71<200	24(48%)	26(52%)	0.689	24(48%)	27(54%)	0.533
≥200	26(52%)	24(48%)		25(50%)	23(46%)	

Table 5: 2 Hour Post Dinner Blood Glucose Values 48 To 96 Hours After Admission-Cases and Controls

2 hour post dinner BG (mg/dl)	48-72 hours		p value	72-96 hours		p value
	Cases	Controls		Cases	Controls	
≤70	-	-		-	-	
≥71<200	16(32%)	18(36%)	0.673	17(34%)	23(46%)	0.221
≥200	34(68%)	32(64%)		33(66%)	27(54%)	

Table 6: 2 Am Blood Glucose Values 48-96 Hours After Admission - Cases and Controls

2 A M blood glucose(mg/dl)	48-72 hours		p value	72-96 hours		p value
	Cases	Controls		Cases	Controls	
≤70	-	-		-	2(4%)	
≥71<200	30(60%)	31(62%)	0.838	33(66%)	26(52%)	0.176
≥200	20(40%)	19(38%)		17(34%)	22(44%)	

Table 7. Number of Times Blood Glucose Values Within the Optimal Range (≥71<200 Mg/Dl) Between 48-96 Hours After Admission

Number of BG values within optimal range (≥71 <200mg/dl)	Cases	%	Controls	%
0	3	6	1	2
1	5	10	6	12
2	5	10	3	6
3	2	4	8	16
4	6	12	6	12
5	10	20	4	8
6	6	12	5	10
7	3	6	4	8
8	2	4	3	6
9	3	6	5	10
10	5	10	5	10

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Table 8: Number of Blood Glucose Values in The Hyperglycemic Range (≥200 Mg/Dl), Between 48 To 96 Hours After Admission

Number of BG values in hyperglycemic range(≥200 mg/dl)	Cases	%	Controls	%
0	5	10	6	12
1	3	6	4	8
2	3	6	5	10
3	2	4	2	4
4	6	12	6	12
5	10	20	3	6
6	6	12	6	12
7	2	4	8	16
8	5	10	3	6
9	5	10	6	12
10	3	6	1	2

Table 9: RESULTS

	CASES (N=50)	CONTROLS (N=50)	p value
FBS :48-72hours Mean ± SD(mg/dl)	177.1 ± 72.6	172.3 ± 63.8	0.877
FBS :72-96 hours Mean ± SD(mg/dl)	195.9± 82.6	177 ± 64.3	0.333
Pre-lunch BG : 48 to 72 hours Mean ± SD(mg/dl)	220.9 ± 82	213.1 ± 75.3	0.62
Pre-lunch BG : 72 to 96 hours Mean ± SD(mg/dl)	226.2±74.2	224.3 ± 77.8	0.898
Pre-dinner BG : 48 to 72 hours Mean ± SD(mg/dl)	209.9±83.4	207.2±85.1	0.873
Pre-dinner BG : 72 to 96 hours Mean ± SD(mg/dl)	212.2±85.9	211±78.1	0.941
2 hour post dinner BG 48 to 72 hours Mean ± SD(mg/dl)	241.7±87.2	216.8±72.5	0.124
2 hour post dinner BG 72 to 96 hours Mean ± SD(mg/dl)	226.5 ± 66.8	215.1 ± 77.4	0.433
2 AM BG: 48 to 72 hours Mean ± SD(mg/dl)	200.5 ± 92.4	180.1 ± 57.9	0.694
2 AM BG 72 to 96 hours Mean ± SD(mg/dl)	179.2 ± 50.2	185.8± 67.9	0.586
Primary outcome- BG values in optimal range (%) Mean ± SD	49 ± 29.3	51.4± 29.9	0.771
BG values in hyperglycaemic range (%) Mean ± SD	50.8 ± 29.5	47.8 ± 30.5	0.7
BG values in hypoglycaemic range (%) Mean ± SD	0.2 ± 1.4	0.8 ± 2.7	0.171
Duration of hospital stay (days) Mean ± SD	8.2 ± 4.1	7 ± 1.9	0.992
Follow up FBS Mean ± SD (mg/dl)	178.2± 54.9	170.4 ± 58.1	0.178
Follow up PPBS Mean ± SD (mg/dl)	205.8 ± 49.4	224.5 ± 69.1	0.123

DISCUSSION

The primary outcome of the study was to compare blood glucose control in patients with Type 2 Diabetes mellitus managed using flash glucose monitoring versus standard capillary glucose measurements and secondary outcomes were to compare in-hospital hypoglycemic episodes, total days in hospital and blood glucose control on first follow up in patients managed using flash glucose monitoring versus standard capillary glucose measurements.

Gender Distribution

In this study, the male to female ratio was 0.85 and 0.78 in cases and controls respectively.However in the study by Haak et al, on Flash Glucose-Sensing Technology as a Replacement for Blood Glucose Monitoring on the management of Insulin treated Type 2 Diabetes between March 13 and October 15, 2014, there were more males in both the case (63%) and control group(75%).[10]

Another study by M Reddy et al, was conducted in the United Kingdom (UK), where participants were randomly assigned to CGM (Dexcom G5) or flash glucose monitoring (Abbott Freestyle Libre) in a 1 :1

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ratio using an online randomization tool. In this pilot study 20 subjects were enrolled in each group with a total of 24 males and 16 females.[11]

Age Distribution

Majority of the patients in this study were between ages of 50 and 70 years.In a pilot study by M Reddy et al conducted in the United Kingdom (UK), the median age was found to be 49.5 years.

In the study by Haak et al, the mean age was found to be 59.0 ± 9.9 years in the cases and 59.5 ± 11.0 years in the controls.

BMI Distribution

In this study there were only 12(24%) cases and 9(18%) controls with BMI in the normal range of 23-24.9 kg/m2.There were 6 patients in both the groups with BMI of more than 30 kg/m2.In the study by Haak et al the BMI of the cases was 33.1 ± 6.2 kg/m2 and that of controls was 33.3 ± 5.5 kg/m2

Duration Of Diabetes Mellitus

In this study there were 40(80%) of cases and 35(70%) of controls with Diabetes mellitus of more than 5 years with majority i.e. 62% of cases and 46% of controls having a duration of diabetes of more than 10 years.

Haak et al, in their study noted the mean duration of diabetes mellitus to be 17 ± 8 years in cases and 18 ± 8 years in controls.

M Reddy et al in their study found the mean duration of diabetes to be 30 years.

Comorbidities

Hypertension was the commonest comorbidity present in 28(56%) in both groups followed by IHD in 22(44%) and 15(30%) in cases and controls respectively. There were 11(22%) patients in both groups with CKD.

Current Medications for Diabetes

Majority of the patients in this study were on OHA's for management of Diabetes mellitus{29(64.4%) cases and 38(84.4%) controls}.In a study conducted by Banshi Saboo et al, in Gujarat to demonstrate glycemic variability in type 2 diabetic patients using flash glucose monitoring majority of the patients i.e. 36.11%, were on combination of Basal Insulin and OHA's.[12]

RBS on Admission

In this study, RBS of more than 400mg/dl on admission was present in 11(22%) and 14(28%) cases and controls respectively with a mean RBS of 266.56mg/dl for cases and 264.66mg/dl for controls.

In a randomised control trial by Stuart Weinzimer et al,[13] evaluating CGM in children, adolescent and adult with Type 1 diabetes mellitus patients the mean random blood sugar was 157±25 mg/dl in patients with age more than 25 years.

HbA1c

In this study, there were only 3(6%) cases and 4(8%) controls with HbA1c of less than 6.5%. The mean HbA1c was 10.21%.

Haak et al, found the mean HbA1c to be 8.74% in cases and 8.8% in controls.

M Reddy et al in their study conducted on people with Type 1 Diabetes Mellitus found the mean HbA1c of the patients in the study to be 7.3 %. As an outcome of the study, it was noticed that both CGM and flash glucose monitoring improved HbA1c.

ADMITTING DIAGNOSIS

In this study there were 14 (28%) cases and 18(36%) controls who were diagnosed with urinary tract infection.

In this study, after 48 hours of blood sugar monitoring in both cases and controls, the 5 point blood glucose monitoring was continued using a glucometer in both groups.

The fasting blood glucose in both the case and control groups were comparable at 48 to 72 hours (p value: 0.877) and 72 to 96 hours (p value: 0.333), and the p value was not significant. (Table 2, figure 2(A) and (B))

The Prelunch blood glucose in both groups were comparable at 48 to 72 hours (p value: 0.62) and 72 to 96 hours (p value: 0.898), and the p value was not significant. Prelunch hypoglycaemia was present in 1(2%) patient of the control group between 48-72 hours (Table 3 and Figures 3(A) and (B)).

The Predinner blood glucose in both groups were comparable at 48 to 72 hours (p value: 0.873) and 72 to 96 hours (p value: 0.941), and the p value was not significant. Predinner hypoglycaemia was present in 1 patient in the case group between 72 to 96 hours. (Table 4, figure 4(A) and (B)).

The 2 hour post dinner blood glucose in both groups were comparable at 48 to 72 hours (p value: 0.124) and 72 to 96 hours (p value: 0.433), and the p value was not significant (Table 5, figure 5(A) and (B)).

The 2 AM blood glucose in both groups were comparable at 48 to 72 hours (p value: 0.694) and 72 to 96 hours (p value: 0.586), and the p value was not significant. Hypoglycaemia was noticed at 2 AM in 2(4%) patients of the control group between 72 to 96 hours after admission (Table 6, figure 6(A) and (B)).

Primary Outcome

The primary outcome of the study was to compare blood glucose control in patients with Type 2 Diabetes mellitus managed using flash glucose monitoring versus standard capillary glucose measurements. There were 29(58%) cases and 26(52%) controls whose blood glucose values were 50% of the time (5/10 readings) within the optimal range. There were 5(10%) cases and controls who had all the blood glucose values (10/10 readings) within the optimal range (Table 7 and figure 7). However the p value was 0.771 and not statistically significant.

However, in study conducted by Banshi Saboo et al, on 108 patients with Type 2 Diabetes Mellitus using Freestyle Libre Pro AGP sensor , the achievement of near to normal glycaemic status at the end of 14 days.

In the IMPACT study by Bolinder J et al,[14] in patients with Type 1 Diabetes mellitus, there was marked improvement in quality of glycemic control, time in target range and reduction in glycemic variability with the use of flash glucose monitoring.

Thabit et al. conducted a similar study on continuous glucose monitoring in hospitalized patients and

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observed that the proportion of time spent in the target glucose range was 59.8% in the cases using CGM and 38.1% in the control group. There was 21.8% difference observed in the percentage of time spent in the target range between cases and controls which was found to be statistically significant.[15]

Secondary Outcome

The secondary outcomes of the study were to compare in-hospital hypoglycemic episodes, total days in hospital and blood glucose control on first follow up in patients managed using flash glucose monitoring versus standard capillary glucose measurements.

There were 31(62%) cases and 27(54%) controls whose blood glucose values were 50% of the time (5/10 readings) in the hyperglycemic range. There were 3(6%) cases and 1(2%) controls who had all the blood glucose values (10/10 readings) in the hyperglycemic range (Table 8 and figure 8). However the p value was 0.7 and was not statistically significant.

In a randomised control trial by Stuart Weinzimer et al, evaluating CGM in children, adolescent and adult with Type 1 diabetes mellitus patients for 6 months, a decrease in time in the hyperglycemic range was observed in patients more than 25 years of age.

Hypoglycemia

Hypoglycaemia was reported only once in the cases whereas it was reported four times in control group and all these episodes were asymptomatic hypoglycaemia. The p value was 0.171 and was not found to be statistically
significant.

M Reddy et al conducted a study on 40 patients with Type 1 Diabetes mellitus, and noted that an 8-week intervention with CGM had a greater benefit in reducing time in hypoglycaemia compared with flash glucose monitoring in people with Type 1 diabetes and impaired awareness of hypoglycaemia and percentage time spent in target range.

In the IMPACT study conducted on 328 patients with Type 1 Diabetes mellitus using flash glucose monitoring for 6 months, the average time spent in hypoglycemia was reduced by 38%. There was a reduction in the number, duration, and magnitude of hypoglycaemia.

Haak et al, demonstrated similar results with the use of flash glucose monitoring in Type 2 Diabetics with reductions in the risk of hypoglycemia. Time in hypoglycemia reduced by 43% for intervention participants compared with controls

Similarly, in a study conducted by Banshi Saboo et al, in 108 patients with Type 2 Diabetes mellitus, a reduction in the frequency of hypoglycaemia by using flash glucose monitoring system was reported.

Number Of Days in Hospital

The total number of days spent in hospital amongst the cases and controls were comparable. There were 20(40%) cases and 10(20%) controls who were hospitalized for less than 6 days.

Summary

1) In this study, the male to female ratio was 0.85 and 0.78 in cases and controls respectively.
2) Majority of the patients were between the ages of 50 and 70 years in both groups. The mean age was 61.54 and 59.7 years for cases and controls respectively.
3) The mean BMI was 25.68 kg/m2 and 25.484 kg/m2 in the case and control group respectively.
4) Majority of the patients i.e. 62% of cases and 46% of controls, had a duration of diabetes of more than 10 years.
5) Hypertension was the commonest comorbidity present in 28(56%) in both groups followed by IHD in 22(44%) and 15(30%) in cases and controls respectively.
6) Majority of the patients amongst both cases and controls were on OHA's.
7) The mean random blood sugar (RBS) on admission was 266.56mg/dl and 264.66mg/dl in the cases and controls respectively.
8) The mean HbA1c in cases and controls was 10.71% and 9.74% respectively.
9) Urinary tract infection was the commonest infection diagnosed on admission, in 14(28%) cases and 18(36%) controls.
10) The fasting blood glucose in both the case and control groups were comparable at 48 to 72 hours (p value: 0.877) and 72 to 96 hours (p value: 0.333).
11) The prelunch blood glucose in both groups were comparable at 48 to 72 hours (p value: 0.62) and 72 to 96 hours (p value: 0.898).
12) The Predinner blood glucose in both groups were comparable at 48 to 72 hours (p value: 0.873) and 72 to 96 hours (p value: 0.941).
13) The 2 hour post dinner blood glucose in both groups were comparable at 48 to 72 hours (p value: 0.124) and 72 to 96 hours (p value: 0.433).
14) The 2 AM blood glucose in both groups were comparable at 48 to 72 hours (p value: 0.694) and 72 to 96 hours (p value: 0.586)

Primary outcome

15) There were 29(58%) cases and 26(52%) controls whose blood glucose values were 50% of the time (5/10 readings) within the optimal range. However the p value was 0.771 and not statistically significant.
16) There were 5(10%) patient each in the case and control group who had all the blood glucose values (10/10 readings) within the optimal range.

Secondary outcome

17) There were 31(62%) cases and 27(54%) controls whose blood glucose values were 50% of the time (5/10 readings) in the hyperglycemic range. The p value was 0.7 and not statistically significant. ii. There were 3(6%) cases and 1(2%) controls who had all the blood glucose values (10/10 readings) in the hyperglycemic range.
18) Hypoglycaemia was reported only once in the cases whereas it was reported four times in the

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controls and all these episodes were asymptomatic hypoglycaemia. The p value was 0.171 and not statistically significant.

19) There were 20 (40%) cases and 10 (20%) controls who were admitted for less than 6 days in the hospital.
20) The correlation between mean Fasting blood glucose values amongst the cases and controls on OPD visit was 178.82 and 170.42mg/dl respectively, which was not found to be statistically significant (p value was 0.178)
21) The correlation between mean PPBS values amongst the cases and controls on OPD visit was 205.82 and 224.54mg/dl respectively, which was not found to be statistically significant (p value was 0.123).

CONCLUSION

1) In this study, no significant difference in the glycaemic control was found using the flash glucose monitor compared to standard capillary glucose monitoring.
2) However, Ambulatory glucose profile helps in reducing hypoglycemic events.
3) As hypoglycemia is the major limiting factor in the glycemic management and is considered as one of the greatest challenges in good glycemic targets in diabetic patients, the flash glucose monitoring helps in reducing the frequency of hypoglycemic episodes.

Limitations of this study

1) The study analysed glycaemic control using flash glucose monitoring over a short duration of time.
2) Flash glucose monitoring patches are expensive comparing to other methods of glucose monitoring.

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