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FROM PREDIABETES TO DIABETES: A CRITICAL ANALYSIS OF DIAGNOSTIC PARAMETERS IN GUJRANWALA'S POPULATION, PUNJAB, PAKISTAN

Muhammad Awais[1], Kashif-Ur-Rehman[2], Naeem Rasool[1], Hafiz Muhammad Aamir Farooq[3], Muneeb Sarfraz[4], Muhammad Mubashar Beig[5*]

[1]Department of Pharmacy, Al-Shifa Institute of Health Sciences, Narowal
[2]School of Biochemistry, Minhaj University, Lahore
[3]Department of Operation Theatre Technology, Al-Shifa Institute of Health Sciences, Narowal
[4]Combined Military Hospital, Lahore
[5*]Institute of Microbiology, University of Veterinary and Animal Sciences, Lahore

***Corresponding Author:** Muhammad Mubashar Beig
*E-mail: mubasharbeig98@gmail.com

Abstract:
In Pakistan, diabetes is a serious public health concern, as the country has the highest death rate (35.5%) from complications connected to diabetes among those under the age of 60. Continuous blood glucose monitoring is necessary for effective diabetes care in order to avoid or prevent complications and diabetes related morbidities. This study seeks to compare glycemic control, by assessing HbA1c, Fasting Blood Glucose (FBG), and Random Blood Glucose (RBG) values in various patient groups. Using a longitudinal study design, 50 participants were recruited and divided into four groups: Group I was designated as the control group, Group II as prediabetics, Group III as type 1 diabetics, and Group IV as type 2 diabetes. Three months of HbA1c, FBG, and RBG measurements were used to evaluate the patient's state of glucose management. According to the International Diabetes Federation (IDF) and American Diabetes Association (ADA) standards, glucose control was divided into three categories: good glucose control (GGC), moderate glucose control (MGC), and poor glucose control (PGC). The average HbA1c levels improved dramatically in all groups, according to the results: in Type 1 diabetes, they decreased from 9.4% to 6.7%; in Type 2 diabetes, they decreased from 8.2% to 7.1%; and in prediabetics, they decreased from 6.1% to 5.8%. While RBG levels were slightly increased, FBG levels stayed within the usual range. In conclusion, proper assessment and maintenance of glycaemic control in diabetic patients require regular monitoring of HbA1c in addition to FBG and RBG measures.

Keywords: Diabetes, HbA1c, FBG, RBG, Glycemic Control

INTRODUCTION:

One of the most concerning public health concerns of the twenty-first century is the diabetes epidemic, particularly among lower middle-class people nations (Ogurtsova, da Rocha Fernandes et al. 2017). It was estimated that the prevalence of diabetes in these countries would rise by 67% between 2010 and 2030 (Shaw, Sicree et al. 2010). An estimated 537 million adults globally, or 10.5% of all adults in this age range, suffer from diabetes. Globally, the number of persons with

diabetes will rise from 643 million in 2030 to 783 million in 2045. Diabetes was the cause of 6.7 million fatalities in the year 2021 (Atlas 2022).

In South East Asian region of world ninety million individuals (11%) have diabetes; estimates suggest that number will increase to 113 million by 2030 and 151 million by 2045. Over half of persons do not receive a diagnosis, which will result in 747,000 diabetes-related deaths in 2021 and a ten billion dollar cost burden. The IDF 10th edition states that for at least 20 years, the incidence of diabetes has been rising in South-East Asian (SEA) countries, and that current figures have surpassed all earlier projections (Atlas 2022). In the South Asian region, almost 122 million people were diagnosed with diabetes in 2021. This corresponds to a prevalence of 8.7%, 9.6%, 10.4%, 11.3%, 14.2%, and 30.8% in the following countries: Bangladesh, India, Nepal, Bhutan, Sri Lanka, and Pakistan (Subhan, Fernando et al. 2023).

Pakistan is the fifth most populous country in the world, with 243.7 million people, and accounts for 2.99% of all people on Earth. The nation's population density is 312 people per km^, with 34.7% living in cities, and its median age is 20.6 years (Worldometer 2024). In 2021, Pakistan had the highest death rate (35.5%) from complications related to diabetes among those under 60. Sindh has the highest diabetes incidence prevalence (32.3%) among Pakistani provinces, followed by Punjab (30.2%), Baluchistan (29.5%), and KPK (13.2%) (Ijaz, Ali et al. 2020). Unfortunately, about 25% (26.9%) of Pakistan's diabetic population remains undiagnosed nation (Welle 2022). Less than 1% of GDP is allocated to health care, which exacerbates the problem of undiagnosed diabetes due to the low quality and penetration of primary care services in the nation (Uddin, Ali et al. 2019).

The three forms of diabetes that are most commonly reported and researched are type 1 diabetes, type 2 diabetes, and gestational diabetes. Insulin-producing pancreatic cells are attacked by the immune system, which prevents the body from producing insulin, leading to type 1 diabetes. Elevated blood sugar levels result from glucose's inability to enter cells without insulin (Eisenbarth 1986). In type 2 diabetes, there is a chronic rise in blood glucose levels due to impaired or insufficient insulin efficacy. Even though type 2 diabetes is a serious and permanent condition, people can manage and live well with it if they receive the right care and treatment, which can reduce the risk of complications (Edelman 1998). Pregnancy-related high blood sugar levels that necessitate particular diet and exercise regimens are known as gestational diabetes, which is detected by a blood test at 24 to 28 weeks and usually goes away after delivery (Buchanan and Xiang 2005).

Diabetes management is the all-encompassing care and tactics used to successfully control blood glucose levels, reduce related risks, and improve the general health of people with diabetes. To maintain ideal glycemic control and avoid problems, this involves lifestyle changes, medication adherence, routine monitoring, and tailored interventions (Association 2022). Blood glucose monitoring (BGM) plays a critical role in the management of diabetes, particularly in non-insulin-using type 2 diabetics. Effective tracking and modification of treatment programs is facilitated by the monitoring of blood glucose levels (Weinstock, Aleppo et al. 2020). The development of continuous glucose monitoring (CGM) technology can improve overall glycemic management and lower the risk of hypoglycemia in diabetics. CGM offers real-time glucose readings, making it possible to better control blood sugar levels (Bolen, Tseng et al. 2016, Shrivastav, Gibson et al. 2018).

There are free amino acids residue accessible for binding to monosaccharides like glucose, fructose, and their derivatives, all structural and circulation proteins are susceptible to glycation in blood. Hemoglobin undergoes posttranslational alteration known as glycation. Glycated hemoglobin (HbA1C or A1C) is the product of non-enzymatic covalent interaction of valine, which is found at the N-terminal of beta globin, with glucose (Jeffcoate 2004). HbA1, which is made up of the charge-separated hemoglobin of a normal adult HbA0, can be further divided into its component portions, HbA1a1, HbA1a2, HbA1b, and HbA1c (Kilpatrick 2000). The capacity to reflect the cumulative glycemic history of the two to three months prior, HbA1c is a significant indicator of long-term glycemic management. In addition to offering a trustworthy indicator of persistent

hyperglycemia, HbA1c has a strong correlation with the likelihood of developing long-term diabetic problems (Sherwani, Khan et al. 2016). The hemoglobin biomarker's particular feature is used to estimate the average blood glucose levels over the preceding two to three months (Khan, Ola et al. 2014). The study attempts to evaluate glycemic management in individuals with diabetes and prediabetes through measures of fasting blood glucose, random blood glucose, and glycated hemoglobin A1C,. Additionally, the inter-reliability of these indicators is also assessed.

MATERIALS AND METHODS

Study design:

A transverse study design was adopted to investigate control of diabetes in patients of diabetes and prediabetes by measuring FBG, RBG and HbA1c in a period of three months from July to October, 2020. Patients were inducted in the study for collection of blood samples from a popular nursing center of Gujranwala that provide diabetes care services at clinics and homes. Four groups of participants are formed: Group I, the control group, Group II with the people suffering from prediabetes, Patients in Group III have Type 1 Diabetes, and Group IV was comprised of people with Type 2 Diabetes.

Ethical consideration:

All the ethical considerations were kept in mind while enrolling patients and during sampling. Sample size and integrity were given importance when blood samples were collected. Data related to diabetes and relevant health condition was collected from patients with their consent.

Glycemic Diagnostic Markers

This study evaluates glycaemic control by analysing multiple diagnostic markers. To assess long-term blood glucose control, the Glycated Haemoglobin A1c (HbA1c) test is performed twice, separated by three months (Arif, Rasheed et al. 2024). Over the course of three months, fasting blood glucose (FBG) levels are monitored every two weeks to offer regular insights into baseline glucose levels (Thmail, Hussain et al. 2023). In a similar vein, during the course of the three months, Random Blood Glucose (RBG) is measured every two weeks to track variations in glucose levels during the day. Together, these metrics make it easier to assess and contrast glycaemic control amongst various groups (Abduallah, Ahmed et al. 2024).

Table.1: Diagnostic Parameters, their frequency, and duration

Diagnostic Parameter	Frequency	Duration
HbA1c Test	Twice	3 months
Fasting Blood Glucose (FBG)	Fortnightly	3 months
Random Blood Glucose (RBG)	Fortnightly	3 months

Statistical Analysis:

SPSS 23 was used for statistical analysis of the data. Values of FBG, RBG and HbA1c were converted into categorical parameters like Good Glycemic Control (GGC), Moderate Glycemic Control (MGC) and Poor Glycemic Control (PGC) for all the subjects (Rizvi, Deeba et al. 2023). One way ANOVA test was applied to find variance among the groups of this study. Descriptive statistical analysis and paired t test was performed to analyze continuous parameters (Thomas, Moring et al. 2023).

Table.2: Criteria adopted for glycemic control assessment(Association 2023)

Parameters	Good Glycemic Control	Moderate Glycemic Control	Poor Glycemic Control
HbA1c	<6.5%	6.5 – 7.0 %	>7.0 %
FBG	<110 mg/dL	110 – 130 mg/dL	>130 mg/dL
RBG	<140 mg/dL	140 – 180 mg/dL	>180 mg/dL

RESULTS

Fast Blood Glucose:

Every two weeks, fasting blood glucose (FBG) levels were measured in order to evaluate the short-term glycemic management. With regard to Type 1 Diabetes, there was a discernible improvement over time; by the eleventh week, eight individuals had good control, up from just six at the start. Patients with type 2 diabetes experienced ups and downs, but overall their condition improved, with more showing satisfactory glycaemic control by the eleventh week. Patients with prediabetes mostly stayed in the good control group; there were not many changes to the moderate or poor control groups. Throughout the course of the trial, the control group's FBG levels were constantly stable and satisfactory, demonstrating the lack of problems connected to diabetes.

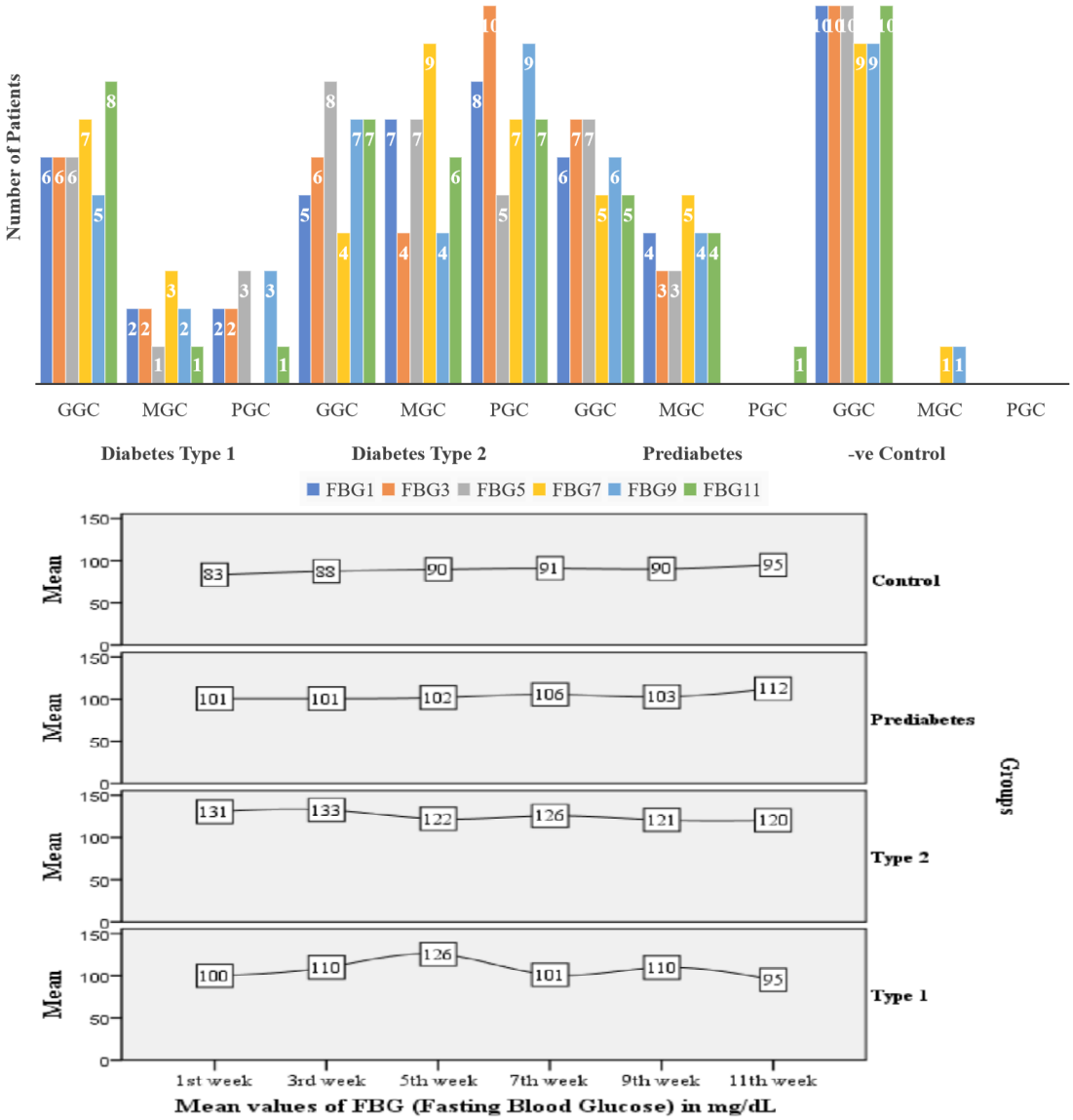


Figure 1: Graph comparing count of glycemic control between groups on the basis of Fortnightly FBG over the period of 3 months

Random Blood Glucose:

Without fasting, glycemic control was assessed using random blood glucose (RBG) readings, which represent changes in blood sugar in real time. Control of patients with Type 1 Diabetes varied greatly, with a major fraction fluctuating between poor and moderate control during 12 weeks. Patients with type 2 diabetes showed continuous variability in their RBG levels, and a considerable proportion of them continued to have poor control, particularly by the eleventh week, when 12 patients had not improved their control. Patients with prediabetes had RBG levels that were more variable than FBG, with occasional movements into poor control groups. Similar to the FBG results, the control group's RBG levels remained largely consistent and good during the course of the investigation, supporting the constancy of glycaemic management in people without diabetes.

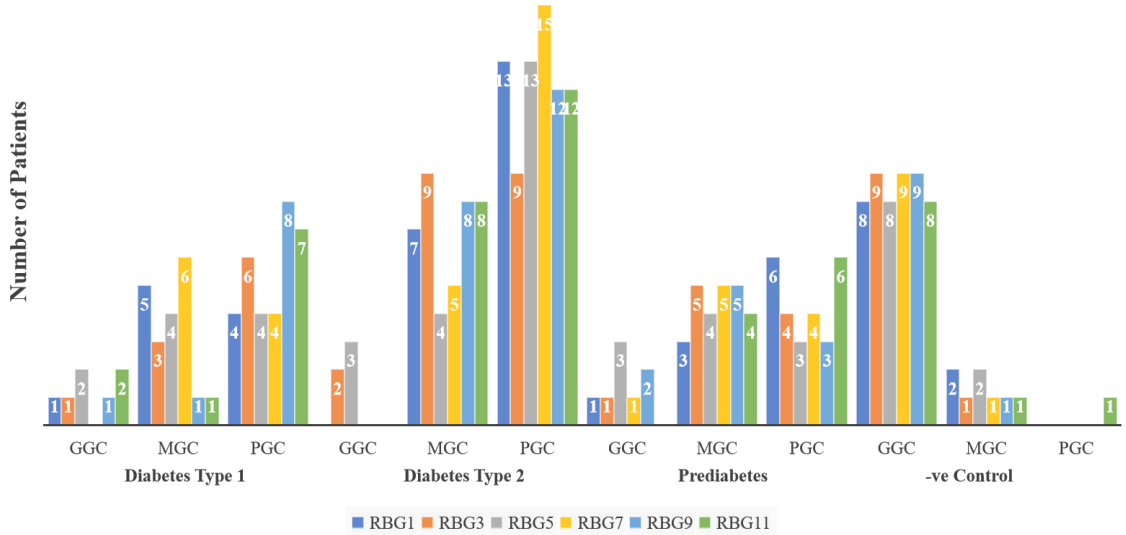
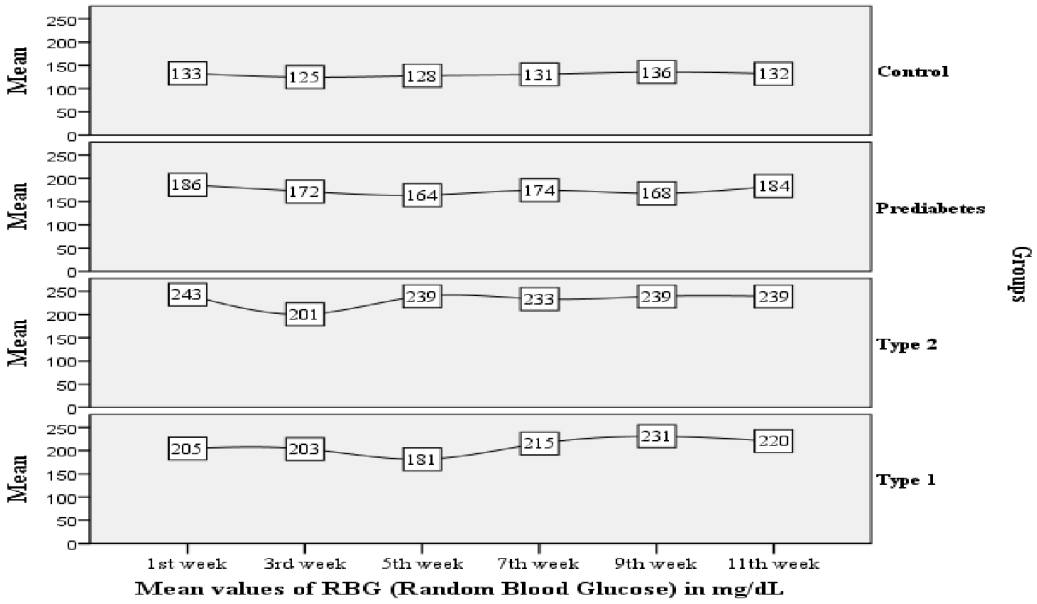


Figure 2: Graph comparing count of glycemic control between groups on the basis of Fortnightly RBG over the period of 3 months



Glycemic Hemoglobin control HbA1c:

At the beginning, all Type 1 Diabetes patients had poor glycemic control, which suggested insufficient control over blood glucose levels. But after three months, there was a noticeable shift in the patients' condition, with six out of ten falling into the category of good glycemic control.

Patients with type 2 diabetes also exhibited improvements: the number of patients in good control increased from 6 to 10, while the number of patients in poor control decreased from 12 to 8. Patients with prediabetes often had good control throughout the study, suggesting that early intervention techniques and successful management were in place. The control group continuously showed excellent glycemic control, indicating efficient maintenance free of the problems noted.

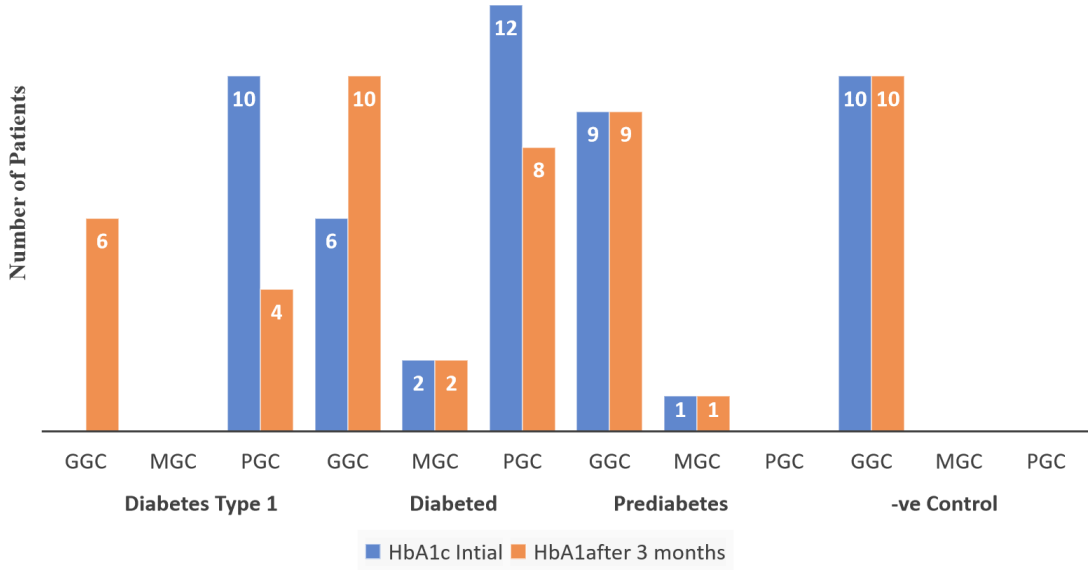
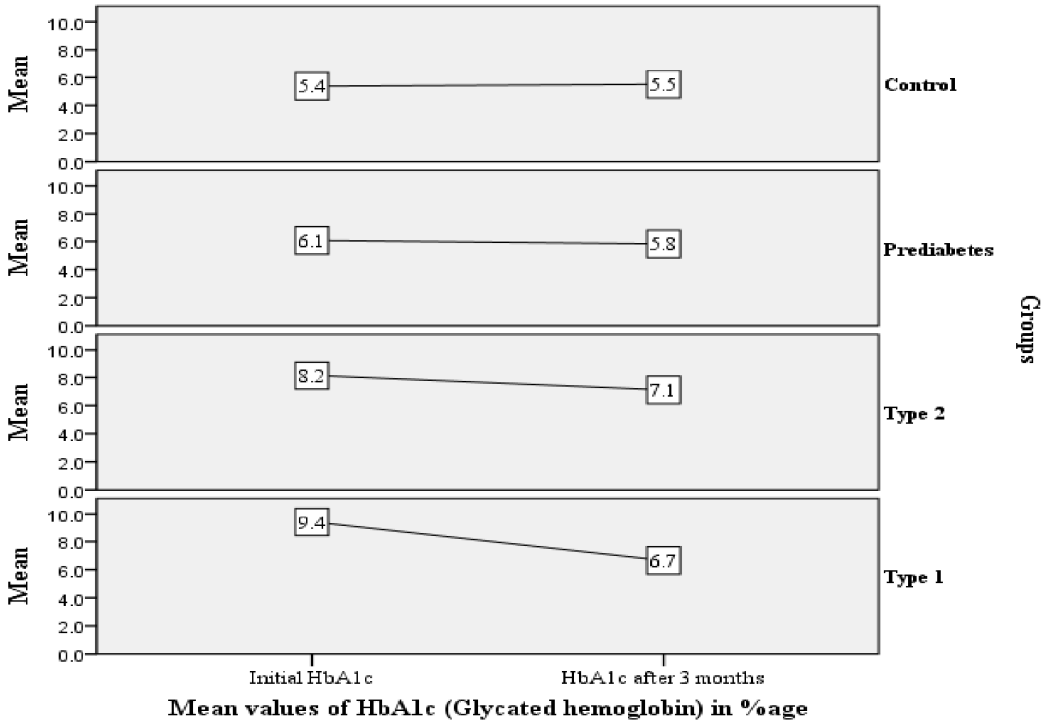


Figure 3: Graph comparing count of glycemic control between groups on the basis of Fortnightly HbA1c over the period of 3 months



DISCUSSION

Goal of diabetes management is to attain optimum glycemic control that help in prevention or delay of the complication of the diabetes like cardiovascular diseases, nephropathy and neuropathy (Kawa

2023). HbA1c is used as a diagnostic tool for diabetes and glycemic control is also evaluated by healthcare providers by using HbA1c but in resource poor settings FBG and RBG are used to evaluate glycemic control. There are certain limitations of HbA1c which can result in misinterpretation of the glycemic levels so medical practitioners use FBG and RBG values to adjust the medication plan of the patients of diabetes (Ghosh 2024).

44 % of the total subjects were having PGC according to initial HbA1c and only 24 % were having PGC after three months. Number of subjects with good glycemic control were higher according to HbA1c after three months as compared to HbA1c initially (70% vs 50 %) but number of subjects with moderate glycemic control were equal for both measured values of HbA1c as given in table 4.3. According to initial HbA1c all of the type 1 patients were having poor glycemic control but three months later 60 % of them were showing good glycemic control. Quarterly estimation of HbA1c during the year in type 1 patients is help in acquiring GGC (Yuan, Lai et al. 2014, Yuan, Zhou et al. 2023). Number of cases with good glycemic control were comparatively less in type 2 patients as compared to type 1 patients of the study population. This poor glycemic control is responsible for debilitating complications of diabetes and it is also linked with longer duration of diabetes, increased body weight and lack of regular physical activity (Mohamed 2023). In another study, similar type of results in population of Jordan were found with 65.1 % of the patients having PGC with HbA1c of more than 7.0 %, a study in Saudi population claimed 42 % type 2 patients achieved good glycemic control, 31% diabetic patients in UAE with HbA1c less than 7.0 % (King, Sheek-Hussein et al. 2023, Legese, Asres et al. 2023).

FBG (Fasting Blood Glucose) and RBG (Random Blood Glucose) were also measured fortnightly during three months of the study for 1^{st}, 3^{rd}, 5^{th}, 7^{th}, 9^{th} and 11^{th} week to evaluate glucose levels of the study population. Interestingly FBG values recorded relatively higher number of cases with good glycemic control as compared to RBG values. According to 5^{th} week FBG and RBG values number of subjects with good glycemic control were 31 and 16 respectively and similar trend was observed in the FBG and RBG data of rest of the weeks. It indicates that most of the patients have maintained their FBG within the normal range but they struggled to control their RBG. Post meal hyperglycemia or elevated RBG is common in both type 1 and type 2 patients of diabetes and many patients have elevated RBG despite having normal metabolic control as assessed by HbA1c (Bonora, Corrao et al. 2006). Previously it was thought that lowering of FBG is important for achieving optimum HbA1c but now it is established that controlling RBG is equally important like FBG (Ceriello, Colagiuri et al. 2008).

HbA1c is preferably used for diagnosis of diabetes and prediabetes but there are discrepancies in the diagnosis based on HbA1c versus FBG or RBG (Lee, Lee et al. 2019). Similarly HbA1c is gold standard for assessment of glycemic control in patients of diabetes but it shows disagreements when compared with FBG or RBG. In the present study kappa coefficient indicated poor agreement (0.177) or fair agreement (0.394) between initial HbA1c and FBG values of 11^{th} and 3^{rd} week. Similar type of agreement was found between initial HbA1c and RBG values of 11^{th} and 9^{th} week i.e. 0.144 and 0.454 respectively. Surprisingly low and negative values of kappa coefficient were noted for HbA1c after three months showing no agreement or poor agreement when compared with FBG or RBG values for glycemic control.

Assessment of glycemic control is usually done by measuring HbA1c and FBG and RBG but there is discordance between these parameters for diagnosis of diabetes as well as assessment of glycemic control (Kim, Hahm et al. 2015). Patients having good glycemic control according to HbA1c were found having poor glycemic control according to FBG or RBG. Sensitivity, specificity, PPV (positive predictive value) and NPV (Negative predictive value) of initial HbA1c and HbA1c after three months when compared with FBG and RBG showed wide range variations. Sensitivity of initial HbA1c ranged from 70.4% to 56.7% when compared with FBG 1^{st} week and FBG 11^{th} week respectively. Whereas when compared with RBG the sensitivity of initial HbA1c was found much better ranging from 80% to 100% for RBG 11^{th} week and RBG 7^{th} week respectively. Positive Predictive Value for initial HbA1c were showing much better when compared with FBG ranging up

to 88% whereas it was much lower 52% when compared with RBG. Negative Predictive Value for initial HbA1c were up to 45.5% and 81.8% when compared with FNG and RBG respectively. This disparity among the HbA1c and FBG and RBG is due to the fact that HbA1c do not indicate daily glycemic excursions it gives an average blood glucose of three months (Oyekemi Funke 2015).

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