

Research Article

Significant Differences in the Prevalence of Elevated HbA1c Levels for Type I and Type II Diabetics Attending the Parirenyatwa Diabetic Clinic in Harare, Zimbabwe

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Diabetics have chronically elevated glucose levels. High levels of glucose result in nonenzymatic formation of glycosylated haemoglobin (HbA1c). Therefore, elevated HbA1c is a good indicator of poorly controlled diabetes. We used the standard HbA1c method to determine glycemic control in diabetics attending a public health facility in Harare, Zimbabwe. Our study sought to assess the prevalence of elevated HbA1c amongst treated diabetics and compare the HbA1c levels by type of diabetes. The cross-sectional study was carried out at one of the main public health centres in Zimbabwe: the Parirenyatwa Group of Hospitals in Harare. Type I and type II diabetics were recruited and had their blood HbA1c levels measured. The standard one tailed proportion z test was used to test the hypothesis at 5% significance level. Combined prevalence of type I and type II diabetics with elevated HbA1c was 27%. There was no significant difference in levels of HbA1c by age and sex. Over half (54%) of Type I diabetics had elevated HbA1c, suggesting poor glycemic control. In contrast only 24% of the Type II diabetics studied had elevated HbA1c. The difference in proportion of Type I and Type II diabetics with elevated HbA1c suggestive of poor glycemic control was significant ($P = 0.0067$).

1. Introduction

According to the World Health Organization (WHO) diabetes mellitus is a state of chronic hyperglycaemia due to genetic and environmental factors. In Type 1 diabetes mellitus there is no production of insulin whereas in Type 2 diabetes mellitus there is insufficient insulin or cells do not respond to insulin present in the body (insulin resistance). The most frequent form is Type 2 diabetes (80% of cases) whilst Type 1 diabetes accounts for 10% of cases and specific diabetes such as gestational diabetes accounts for 5% of cases [1, 2].

In 2004 it was estimated that up to 3.4 million people died from diabetes and 80% of these deaths occurred in low and middle income countries such as Zimbabwe [3–5]. Half of the people who died as a result of diabetes were under the age of 70, 55% of them women [3–5]. Diabetes mellitus was generally considered to be a rare condition in

Africa before the 1990s. Evidence of increased incidence and prevalence of type 2 diabetes mellitus was provided by some epidemiological studies carried out in that decade [5–7]. Africa is experiencing a demographic and epidemiological transition with a rise in diseases like diabetes mellitus. Most reports published between 1959 and 1985 indicated a prevalence of diabetes below 1.4% with the exception of those from South Africa where higher prevalence was seen [5–7].

Different tests are used in diabetes mellitus patients and these include random and fasting blood glucose, oral glucose tolerance test, blood urea, blood hydrogen, urinary protein, blood insulin, blood fructosamine, and glycosylated haemoglobin (HbA1c) [8]. For diagnosis the oral glucose tolerance test (OGTT), fasting and random blood glucose tests are ideal. According to the WHO guidelines, if the plasma glucose is less than 5.5 mmol/L, then diabetes is highly unlikely [1]. A fasting plasma glucose of 7.0 mmol/L

or more or a random glucose of 11.1 mmol/L or more makes diabetes likely and the diagnosis is confirmed by a repeated abnormal test. If the fasting plasma glucose is between 5.5 and 6.9 mmol/L or between 5.5 and 11.0 mmol/L nonfasting an OGTT with 75 g anhydrous glucose should be done [1]. Blood hydrogen, blood urea, and urinary protein can also be used in diagnosis of diabetes but only as confirmatory tests for fasting, random blood glucose, and OGTT. Blood insulin is rarely measured in diagnosis of diabetes mellitus [1].

In the management and control of diabetes, blood glucose determined at the time of the clinic attendance can only give limited information and may not represent the overall closeness of control at other times. The glycosylated haemoglobin (HbA1c) test provides a better index of diabetic control than plasma glucose since it is not greatly affected by short-term fluctuations in plasma glucose [9]. HbA1c is a form of haemoglobin used primarily to identify the average plasma glucose concentration over prolonged periods of time (three to four months). In the normal 120-day lifespan of the red blood cell glucose molecules combine with haemoglobin forming HbA1c. In individuals with poorly controlled diabetes, increases in the quantities of the HbA1c have been noted. Once a haemoglobin molecule is glycosylated, it remains that way. HbA1c levels within the red blood cell reflect the average level of glucose to which the cell has been exposed during its life cycle [1, 8]. The American Diabetic Association and National Institute for Health and Clinical Excellence (NICE) both recommend that %HbA1c should be below 6.5 in nondiabetics and 7% in diabetics [10, 11].

The HbA1c test mainly measures level of glycemic control in diabetic patients. It has recently been added as a diagnostic test by the World Health Organization (WHO) but the test requires quality assurance and controls [11]. HbA1c recommended that cut-off point for diagnosing diabetes is 6.5% [11]. Traditionally, measuring HbA1c assesses the effectiveness of therapy by monitoring long term-plasma glucose regulation. Monitoring of glyco-genic status is considered a cornerstone of diabetes care and affects how physicians and patients adjust medical therapy as well as behavioural therapy (diet and exercise). It has been shown in a randomised study that when health care providers and patients are informed about the HbA1c results blood glucose control is improved. Simply knowing the results improves glycemic control, either through improved efforts by the patient or by the provider [12–14].

In a study done to determine the relationship of HbA1c levels to hospital admission of patients, it was found that the likelihood of admission increased with higher HbA1c levels. The number of admissions of diabetic patients with HbA1c levels in the range 10.8%–18.4% was higher with 5 481 admissions in a 3-year period compared with 2 566 admissions of patients with HbA1c levels in the reference region of 7.7%–8.1% [15]. One other study showed that an average HbA1c level of 7.2% resulted in a 76% reduction in retinopathy, a 60% reduction in neuropathy, a 50% reduction in kidney disease, and a 35% reduction in cardiovascular disease [16]. Another study in the United States of America demonstrated unequivocally that maintaining close to normal blood glucose levels significantly lowers

a person's risk of developing complications of diabetes mellitus [17].

A study by Gerstein et al. showed that high HbA1c levels are associated with increased risk of mortality [18] and this was partially explained by the fact that high HbA1c levels are associated with increased risk of diabetic macrovascular and microvascular complications [19, 20]. These may contribute to deteriorating kidney function. Anemia has also been suggested to account for increased risk of mortality associated with increased levels of HbA1c. The reference ranges for our study were <7% desirable, 7–9% suboptimal, and >9% poor based on literature [18–20].

Public health laboratories in Zimbabwe do not offer the HbA1c assay for diabetic patients. Many patients are from poor socioeconomic background and rely solely on public health facilities as they cannot afford private healthcare facilities. Thus, most Zimbabwean diabetics do not have any form of long-term monitoring of their blood glucose levels and are at a risk of having high levels of HbA1c without them or their health care providers knowing it. This study seeks to determine the prevalence of elevated HbA1c (a measure of poor glycemic control) in diabetics at Parirenyatwa Group of Hospitals Diabetic Clinic in Harare, Zimbabwe.

2. Materials and Methods

An analytical cross-sectional study was done on blood samples of diabetes mellitus patients attending Parirenyatwa Group of Hospitals Diabetic Clinic in Harare, Zimbabwe.

The minimum sample size (202) was calculated as $S = Z^2 pq/E^2$, where Z = test statistic, E = standard error, p = population proportion with desired characteristic, $q = 1 - p$, and S = minimum sample size:

$$S = \frac{1.645^2 \times 0.25 \times 0.75}{0.05^2} = 202.09. \quad (1)$$

Ethical clearance was given by the joint Parirenyatwa Hospital-University of Zimbabwe Ethics Committee, and permission to carry out the study was granted by the Clinical Director and Diabetics Clinic Staff. No patient names were used and samples were allocated a research number. Samples, results, and data collected were treated with strict confidentiality and were not accessible to unauthorized persons.

Sequential sampling technique was used to recruit diabetics eligible for the study who had come for routine checkup or monitoring at Parirenyatwa Group of Hospitals Diabetic Clinic. Blood samples were collected from eligible consenting diabetic patients. Blood samples in EDTA tubes were later spun in a centrifuge at 3000 rpm for five minutes in the Department of Medical Laboratory Sciences laboratory. The required amount of packed cells (25 microlitres) was aspirated into serum pots and samples were stored at 2–8°C.

Samples were then assayed at the Department of Medical Laboratory Sciences on the Mindray BS 120 Chemistry Analyzer. 500 microlitres of pretreatment solution was added to 25 microlitres of thawed samples and gently mixed with the cells. The samples were left to stand for five minutes after which the samples were loaded into the analyzer for processing.

TABLE 1: Descriptive measures in study population.

	HbA1c (%)	Age (years)
Mean	7.5	54
Median	6.8	55
S.D	2.92	14.21
Q1	5.2	44
Q2	9.5	64
Inter-Quartile Range	4.3	20
Range	3.4–16.7	19–80

TABLE 2: Reference range levels of long-term glucose control used in the study.

Level of long-term glucose control	Optimal	Suboptimal	Poor
HbA1c level	Desirable	Reasonable	Elevated
HbA1c percentage	<7%	7–9%	>9%

An enzymatic method was used to determine the levels of HbA1c in the blood samples. In the first reaction the concentration of haemoglobin is measured at absorbance of fixed wavelength. In a second reaction, fructosyl dipeptides are generated from the N-terminus amino groups of the beta chain of HbA1c by the reaction of protease enzyme. The fructosyl dipeptides react with fructosyl peptide oxidize (FPOX) to generate hydrogen peroxide. Hydrogen peroxide formed reacts with 10-(carboxymethylaminocarbonyl)-3,7-bis (dimethylamino) phenothiazine sodium salt to develop a colour in the presence of peroxidase. The change in absorbance is measured for HbA1c determination. The combined assay results (haemoglobin and HbA1c) are used by the system to calculate and express percentage HbA1c.

The standard one tailed proportion z test was used to test the hypothesis at 5% significance level.

3. Results and Analysis

A total of 290 diabetics (117 men and 173 women) who attended Parirenyatwa Diabetic Clinic during the time of study had their samples analysed for HbA1c. Twelve percent ($N = 35$) of the patients studied were type 1 and 255 were type 2 diabetics. Mean age (IQR) was 54 years (20), whilst mean % HbA1c (IQR) was 7.5% (4.3) (Table 1).

HbA1c levels and age did not follow a normal distribution ($P = 0.0$ for HbA1c and $P = 0.00195$ for age) both calculated using the Shapiro-Wilk test for normal distribution.

The level of glucose control was defined using % HbA1c as shown in Table 2.

The distribution of glycaemic control was optimal for 55% of the diabetics, whilst 45% did not have good glycaemic control (Figure 1).

Level of glycaemic control was also compared by age group of patients (Table 3). There was no statistically significant difference in distribution of glycaemic control among the three age categories, $P = 0.9790$.

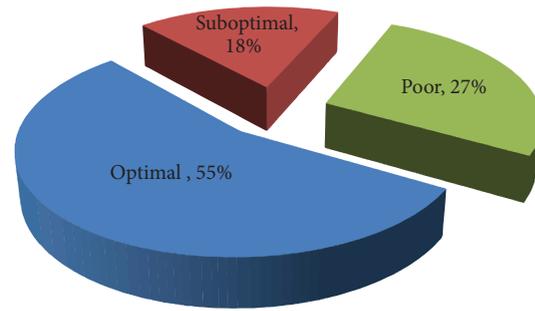


FIGURE 1: Distribution of levels of glycaemic control in the study population.

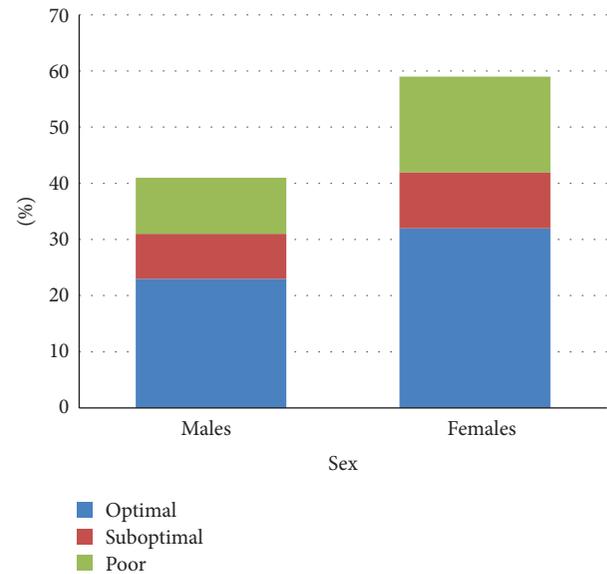


FIGURE 2: Distribution of glycaemic control levels by sex in the study population.

The distribution of glycaemic control between males and females was compared (Figure 2). Using the Wilcoxon rank sum (Mann-Whitney) method, there was no statistically significant difference in glycaemic control between the two sexes, $P = 0.7537$.

Figure 3 shows a comparison of the levels of glycaemic control by type of diabetes. There was a statistically significant difference in glycaemic control of study participants by types of diabetes mellitus, $P = 0.00867$.

4. Discussion

In a diet control study of diabetics with HbA1c results available, in the United States, it was shown that 39% had good control ($HbA1c < 7\%$), 36% had suboptimal control ($HbA1c 7-9\%$), and 25% had poor control ($HbA1c > 9\%$) [21]. Our data indicated that the prevalence of elevated HbA1c levels (27%) among diabetics attending the Parirenyatwa Diabetic Clinic in Zimbabwe was greater than the proportion of 25% found in the American study, z -score = 1.665 [21]. This contradicts the epidemiological studies showing that

TABLE 3: Levels of glycemic control in different age groups of study population.

Age Group	Optimal control N (%)	Suboptimal control N (%)	Poor control N (%)	Total participants N (%)
18–40 years	33 (70)	3 (6)	11 (24)	47 (100)
41–60 years	68 (56)	22 (18)	32 (26)	122 (100)
61–80 years	59 (49)	28 (23)	34 (28)	121 (100)

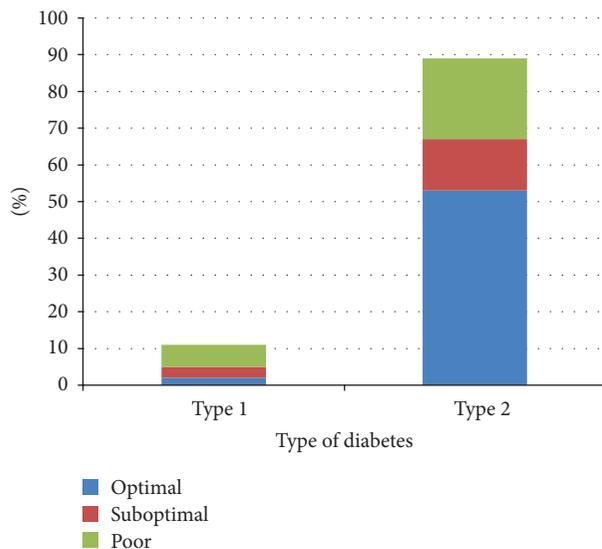


FIGURE 3: Distribution of levels of glycemic control in type 1 and 2 diabetics in the study population.

diabetes mellitus has a higher prevalence in developed than in developing countries [4, 22, 23]. Glycemic control was not significantly different by age and sex but was significantly different by type of diabetes. 54% of type 1 diabetics had poor control compared to 24% in type 2 diabetics ($P < 0.05$). No study to date puts across scientific evidence for why type of diabetes affects long-term glycemic control.

Our results were from a pilot study which warrants further investigation and should be interpreted with caution. This is because all the samples were collected from one study centre and are not necessarily representative of the entire Zimbabwean population. The study was also not independent of some confounding variables such as effect of basal glucose levels which are naturally high in some people.

Studies to determine correlation between fasting glucose at a particular time and HbA1c levels should be carried out in the Zimbabwean population, in future. If a correlation is established, this can be used to estimate HbA1c levels in resource constrained settings. Similar studies have been done in other populations but may not be applicable to our population due to differences in diet and basal glucose levels [9, 14]. Further studies to explain differences in long-term glycemic control among different types of diabetes should

yield interesting results. This will provide better understanding and better interpretation of results and improve handling of diabetics depending on their type of diabetes.

5. Conclusion

In conclusion and according to the data obtained, 27% of type 1 and 2 diabetics had elevated plasma HbA1c levels representing poor long-term glycemic control. This may be an indication of poor adherence to both dietary and medicinal therapy and can predispose patients to developing long-term complications of diabetes mellitus. Regular HbA1c measurements at Public Diabetic Clinics should be done and results should be used to counsel and closely monitor patients with continuously elevated HbA1c.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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