



Average HbA1c in Diabetic Patients in Southern KPK-Pakistan

Tahir Ullah Khan¹, Nafid Ullah Khan¹, Hasnain Gul², Raza Muhammad Khan², Atif Masood³, Atta Ullah Khan⁴

¹DHQ Teaching Hospital MTI, Bannu.

²Bannu Medical College, Bannu.

³University of Lahore teaching hospital Lahore

⁴DHQ Hospital Bannu.

Abstract

Diabetes mellitus is a complex metabolic syndrome characterized by either insulinopenia or insulin resistance. This study is focused on the ever-growing prevalence of diabetes mellitus and its poor glycemic control in southern KPK. This descriptive cross-sectional study was conducted at the outdoor unit, Department of medicine DHQ hospital Bannu, over six months, extending from 30th December 2021 to 30th June 2022. The sample size was 91 and was calculated using the standard WHO formula. The confidence interval used was 95%, with a 5% margin of error. P value <0.05 was taken as statistically significant. Consecutive non-probability sampling technique was applied. Diabetic patients under treatment below 70 years were included in the study. HbA1c was used as an assessment tool for glycemic control and divided into three categories: good glycemic control with HbA1c <7%, poor glycemic control with HbA1c >9%, and very poor glycemic control with HbA1c >10%. Data was entered and analyzed using SPSS version 19.0. About 18.6% diabetic patients had HbA1c >6%, 25.6% patients had HbA1c between 6-8%, 26.7 % patients had HbA1c between 8-10% and 29.6 % had HbA1c >10%. This study revealed that the majority (55%) of diabetic patients belonging to southern KPK had poor glycemic control, as revealed by HbA1c, more than 8%.

Keywords Diabetes mellitus, HbA1c, Glycemic control.

1. Introduction

Diabetes mellitus is a metabolic syndrome characterized by increased blood glucose either due to decreased production or decreased response of body tissues to insulin, a hormone that helps in effectively utilizing glucose along with other functions (1,2). There are two types of DM: type I and type II. Gestational diabetes is a separate entity occurring in pregnant women, but type I & II have got more emphasis (1,3). Despite great improvements in health care facilities and efforts to prolong life in diabetic patients, it is still the 5th leading cause of mortality worldwide.

According to the statistics of the International Diabetes Association (IDA) in 2017, Pakistan is the 10th leading country in terms of diabetes prevalence. In between the age group 21 and 79 years, Pakistan has 75 million cases (4,5).

Random blood glucose levels, fasting blood glucose levels, and HbA1c levels are usually used as diagnostic tools, but HbA1c is considered a standard gold test (6).

For decades HbA1c measurement has been considered one of the vital laboratory medical advances in diabetes care since its recommendation by the American Diabetes Association (ADA) in 1988 (7). Before HbA1c, glucose

criteria, either random or fasting or 75g oral glucose tolerance, were used. Still, in 2010 after assay improvement, ADA validated its use (7) as a Diabetes diagnostic criterion with cutting-off values of $\geq 48\text{mmol/mol}$ (6.5%). Normal <5.6%, and pre-diabetics between 5.7% and 6.4%. and the target value should be below 42mmol/mol (6%) (6).

Hemoglobin is the Fe-containing oxygen-transport metalloprotein present in RBCs. Normal adult hemoglobin (HbA) consists of haem and four globin chains, the α and β globin chains ($\alpha 2 \beta 2$), making up to 97% of adult human hemoglobin (8,9). Within hemoglobin A, approximately 6% is glycated, HbA1c (5%) is the main component, and HbA1a and HbA1b are minor components, comprising the remaining 1% (13). HbA1c results from glycation, a non-enzymatic formation of a covalent bond between serum glucose and N-Terminal amino acid valine of beta-chains of hemoglobin A (12).

HbA1c depends on the interaction between the concentration of serum glucose and the lifespan of the red blood cells (8). As the mean erythrocyte lifespan is approximately 120

days, HbA1c acts as a surrogate marker of glucose concentration during the preceding 8–12 weeks (11).

Measuring HbA1c for diagnosis of diabetes carries Advantages of its convenience because it does not need pre-test preparation, sample stability when collected and low day-to-day variability. However, it is limited by greater cost, low sensitivity (7), and some conditions which falsely elevate or lowers the HbA1c values such as acute and chronic blood loss, hemolytic diseases, hypersplenism, hemoglobin variants and iron, vitamin B12, folate deficiency, asplenia and blood transfusions etc (10-12). Measurements of HbA1c work by separating non glycated and glycated by structural differences and isoelectric point differences (10,11). The National Glycohemoglobin Standardization Program (NGSP) shows values in %, and International Federation of Clinical Chemistry (IFCC) shows in mmol/mol. The conversion equation is NGSP= 0.0915×IFCC (6).

Point-of-care devices which quantify HbA1c on structural differences from non-glycated Hb use is increasing, and give immediate results. Based on studies it is indicated that HbA1c cannot solely explain complications of diabetes because it does not show day-to-day variations in blood glucose (6,13).

Self-Monitoring Blood Glucose (SMBG) and Continuous Glucose Monitoring (SGM) provide alternate methods for HbA1c measurement (11,14). Fructosamine is another alternative to HbA1c, giving a clue about the past 2 to 3 weeks of glycemic control. Fructosamine is formed by glycation of proteins specially albumin, but there are limitations to fructosamine, such as hypoproteinaemia and hypoalbuminemia, as in renal failure and liver diseases (9,15).

In pregnancy, 75g OGTT rather than HbA1c should be used for medication adjustments. Glucose monitoring methods such as SMBG and CGM are particularly effective for young and type 1 diabetic patient (9).

Incidence and prevalence of DM in Pakistan are increasing very rapidly in line with many developed countries across the world, to an alarming level, placing a heavy burden on the health care system socially and economically (17). The govt, along with the general public, share a huge responsibility in terms of adopting and implementing preventive measures amid the rising prevalence. In Khyber Pakhtunkhwa (KPK) province of Pakistan, prevalence ranges from 9% to 12% of the population (16). There are no studies conducted regarding glycemic control of diabetic patients residing in Southern KPK. This study is aimed to

assess the glycemic control of patients with diabetes in southern KPK using HbA1c laboratory reports.

2. Methodology

This descriptive cross-sectional study was conducted at the outdoor unit, Department of medicine DHQ hospital Bannu over 6 months, extending from 30th December 2021 to 30th June 2022. The sample size was 91 and was calculated using standard WHO formula. The confidence interval used was 95% with 5% margin of error. P value <0.05 was taken as statistically significant. Consecutive non-probability sampling technique was applied. Diabetic patients under treatment below 70 years were included in the study. Demographic data was obtained from all patients on the designed Performa. All the patients were interviewed in details regarding glycemic control and worsening of hyperglycemia symptoms including frequency of urination at nights and peripheral neuropathy. HbA1c was used as an assessment tool for glycemic control and divided into 4 categories: good glycemic control with HbA1c <6%, reasonable glycemic control with HbA1c 6-8 %, poor glycemic control with HbA1c 8-10% and very poor glycemic control with HbA1c >10%. Data was entered and analyzed using SPSS version 19.0. Mean + SD were calculated for quantitative variables like age, duration of diabetes, HbA1c. Frequencies and percentages were calculated for sex, education, and dietary habits. All results were presented as tables and graphs.

3. Results

The study included 86 patients. Forty-three were males, and 43 were females. The mean age of our studied population was 46.9 ± 12.4 years, while the mean HbA1c was 8.6 ± 2.3 mg/dl (Table 1). About 11.6% of patients were below the age of 50 years, 51.2% in the age group 51-70 years and 37.2% above the age of 70 years. About 18.6% patients had HbA1C <6%, 25.6% HAD HbA1c between 6-8%, 26.7% had HbA1c between 8-10% and 29.1 % had HbA1c >10% (Table 2). HbA1C correlated with age had a significant p value (<0.001), while it was insignificant when correlated with gender (0.173) (Table 3). The distribution of patients' glycemic control based on HbA1c values was: 18.6% diabetic patients had HbA1c >6% manifesting good glycemic control, 25.6% patients had HbA1c between 6-8% manifesting reasonable glycemic control, 26.7 % patients had HbA1c between 8-10% manifesting poor glycemic control, and 29.6 % had HbA1c >10% manifesting very poor glycemic control (Fig 1).

Table 1: Mean and standard deviation of numerical variables.

Variable	Minimum	Maximum	Mean	Standard Deviation
Age (years)	8	70	46.9	12.4
HbA1c (mg/dl)	5.1	14.1	8.6	2.3

Table 2: Frequency distribution of numerical variables.

Variable	Distribution	Frequency (n)	Percentage (%)
Age (years)	Less than 50 years	10	11.6
	51-70 years	44	51.2
	More than 70 years	32	37.2
HbA1c (mg/dl)	Less than 6	16	18.6
	6.1-8	22	25.6
	8.1-10	23	26.7
	More than 10	25	29.1

Table 3: Correlation of HbA1c with age and gender.

Variable 1	Variable 1	P value
HbA1c (mg/dl)	Age (years)	<0.001*
	Gender	0.173

*P value calculated using Pearson Square Test

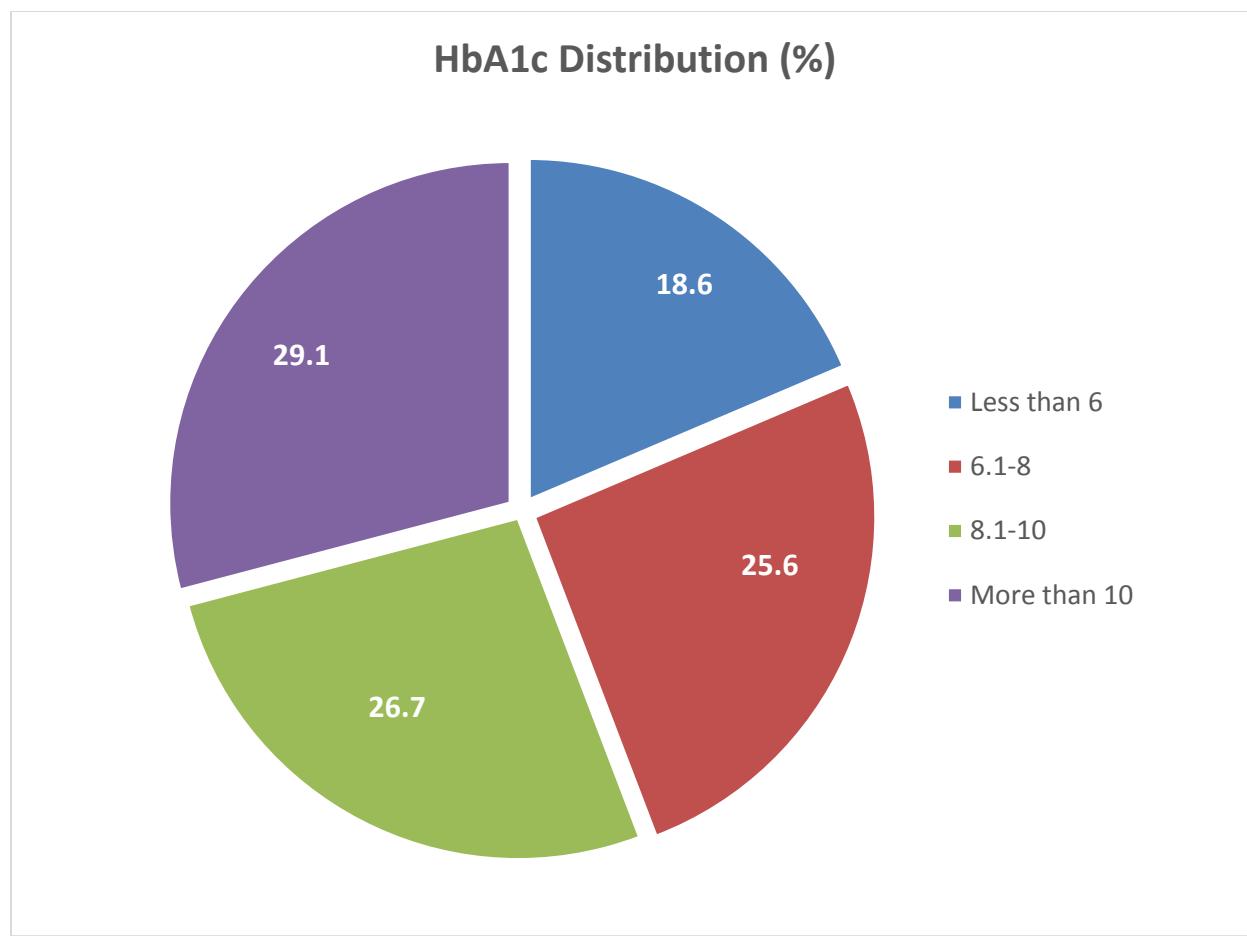


Figure 1: Patient glycemic control based on HbA1c values.

4. Discussion

Due to the high prevalence of diabetes mellitus in Pakistan, optimal glycemic control is paramount to prevent the catastrophic complications linked with prolonged, persisting hyperglycemia. To achieve this purpose, not only dietary and lifestyle modifications are needed, but also effective and regular pharmacotherapy is the need of the day.

In the current study, most patients (29.1%) had very poor glycemic control with HbA1c $>10\%$. About 26.7% had HbA1c between 8-10% while only 25% patients had HbA1c $<8\%$. Almost similar results were reported from other cities of Pakistan (Peshawar and Rawalpindi), about 31% and 30%, respectively (18). The prevalence of poor glycemic control in other regions of Asia is even more alarming, with Iran showing 58.3% people with suboptimal glycemic control (20) and India with 65.4% (21). Our results seem compatible with a Thailand study conducted by Aekplakorn *et al.*, where 30% of patients had suboptimal glycemic

control (21). This difference might be due to cultural differences and dietary patterns observed in Thailand.

In the current study, suboptimal glycemic control was observed more in the younger population than in the elderly population. Age was found to be associated with suboptimal glycemic control. This finding coincided with another study from Pakistan, which revealed that the younger population was more at risk for poor glycemic control (22). However, a study from Ghana contradicted this finding (23). Similar contradiction was observed in a study from eastern Sudan. According to a study from Saudi Arabia, old age had a significant relationship with poor glycemic control (24). No gender discrimination was observed in our present study, with 43 patients being male and 43 females. However, most of the diabetic patients having suboptimal glycemic control in China's Chiang Rai Province (26) were observed to be female having poor socioeconomic conditions. A large number of the diabetic population had poor self-esteem and disease awareness. Compliance with diet and medications was frequently observed.

Like all studies, this study was not without limitations. It was mainly focused on the prevalence of poor glycemic control in the local population of southern KPK, ignoring the key factors and contributors to the phenomenon. Secondly, the duration of diabetes was not taken into consideration which could impact glycemic control in the long run.

5. Conclusion

This study revealed that 26% of diabetic patients belonging to southern KPK had poor glycemic control with HbA1c, more than 8% necessitating either triple-drug therapy or insulin. In comparison, 29% of patients had poor glycemic control, with HbA1C >10% necessitating insulin initiation.

Conflict of Interest The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

Acknowledgement Department of medicine is indebted to the paramedical staff of the medicine department at DHQ Hospital Bannu.

References

- Khan RMM, Chua ZJY, Tan JC, Yang Y, Liao Z, Zhao Y. From Pre-Diabetes to Diabetes: Diagnosis, Treatments and Translational Research. *Medicina (Kaunas)*. 2019 Aug;29;55(9):546. doi: 10.3390/medicina55090546. PMID: 31470636; PMCID: PMC6780236.
- Edgerton DS, Kraft G, Smith M, Farmer B, Williams PE, Coate KC, Printz RL, O'Brien RM, Cherrington AD. Insulin's direct hepatic effect explains the inhibition of glucose production caused by insulin secretion. *JCI Insight*. 2017 Mar 23;2(6):e91863. doi: 10.1172/jci.insight.91863. PMID: 28352665; PMCID: PMC5358484.
- Marciano L, Camerini AL, Schulz PJ. The Role of Health Literacy in Diabetes Knowledge, Self-Care, and Glycemic Control: a Meta-analysis. *J Gen Intern Med*. 2019 Jun;34(6):1007-1017. doi: 10.1007/s11606-019-04832-y. Epub 2019 Mar 15. PMID: 30877457; PMCID: PMC6544696.
- International Diabetes Federation [Internet]. IDF Diabetes Atlas, 8th edition. Brussels, Belgium: International Diabetes Federation; <http://www.diabetesatlas.org>. Accessed March 29, 2019.
- Adnan M, Aasim M. Prevalence of Type 2 Diabetes Mellitus in Adult Population of Pakistan: A Meta-analysis of Prospective Cross-Sectional Surveys. *Ann Glob Health*. 2020 Jan 31;86(1):7. doi: 10.5334/aogh.2679. PMID: 32025503; PMCID: PMC6993597.
- Wang M, Hng TM. HbA1c: More than just a number. *Australian Journal of General Practice*. 2021 Sep;50(9):628-32.
- American Diabetes Association. 2. Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes-2021*. *Diabetes Care*. 2021 Jan;44(Suppl 1):S15-S33. doi: 10.2337/dc21-S002. Erratum in: *Diabetes Care*. 2021 Sep;44(9):2182. PMID: 33298413.
- Lenters-Westra E, Schindhelm RK, Bilo HJ, Slingerland RJ. Haemoglobin A1c: Historical overview and current concepts. *Diabetes Res Clin Pract*. 2013 Feb;99(2):75-84. doi: 10.1016/j.diabres.2012.10.007. Epub 2012 Nov 20. PMID: 23176805.
- Radin MS. Pitfalls in hemoglobin A1c measurement: when results may be misleading. *J Gen Intern Med*. 2014 Feb;29(2):388-94. doi: 10.1007/s11606-013-2595-x. Epub 2013 Sep 4. PMID: 24002631; PMCID: PMC3912281.
- Little RR, Sacks DB. HbA1c: how do we measure it and what does it mean? *Curr Opin Endocrinol Diabetes Obes*. 2009 Apr;16(2):113-8. doi: 10.1097/MED.0b013e328327728d. PMID: 19300091.
- Phillips PJ. HbA1c and monitoring glycaemia. *Aust Fam Physician*. 2012 Jan-Feb;41(1-2):37-40. PMID: 22276282.
- Homa K, Majkowska L. Difficulties in interpreting HbA(1c) results. *Pol Arch Med Wewn*. 2010 Apr;120(4):148-54. PMID: 20424541.
- Whitley HP, Yong EV, Rasinen C. Selecting an A1C Point-of-Care Instrument. *Diabetes Spectr*. 2015 Aug;28(3):201-8. doi: 10.2337/diaspect.28.3.201. PMID: 26300614; PMCID: PMC4536639.
- Danne T, Nimri R, Battelino T, Bergenstal RM, Close KL, DeVries JH, Garg S, Heinemann L, Hirsch I, Amiel SA, Beck R, Bosi E, Buckingham B, Cobelli C, Dassau E, Doyle FJ 3rd, Heller S, Hovorka R, Jia W, Jones T, Kordonouri O, Kovatchev B, Kowalski A, Laffel L, Maahs D, Murphy HR, Nørgaard K, Parkin CG, Renard E, Saboo B, Scharf M, Tamborlane WV, Weinzimer SA, Phillip M. International Consensus on Use of

- Continuous Glucose Monitoring. *Diabetes Care*. 2017 Dec;40(12):1631-1640. doi: 10.2337/dc17-1600. PMID: 29162583; PMCID: PMC6467165.
15. Ng JM, Cooke M, Bhandari S, Atkin SL, Kilpatrick ES. The effect of iron and erythropoietin treatment on the A1C of patients with diabetes and chronic kidney disease. *Diabetes Care*. 2010 Nov;33(11):2310-3. doi: 10.2337/dc10-0917. Epub 2010 Aug 26. PMID: 20798337; PMCID: PMC2963485.
 16. Meo SA, Zia I, Bukhari IA, Arain SA. Type 2 diabetes mellitus in Pakistan: Current prevalence and future forecast. *J Pak Med Assoc*. 2016 Dec;66(12):1637-1642. PMID: 27924966.
 17. Akhtar S, Ali Shah SW, Javed S, Alina A. Prevalence of diabetes and prediabetes in district Swat Pakistan. *J Pak Med Assoc*. 2021 Jan;71(1(B)):243-246. doi: 10.47391/JPMA.548. PMID: (1)35157657.
 18. Ullah Khan A, Zafar Ali Khan M, Nadeem M, Yasmeen Bangash R, Fakhr A. Status of glycemic control in patients of type 2 diabetes mellitus. *Pak Armed Forces Med J*. 2013;63(2):205.
 19. Mirzaei M, Rahmaniman M, Mirzaei M, Nadjarzadeh A, and tafti BAD. Epidemiology of diabetes mellitus, pre-diabetes, undiagnosed and uncontrolled diabetes in Central Iran: results from Yazd health study. *BMC Public Health*. 2020; 20(166): 1–9. doi: 10.1186/s12889-020-8267-y.
 20. Anusuya GS, Ravi R, Gopalakrishnan S, Abiselvi A, Stephen T. Prevalence of undiagnosed and uncontrolled diabetes mellitus among adults in South Chennai. *International Journal of Community Medicine and Public Health*. 2018; 5(12): 5200–5204.
 21. Aekplakorn W, Chariyalertsak S, Kessomboon P, Assanangkornchai S, Taneepanichskul S, Putwatana P. Prevalence of diabetes and relationship with socioeconomic status in the Thai population: national health examination. *Journal of Diabetes Research*. 2018; 1–8. doi: 10.1155/2018/1654530.
 22. Siddiqui FJ, Avan BI, Mahmud S, Nanan D, Jabbar A, Assan PN. Uncontrolled diabetes mellitus: prevalence and risk factors among people with type 2 diabetes mellitus in an urban district of Karachi, Pakistan. *Diabetes Res Clin Pract*. 2015; 107(1): 148–56. doi: 10.1016/j.diabres.2014.09.025.
 23. Fiagbe J, Bosoka S, Pong J, Takramah W, Axame WK, Owusu R, et al. Prevalence of controlled and uncontrolled diabetes mellitus and associated factors of controlled diabetes among diabetic adults in the hohoe municipality of Ghana. *Diabetes Management*. 2017; 7(5): 343–354.
 24. Fiagbe J, Bosoka S, Pong J, Takramah W, Axame WK, Owusu R, et al. Prevalence of controlled and uncontrolled diabetes mellitus and associated factors of controlled diabetes among diabetic adults in the hohoe municipality of Ghana. *Diabetes Management*. 2017; 7(5): 343–354.
 25. Riaz F, Shaikh AA, Anjum Q, Alqahtani YW, Shahid S. factors related to the uncontrolled fasting blood glucose sugar among type2 diabetes patients attending primary health care center, Abha city, Saudi Arabia. *The International Journal of Clinical Practice*. 2021; doi: 10.1111/ijcp.14168.
 26. Bai YL, Chiou CP, Chang YY. Self-care behaviour and related factors in older people with type 2 diabetes. *J Clin Nurs*. 2009;18(23):3308–3315.