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Glycemic Variability and Associated Individual and Clinical Factors among Type 2 Diabetic Patients Attending Out-Patient Clinic at Diabetes Center of Excellence in Kenya (Formally Diabetic Comprehensive Care Clinic)

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Abstract: ***Background: Diabetes mellitus a common health challenge having expanded its incidence and prevalence globally. The association between chronic complications, sociodemographic and patients' HbA1c glycemic levels are not well understood in developing countries such as Kenya. Methods: A cross-sectional hospital-based study was carried out among 275 type 2 diabetic respondents attending out-patient Diabetes Centre for Excellence in Nakuru County in south-western Kenya. A standard questionnaire was employed to obtain information on sociodemographic characteristics, HbA1c glycemic levels, relevant chronic complications and adherence to insulin medication. Results: The mean age of the 275 respondents was 49.4 years with 152 (55%) being female. While anon-adherence rate of insulin medication of 9% was realized, only 32.4% (n=89) monitored their HbA1c glycemic levels. At least one chronic complication was documented among 59% of the respondents (n=162) The prevalence of key complications was: hypertension 56% (n=155), retinopathy and eyesight complications (30%, n=83), foot ulcers (6%n=17) and others 7% (n=9). Among the hypertensive and those with eyesight complications, 57% and 66% were females respectively. 41% and 23% of respondents aged >51 years were hypertensive and reported eyesight complications respectively. Of the 89 who monitored their HbA1c levels, 58% were females but overall, only 7.9% (n=7) had good glycemic control (HbA1c <= 6%) constituting of 3 females. Of the 82 respondents who had poor glycemic control (HbA1c > 6.1%), 58% were female (n=34). 30.3% (n=27) of those aged >51 years had HbA1c >6.1% compared to 62% (n=55) aged ≤51 years. 50.6% (n=45) with poor glycemic control (HbA1c >6.1%) had hypertension. Conclusion: Adherence to anti-diabetic medications is crucial to reach metabolic control while non-adherence is associated with increased levels of HbA1c. In the current study, the non-adherence rate was at 9%. More female than male had poor glycemic control. Chronic complications were seen with advancing age and in those with poor glycemic control. Hypertension and eyesight illnesses were the key complications. Management of diabetes mellitus is resource-intensive in terms of time and direct medication costs, and indirect costs associated with accessing medical care from distant clinics that will burden the economy due to higher medical costs and a reduction in productivity.***

Keywords: Chronic Complications, Glycated hemoglobin Glycemic Levels, Nakuru-Kenya

1. Introduction

The global diabetes prevalence in 20-79 year old in 2021 was estimated to be 10.5% (536.6 million people), rising to 12.2% (783.2 million) in 2045 (Sun, H., Saeedi, *et al* 2022)

The latest Global Burden of Disease Study estimated >500 million individuals with type 2 diabetes mellitus (T2DM) globally in 2017 (Bikbov*et. al* 2017, Cannon, A., *et al*., 2018) Reports of 340 million people estimated to be living with diabetes underpins the mortality, morbidity, and health-system costs associated with the disease globally (Mureyi, D., et; al 2022). The chronically elevated blood sugar in T2DM damages multiple body organs, targeting the cardio-vascular, immune, renal and nervous systems, and the eye (American Diabetes Association, 2014; Zheing *Y, . et al* 2018). Consequently, it causes blindness, cardiovascular failure, Lower limb amputation and other long-term health outcomes that significantly reduce quality of life while significantly contributing to the years of life living with disability (American Diabetes Association, 2018, Harding, J. L., *et al* 2019) Recently, T2DM has been ranked the topmost co-morbidity linked to COVID 19 severity (Rahman, S., *et. al* 2020). Sub-Saharan Africa (SSA) is undergoing a rapidly elevated T2DM prevalence and incidence associated with demographic factors, socio-cultural dynamics linked to lifestyle changes and eating habits, and socioeconomic transition characterized by higher income and urbanization (Sartorius, B., 2015). Close to 800, 000 (3.6%) of Kenyans live with T2DM, with 50% of hospital admissions and 55% of hospital deaths in the country attributed to non-communicable diseases (NCDs) led by T2DM (Maina; 2016).

Studies have characterized positive relationships between low socioeconomic status (SES) or selected demographic factors on the one hand and adverse health outcomes on the other. For instance, in T2DM, studies identified the SES differences in all disease stages of disease evolution and death (Mayega R. W. *et, al* 2014).

Agardh and colleagues (2011) underscored three low SES features associated with an escalated risk of T2DM, including education, income, and occupation. Low SES is also associated with inequalities in diabetes care in large part because patients of low SES are likely to have attained low education levels (Lee, T. C. *et al* 2011). To illustrate this better, education level positively modifies access to and quality of care, influences diabetes-related knowledge, and motivates adherence to treatment by employing educational

skills into health information (Brown, A. F., *et al* 2004, Kirkman, M. S., *et al* 2015). Other reported factors that could explain HbA1c variability and diabetic complications include poor self-management or lack of support (Takao., *et al* 2014, Cunningham, A. T. *et al* 2018).

Though the majority of these studies come from developed countries, they still provide the necessary background for defining associations between chronic complications, sociodemographic and patients' HbA1c glycemic levels but considerable disparities persist in understanding these risk factor relationships in developing countries. Besides the presence of comorbidities defined as existing or consequential chronic complications of T2DM confounds disease-related health outcomes, disease management and care needs, and associated costs (Renner, S., *et al* 2020).

To better define individual and clinical risk factor associations with long-term blood glucose control in developing countries, we explored cross-sectional links between sociodemographic factors, co-morbidity and HbA1c variability among T2DM patients attending an out-patient clinic at Diabetes Center of excellence in Nakuru County in south-western Kenya. Such studies could help identify patient characteristics related to T2DM management, enabling a patient-driven approach to health care support in developing countries. Justifiably, health challenges are emerging in developing countries due to rapid demographic transitions and an advancing health burden attributed to co-morbidity with NCDs (Elissen, A. M., *et al* 2016, Ashrafzadeh, S., & Hamdy O. 2019).

More specifically, the study aimed to explore differences regarding HbA1c levels in regard to sex, age, co-morbidity and other patient characteristics. Sex and age are also critical factors influencing health among people with the prevalence of T2DM and poor glycemic control reportedly higher among females (Iloh, G. U. P., *et al* 2015, Mannan, A. *et al* 2021).

The low levels of assessment of glycemic targets using HbA1c that indicates average blood glucose control over the preceding 2-3 months levels and the low achievements of metabolic targets among low SES people with diabetes exemplifies inequalities in diabetes care. (Grintsova O., *et al* 2014).

2. Materials and Methods

2.1 Study Design and setting

A cross-sectional research design was employed to recruit 275 T2DM patients receiving treatment at Diabetes center of excellence in Nakuru County South-west Kenya. A formula for estimating the population proportion with specific relative precision described by Elashoff & Lemeshow, was applied, setting margin of error at 0.05, and detection rate of 50% with 95% confidence. The ethics and research committee of the Egerton University and National Commission for Science, Technology and Innovation-Kenya approved the study with approval reference no. NACOSTI/P/15896/22177.

2.2 Study Participants

Permission was obtained from the head of the institution to evaluate those who met the study inclusion criteria at the diabetic clinic. Type 2 diabetic patients who were at least 18 years old, receiving care and treatment at the diabetic clinic of Nakuru County Referral Hospital willing to participate in the study and consented for the study were eligible to participate. Those who were less than 18 years of age had other types of diabetes and those who were not willing to consent were excluded from the study.

2.3 Sampling Design

Systematic sampling technique was used to select patients to be surveyed from diabetic clinic. A target of 9 clients per day from a population of 45 being the average number of clients attending the diabetic clinic gives 5 clients. (X=45/9) Therefore, every 5^{th} client was interviewed consecutively from the first randomly selected client of the day. The sampling frame was derived from diabetic register at the diabetes centre of excellence. A total of 275 respondents were interviewed.

2.4 Data Collection

A detailed, pretested semi-structured questionnaire was employed during face-face interview to gather information on socio-demographic characteristics, age, gender literacy level, current treatment, glycemic levels presence of diabetes-related complications (leg or foot ulcers, a decreased vision, loss of sight, vascular complications, cardiovascular disease-hypertension). Twenty-five respondents reported having missed their medication as prescribed giving a non-adherence rate of 9%.

2.5 Data Analysis

All statistical analyses were conducted using the IBM SPSS version 17 at a significant level of $p < 0.05$. Descriptive data were presented in frequencies and percentages using tables and charts. Baseline characteristics were analyzed using Kruskal-Wallis test (non-categorical variables) and $\chi 2$-test or Fisher's exact test (categorical variables). Factors' contributing to glycemic variability was determined using logistic regression analysis.

3. Results

3.1 Socio-demographic Characteristics of Respondents

As summarized in Table 1. The maximum age was 85 years while the minimum was 18 years, the mean age (SD 16.25) was 49.4 years. Of these 275 respondents, 138 (50%) were aged above 50 years, 152 (55%) were female, 197 (72%) were married, 117 (43%) had secondary education while 130 (47%) were self-employed.

3.2 Adherence to medication.

Non-adherence is associated with increased levels of HbA1c. In the current study, the non-adherence rate was at 9%. More females 18 (6.5%) reported non-adherence as compared to

males 7 (2.5%). Education level was noted to contribute to non-adherence. T2DM patients with primary level of education reporting a higher non-adherence rate of4%.

3.3 T2DM Chronic Complication.

Various chronic complications were documented with56% (155) of respondents having hypertension, 83 (30%) eye-sight diseases, 17 (6%) foot-ulcers. However, there was significant difference in prevalence of eye disease between males and female, twice the number of females (20%) (n=55) than males (10%). Advance in age was a risk factor to complication. About 41% (n=113) of the respondents above 51 years had hypertension and 23% (n=63) eye-sight disease (Table 3).

3.4 Glycemic Control among T2DM

Of the 275 respondents, 89 (32.4%) routinely monitored their HbA1c levels, 57.3% (n=51) were females whereas 42.7% (n=38) were male. 92% had poor glycemic. More females (53.93%) (n=48) than males (38.2%) (n=34) had poor glycemic control. About a half (51%n=45) of respondents who had poor glycemic control and 4.5% (n=4) of those with good glycemic control had elevated blood pressure. 3.4% (n=3) of ones with good glycemic control and 37 (42%) with poor glycemic control had normal blood pressure (Table 5, 6).

Based on the recommendation regarding the HbA1c ranges (4-6%), there were 7 (7.9%) respondents who had HbA1c levels <=6% considered with good control. A significant difference between males and females was noted with more males 4 (4.49%) than females 3 (3.37%) having good glycemic control while (Table 5). Respondents exhibited age variation in glycemic control, those above 51 years had poor glycemic control with 37% (n=33) having HbA1c of >6.1% and 26% (n=23) of those aged between 41-50 years had HbA1c above 6.1%. Only 6.7% (n=6) above 51years had good glycemic control with a HbA1c of <= 6% (Table 4)

3.5 Bivariate Analyses

In unadjusted analysis, socio-demographic and clinical characteristics associated with patients' glycemic control, Age, gender, Blood pressure, Concurrent medical conditions, glycated hemoglobin levels and adherence to medication.

Table 1: Demographic and socio-economic characteristic of study respondents (N=275).

Variable	Levels	Frequency	%
Gender	Female	152	55.3
	Male	123	44.7
Age in years	<20	11	4.0
	21-30	32	11.6
	31-40	47	17.1
	41-50	47	17.1
	>50	138	50.2
Marital status	Married	197	71.7
	Single	54	19.6
	Widowed	14	5.1
	Divorced	10	3.6
Level of education	No education	24	8.7
	Primary	102	37.1
	Secondary	117	42.5
	Post-secondary	32	11.6
Employment status	Not employed	102	37.3
	Self employed	130	47.3
	Formal employment	20	7.3
	Retired	23	8.4

Table 2: Gender distribution of diabetes complication (n=162)

Complications	Gender (n=162)	Frequency (%)	P-value
High blood pressure	Females	88 (32.0%)	0.569
	Males	67 (24.4%)	
Eyesight disease	Females	55 (20.0%)	0.016
	Males	28 (10.2%)	
Foot Ulcers	Females	8 (2.9)	0.482
	Males	9 (3.3%)	
Heart disease	Females	3 (1.1)	0.793
	Males	3 (1.1%)	
Kidney (Nephropathy) disease	Females	1 (0.7%)	0.442
	Males	2 (0.4%)	

Table 3: Diabetes chronic complications in various age group (n=162)

Complications	Age (n=162)	Frequency (%)	P-value
High blood pressure	<20 years	0 (0.0%)	<.001*
	21-30 years	2 (0.7%)	
	31-40 years	9 (3.3%)	
	41-50 years	32 (11.6%)	
	>50 years	113 (40.7%)	
Eyesight disease	<20 years	3 (1.1%)	<.001*
	21-30 years	2 (0.7%	
	31-40 years	2 (0.7%)	
	41-50 years	13 (4.7%)	
	>50 years	63 (22.9%)	
Foot Ulcers	<20 years	0 (0.0%)	0.208
	21-30 years	2 (0.7%)	
	31-40 years	1 (0.4%)	
	41-50 years	1 (0.4%)	
	>50 years	13 (4.7%)	
Heart disease	<20 years	0 (0.0%)	0.753
	21-30 years	0 (0.0%)	
	31-40 years	2 (0.7%)	
	41-50 years	1 (0.4%)	
	>50years	3 (1.1%)	
Kidney disease	<20years	0 (0.0%)	0.556
	21-30 years	0 (0.0%)	
	31-40 years	0 (0.0%)	
	41-50 years	0 (0.0%)	
	>50years	1 (1.09%)	

Table 4: Glycemic variation by age (n=89).

Age in Years (n=89)	HbA1c levels	Frequency (%)	P-value
<20 years	<=6%	1 (1.1%)	0.0567
	>6.1%	7 (7.9%)	
21-30 years	<=6%	0 (0.0%)	
	>6.1%	14 (15.7%)	
31-40 years	<=6%	0 (0.0%)	
	>6.1%	11 (12.4%)	
41-50 years	<=6%	0 (0.0%)	
	>6%	23 (25.8%)	
>50 years	**<=6%**	**6 (6.7%)**	
	>6.1%	27 (30.3%)	

Table 5: Glycemic levels by gender (n=89)

Age in Years (n=89)	HbA1c levels	Frequency (%)	P-value
Females	<=6%	3 (3.4%)	0.276
	>6.1%	48 (53.9%)	
Males	<=6%	4 (4.5%)	
	>6.1%	34 (38.2%)	

Table 6: Glycemic control in a comorbidity (Hypertension) (n=89)

(n=89)HbA1c	Frequency (%)		P-value
BP	Normal	Elevated	
<=6%	3 (3.4%)	4 (4.5%)	0.908
>6.1%	37 (41.6)	45 (50.6%)	

4. Discussion

HbA1c test was used as a standard measure for glycemic control, we found that a considerable proportion of our diabetic study participants did not monitor their glycemic levels over time.

The low levels of assessment of glycemic targets using HbA1c that indicates average blood glucose control over the preceding 2-3 months levels and the low achievements of metabolic targets among low SES people with diabetes exemplifies inequalities indiabetes care. (Grintsova O., *et al* 2014).

While non-adherence is unquestionably common, its prevalence remains difficult to gauge due to lack of robust definitions and gold-standard. Participants may appear 'non-adherent' when reduced use is confounded by factors such as variable subjective reporting, or inability to access the insulin medication. An adherence rate of 91% was reported in the current study. However, this did not reflect on glycemic control as over two third (92% n=82) of study participants had poorglycemic control. Non-adherence was biased towards female and those with primary level of education, the study demonstrated the benefits of literacy. An administration's post-secondary strategy shift will be a longer-term policy trend that will increase adherence. Independent risk factors associated with poor glycemic control was concurrent hypertension. Females had a higher prevalence of diabetes complications as opposed to males. A significant association was found between glycemic control and age. A treatment plan should be devised tailored specifically to the needs of the individual patient.

Only 32% (n=89) of the study participants used HbA1c as a standard measure of their glycemia. The overall picture established by our study suggests a generally high prevalence of poor glycemic control, which is a matter of significant concern globally linked to micro-and macro-vascular chronic complications (Ravi, R., *et, al* 2021). The prevalence of chronic complication was high with 59% of participants developing one or more complication. This compared well with similar studies; A study in southwest Ethiopia (Yimam Ahmed, *et al* 2020) found that 59% of study participants had diabetes-related complications, 72.72% in Saudi Arabia (Khan, A. R., *et al* 2014) These complications may continue to appear since the incidence of diabetes in Kenya and Africa is rising (Mohamed, S. F. *et al* 2018).

This study is among the first one in developing countries to investigate glycemic variability among T2DM on insulin medication. In clinical practice, optimal control is difficult to obtain on a long-term basis because the reasons for poor glycemic control in T2DM patients are complex. (Critchley, J. A., 2018). In the current study, almost all of the participants had HbA1c levels considered as poor glycemic control. Those above 50 years constituted about 30% (n=27) as compared to 27% (n=25) of those between 41-50 years. Women, were more likely to have poor glycemic control. 54% (n=48) female compared to 38% (n=34) male had HbA1c levels considered as poor glycemic control. This compared well with a study by (Kamuhabwa, A. R., & Charles, E. 2014) in Dar es salaam which found out that Stratification by age and sex showed that females aged 40-59 years had a significantly higher percentage of poor glycemic control than their male counterparts of the same age group (76.1% vs 65.4%, *P*=0.04). In this study, reasonable glycemic control was defined as having values of HbA1c ≤ 6.0% and poor glycemic control of HbA1c > 6.1%. Lack of health insurance affects accessibility and affordability of medicines and diagnostic services in T2DM patients (Kamuhabwa, A. R., & Charles, E. 2014). Inthe current study we found no association between insurance cover, accessibility to medication and HbA1c test.92% (n=184) of the study participants had NHIF insurance cover, over two thirds (91%) accessed the medication from the attending facility. However only32% (n=89) monitored their glycated hemoglobin. This could be attributed to affordability as the cost it was not provided for by the cover. This finding compared well with similar studies done in other countries. In a study done by (McBrien, K. A., et al 2017) in city of Calgary, Alberta established that Study participants with HbA1c levels of 10% (86 mmol/mol) were more likely to report not having drug insurance.

Chronic complications were reported in about 59% (n=162) of study participants, hypertension (56%) and eyesight (30%) illnesses as most prevalent. Females had a higher prevalence of complications as opposed to males.32% (n=88) female had hypertension as compared to 24% males while 20% (n=55) had eyesight illnesses. This could be due to the fact that in premenopausal women diabetes causes impairment of endothelial function. (Kamuhabwa, A. R., & Charles, E. 2014). Studies have been carried out to explore the variables that may be associated with poor control. A study by (Alzaheb, R. A., & Altemani, A. H. 2018) in Saudi Arabia identified four variables which appeared to be associated with glycemic control as an outcome among which family history and diabetes duration were found to be non-modifiable risk factors. In this study, a significant association was found between glycemic control and age. Study participants in age categories of 41-50 years and above 50 years were observed to have poor glycemic levels. This variation of association control could be explained by the differences in population characteristics such as literacy levels and poor eyesight in drawing correct dosages.

Elevated blood pressure is closely related to increased circulatory fluid volume and peripheral vascular resistance. Patients with diabetes mellitus experience increased peripheral artery resistance caused by vascular remodeling.

Afferent arteriolar remodeling during diabetic nephropathy leads to increased glomerular pressure. (Ohishi, M. 2018).

Hyperglycemia is considered to play an important role in the pathogenesis of retinal microvascular damage, dilatation of blood vessels and blood flow changes being the earliest changes. (Rosen, R. B., *et, al* 2019)

Recent evidence suggests that women with diabetes are still less likely than men to receive guideline-recommended care, even in the most developed nations (Peters, S. A., & Woodward, M. 2018) Females are more likely to forget their treatment regimen possibly due to their gender roles and socioeconomic status. They are more likely to develop complications that may alter their ability to draw appropriate dosages leading to inadequate glycemic control.

5. Conclusions

A high number of diabetes patients' seeking diabetes services at Diabetes Center of excellence at Nakuru County Referral Hospital had poor glycemic control. Glycated hemoglobin was not utilized as a measure of blood sugar over time. HbA1c variability was strongly associated with overall comorbidity. Targets should focus on both stability and absolute level of HbA1c. Despite a high percentage of adherences to diabetes insulin medication, chronic complications were reported in about half of the study participants.

6. Recommendations

A comprehensive understanding of patient and system-level barriers is needed to inform the development of contextually-tailored interventions to support self-management and improve outcomes for diabetes patient. For optimal management of people with diabetes, a treatment plan should be devised tailored specifically to the needs of the individual patient. The treatment plan should include adequate glycemic control based on glycated hemoglobin (HbA1c).

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