Research Article

Clinical Characteristics and Glycaemic Control in Adults Living with Type 1 Diabetes: A 1-Year Retrospective Chart Review at Two South African Public Sector Tertiary Hospitals

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Abstract:

Background: An estimated 11.8% of the South African population are living with diabetes. There is a paucity of data related to the clinical characteristics and glycaemic control in people living with T1DM within the South African public healthcare sector.

Objective: To describe the clinical characteristics and glycaemic control of people living with T1DM in a public health care setting.

Methods: The study was an observational study conducted at two tertiary public sector hospitals in South Africa by means of a chart review. The study involved adults living with T1DM treated with human insulin for 12 months prior to the date of informed consent.

Results: A total of 224 patients with T1DM were enrolled, with 190 (84.8%) from Chris Hani Baragwanath Academic Hospital and 34 (15.2%) from Klerksdorp Tshepong Hospital Complex. One patient withdrew consent, leaving a total analysed population of 223. Of the 223 patients, 37 (16.6%) were controlled (most recent glycosylated haemoglobin (HbA1c) < 7%) while the remainder 186 (83.4%) were uncontrolled (most recent HbA1c ≥ 7%). The mean age of the study group was 33 ± 9 years. The majority of participants were female (122 [54.7%]) and of black ethnicity (215 [96.4%]). The mean number of hypoglycaemic events per patient-year was 151.4 (SD ± 213.9). Diabetic ketoacidosis occurred more frequently in the uncontrolled group.

Conclusion: The majority of patients in this study did not achieve target HbA1c, placing them at higher risk for long-term diabetes complications. Poor glycaemic control, leading to long term complications, as well as hypoglycaemia and diabetic ketoacidosis adds further strain to the resource constrained public healthcare in South Africa.

Keywords: Type 1 diabetes mellitus, HbA1c, macro & microvascular complications, diabetic ketoacidosis, hypoglycaemia

INTRODUCTION

According to the International Diabetes Federation (IDF), 11.8% of the South African population are living with diabetes mellitus (DM).(1) While type 2 diabetes mellitus (T2DM) is more common than type 1 diabetes mellitus (T1DM), the incidence of T1DM is increasing annually at rates of 2%–5%.(1) Estimating the true incidence and prevalence of T1DM in South Africa is challenging due to a lack of comprehensive epidemiologic studies.

T1DM is a potentially debilitating disease with life-threatening complications such as heart disease, stroke, blindness, amputations and kidney failure. The financial burden associated with the management of this disease is significant and estimated to cost South Africa in excess of R27.9 billion per annum.(2,3) Early diagnosis and intervention can improve morbidity and mortality, but in the South African healthcare setting, T1DM is not always managed optimally with less than 17% of patients obtaining the target glycosylated haemaglobin (HbA1c) of <7%.(2,4) Failure to obtain glycaemic control is associated with an increase in micro- and macrovascular complications. In patients with T1DM in South Africa, a 20-year mortality of 43% has been noted, which can be attributed to renal failure, hypoglycaemia and ketoacidosis, all of which are linked to poor glycaemic control.(5) Hence, the management of T1DM is currently still centred around obtaining adequate glycaemic control.

Given the paucity of data on glycaemic control in the public sector in South Africa, we aimed to describe the clinical characteristics and glycaemic control of patients with T1DM in the South African public health care sector.

METHODS

This retrospective, observational study was conducted at two tertiary public sector hospitals, Chris Hani Baragwanath Academic Hospital in Johannesburg and Klerksdorp Tshepong Hospital Complex, in the North West Province of South Africa. The study was compliant with Good Pharmacoepidemiology Practices.(6) From February 2021 to August 2021 a total of 224 patients were enrolled across the two study sites. Criteria for inclusion were adults aged ≥18 years with T1DM treated with human insulin for 12 months preceding the date of informed consent. Exclusion criteria were patients with type 2 diabetes mellitus, gestational diabetes, chronic pancreatitis (type 3 diabetes mellitus), latent autoimmune diabetes of adulthood, maturity onset diabetes of the young, and those on insulin analogue therapy. Patients on analogue insulin were excluded due to the standard of care for insulin therapy in the public sector in South Africa is human insulin. Ethical approval for the study was obtained from the University of Witwatersrand Human Research Ethics Committee.

Diabetes control was defined as a HbA1c <7% as per the American Diabetes Association (ADA) guidelines. Hypoglycaemia was characterized by the ADA standards of care definition as a severe event characterised by an altered physical or mental function, requiring third party assistance.

Data was captured in a case report form which included demographics, duration of DM, risk factors, hypoglycaemia and acute and chronic complications. This work has been reported in line with the Strengthening the Reporting of Cohort Studies in Surgery (STROCCS) criteria.(7)

STATISTICAL CONSIDERATIONS

Sample size calculation

The sample size was calculated using SAS version 9.4, based on the assumption that both hospital sites had a total population of 1129 T1DM patients. Adult patient with T1DM that maintained an HbA1c < 7% were classified as controlled. It was further assumed that approximately 20% of the sample would have HbA1c readings < 7%. For sample size calculation, a proportion of 20% was used. Assuming that the population was normally distributed, using a margin of error of 5% and a confidence level of 95% and adjusting for a 10% rate of patient files that could not be evaluated due to missing or incomplete data, a sample size of 224 patients was calculated.

Macro & Micro vascular Complications

Renal Complications: These were recorded in the patient medical records by the treating clinician. It was presumed the complication was noted based on urine analysis (eg urine dipsticks for proteinurea, spot urine albumin creatinine ratio) urea, creatinine and eGFR.

Hypoglycaemic Events

These were recorded by the treating clinicians based on patient history and glucose levels.

RESULTS

A total of 268 patients were screened for inclusion in the study. Forty-four patients did not meet the eligibility criteria and were excluded. A total of 224 patients were enrolled: 190 (84.8%) patients from Chris Hani Baragwanath Academic Hospital and 34 (15.2%) from Klerksdorp Tshepong Hospital Complex. A total of 223 patients completed the study as one patient withdrew consent.

Of the 223 patients enrolled, 186 (83.4%) were found to be uncontrolled and 37 (16.6%) were controlled.

Demographics

The age of the study population was 33.4 ± 9.4 (range 18–75) years (Table 1). Black female study participants constituted the majority of the study population. The mean age of the controlled and the uncontrolled group were similar (34 ± 8.1 [20–61] years vs 33.1 ± 9.6 [18–75] years, respectively). The proportions of female and male patients

in the controlled and uncontrolled groups were comparable. In both groups, patients of black ethnicity formed the majority of study participants and their proportion in the two groups were comparable. Similarly, anthropometry (height, weight and BMI) and blood pressure were also comparable between the two study groups.

Table 1: Demographics of study population

	Controlled (N = 37)	Uncontrolled (N = 186)	Total (N = 223)
Age (years)			
n	37	186	223
Median	35	32	33
Mean	34.8	33.1	33.4
SD	8.1	9.6	9.4
Min	20	18	18
Max	61	75	75
Sex			
Female	20 (54.1%)	102 (54.8%)	122 (54.7%)
Male	17 (45.9%)	84 (45.2%)	101 (45.3%)
Ethnicity			
Black	35 (94.6%)	180 (96.8%)	215 (96.4%)
Other	2 (5.4%)	3 (1.6%)	5 (2.2%)
White	0 (0.0%)	3 (1.6%)	3 (1.3%)
Asian	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetic medications			
Short acting human insulin	25 (67.6%)	138 (74.2%)	163 (73.1%)
Basal human insulin	25 (67.6)	138 (74.2)	163 (73.1%)
Biphasic human insulin	12 (32.4%)	48 (25.8%)	60 (26.9%)
Oral diabetic medication	1 (2.7%)	2 (1.1%)	3 (1.3%)

HbA1c and average duration of diabetes

For the whole study population, HbA1c (performed at least once within the last 12 months) had a mean value of 10.0 ± 3.0 % (range 4.3–22.0). The controlled group had a significantly lower mean HbA1c as compared to the uncontrolled group (6.6 ± 1.6 [range 4.3–12.8] vs 10.6 ± 2.7 [5.6–22.0], p<0.001). (Table 2)

When considering the most recent HbA1c results (within the last 12 months), the mean value was 10.0 ± 2.9 (range 5.0–19.2). The controlled group had a substantial lower mean value (6.2 ± 0.5 [range 5.0–6.9]) as compared to the uncontrolled group (10.7 ± 2.6 [range 2.6–7.2], (Table 2)

The mean duration of diagnosis of T1DM for the study population was 122.2 ± 106.7 months. The controlled group had a shorter duration of TIDM as compared to the uncontrolled group (94.9 ± 108.4 [range 1–361] vs 127.5 ± 105.8 [range 5–698], respectively).

Presence of complications/comorbidities

Macrovascular complications

Two patients in the uncontrolled group had macrovascular complications, namely left ventricular hypertrophy (LVH) and congestive cardiac failure. None of the patients in the controlled group had any evidence of macrovascular complications.

Microvascular complications

Microvascular complications which included renal disease, blindness, cataract, foot ulcers, retinopathy and neuropathy were more common in the uncontrolled group (11% vs. 2.7%, p<0.001). (Table 3)

Table 2: Glycosylated haemoglobin (HbA1c) of the population

	Controlled group (N = 37)	Uncontrolled group (N = 186)	Total (N = 223)
HbA1c, oldest result (within the last 12 months)			
Number of patients (n)	28	165	193
HbA1c results			
Mean	6.6	10.6	10.0
Min	4.3	5.6	4.3
Max	12.8	22.0	22.0
HbA1c, most recent result (within the last 12 months)			
Number of patients (n)	23	126	149
HbA1c results			
Mean	6.2	10.7	10.0
Min	5.0	7.2	5.0
Max	6.9	19.2	19.2

Table 3: Number of comorbidities/complications

Episodes in the past 12 months	Controlled group (N = 37)	Uncontrolled group (N = 186)	Total (N = 223)
Microvascular			
Renal disease	0	1	1
Blindness	0	1	1
Cataract	0	1	1
Foot ulcers	0	6	6
Retinopathy	1	8	9
Neuropathy	0	3	3

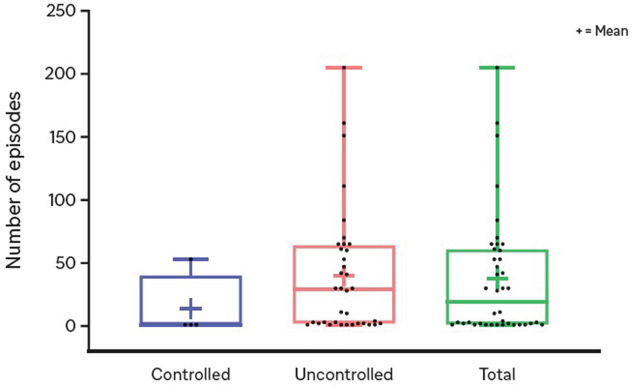

Figure 1. Severe Hypoglycaemic events in 1 year

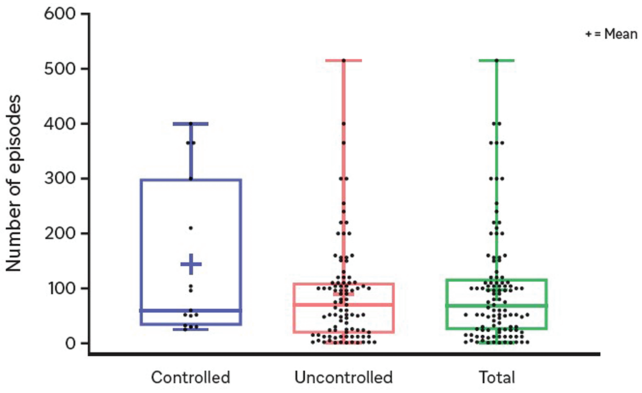

Figure 2. Nocturnal Hypoglycaemic events

Hypoglycaemic events

In the total study population, the mean number of hypoglycaemic events was 151.4 (SD ± 213.9) per year. The most frequent hypoglycaemic events were nocturnal, with a mean of 97.4 ± 103 events, closely followed by symptomatic events (91.6 ± 159.1). Between the study groups, the controlled group had fewer severe events (14.0 ± 26.0 vs 40.2 ± 50.4) but this cohort had more nocturnal (144.7 ± 141.8 vs 89.7 ± 94.1) and symptomatic events (152.0 ± 281.5 vs 79.7 ± 119.7) as compared to the uncontrolled cohort. (Figures 1-4).

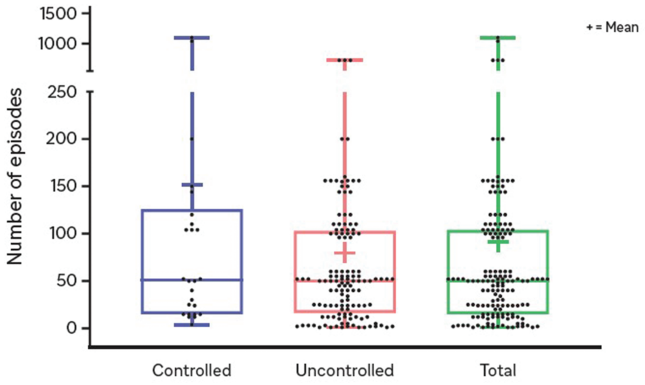

Figure 3. Symptomatic Hypoglycaemic Events

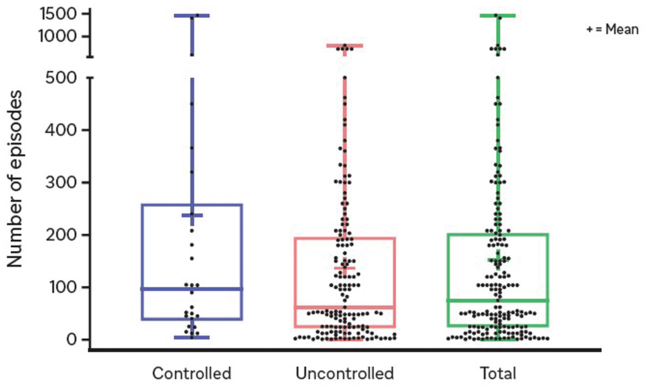

Figure 4. Total Hypoglycaemic events

Diabetic ketoacidosis (DKA)

In the controlled group, 1 patient (2.7%) experienced a DKA episode, as compared to 27 patients (14.5%) in the uncontrolled group.

DISCUSSION

The majority (83%) of patients in this study who were female and of black ethnicity did not attain a target HbA1c of below 7%. The high proportion of patients with poor glycaemic control is concerning, similar to that reported by Hoosen and Mbanya.(2,4) Hoosen,(4) performed a 10-year (2006–2015) chart review of patients with T1DM who attended a tertiary health facility in South Africa and found that less than 10% of patients had attained a glycaemic target defined as a HbA1c < 7%. The average age of this patient population was under 30 years, but already had increased levels of retinopathy and nephropathy. Study participants in the current study had low levels of microvascular complications. The reasons are not clearly apparent but given the nature of a retrospective review, the low levels of micro and macrovascular disease may be due to reporting bias and limited screening for these complications in a busy, resource limited setting of public hospitals in South Africa.

Mbanya,(2) described the findings of the International Diabetes Management Practices Study (IDMPS) which

was an observational study conducted using a questionnaire administered to clinicians and patients in 12 African countries. Of the 788 patients with T1DM, only 17% had an HbA1c <7%, which is similar to our study finding. The authors concluded that African patients with T1DM have suboptimal glycaemic control with frequent hospitalisations (25% of the patient population were hospitalised during the preceding year). Patients cited a lack of insulin titration, fear of hypoglycaemia and poor education as primary reasons for non-attainment of the glycaemic target.

Given that poor glycaemic control is a leading cause of renal failure, one would expect that many uncontrolled patients would eventually require renal replacement. While only one patient in the uncontrolled group had renal complications, the prevalence of complications is likely to increase with time and age of patient. Access to dialysis in the South African public sector is highly constrained, with only 1.5% of patients suitable for renal replacement therapy receiving treatment largely due to resource constraints.(8,9)

The six patients with diabetic foot ulcer disease in the uncontrolled group are at increased risk of lower limb amputations. The rate of lower limb amputations has been described as a surrogate marker for the overall diabetes control.(8) Peripheral neuropathy and poor glycaemic control are frequent contributors to cases of lower limb amputations. When considering the medical, personal, family loss and socio-economic costs, diabetic foot disease is estimated to cost South Africa at least R68 billion per annum.(10) It has been estimated that implementation of a multi-disciplinary amputation prevention approach, including foot education and deployment of a podiatrist in areas of need can lead to a 39%–56% reduction in amputation rate.(10)

Episodes of macrovascular and microvascular complications were generally few in our study but were more prevalent in the uncontrolled group compared to the controlled group. If glycaemic control in the uncontrolled group remains suboptimal, a significant number will develop vascular complications and are likely to have premature mortality. Amongst patients with T1DM from Soweto, Johannesburg, a crude 20-year mortality of 43% has been described, largely related to renal failure and hypoglycaemia.(5) Given that the mean age of the patient population described was 22 ± 5 years, the implication of diabetes as a leading cause of morbidity and mortality amongst the economically active population of the country is apparent.

In this study diabetic ketoacidosis was more frequent in the uncontrolled group. This condition requires intense medical care to ensure that patients survive, adding significant strain to public sector hospitals. The risk to the patient and added strain to the health care system can be minimised if patients have better glycaemic control.

Hypoglycaemia was more pronounced in the controlled group, which may indicate that tight glycaemic control places the patient at risk of severe hypoglycaemia. Apart from the potential to contribute to morbidity and mortality, hypoglycaemia is a deterrent to adequate glycaemic control. As described among patients from the IDMPS cohort, fear of hypoglycaemia, inadequate insulin titration and a lack of diabetes education are barriers to attaining an adequate glycaemic target.(2) Among patients with T1DM, frequent episodes of hypoglycaemia commonly lead to hypoglycaemia-associated autonomic failure, resulting in a reduced counterregulatory hormonal response and consequently asymptomatic hypoglycaemia.(11) Thus, in many patients with T1DM, the immediate fear of hypoglycaemia exceeds the concern around long-term complications of diabetes.(12)

Another plausible explanation for the high occurrence of hypoglycaemic events in this study was that all the patients were receiving human insulin as this is the standard of care in the public sector hospitals of South Africa. Numerous clinical trials have demonstrated lower levels of hypoglycaemia with insulin analogues, in particular, fewer nocturnal and severe episodes of hypoglycaemia.(13–15) The use of insulin analogues is supported by local and international guidelines. The ADA recommends insulin analogues in people with T1DM, as it is associated with less hypoglycaemia and weight gain, as well as lower HbA1c, when compared to human insulin.(16) The Society for Endocrinology, Metabolism and Diabetes of South Africa, Type 2 Diabetes guidelines recommend insulin analogues, when cost is not prohibitive.(17) While real-world evidence does indicate that the hypoglycaemic benefit of analogue insulins may correlate with improved glycaemic control,(18) access to insulin analogues in South Africa is restricted in the public sector health care environment due to its costs.

The controlled group had fewer severe hypoglycaemic episodes. We postulate that the controlled group had better glycaemic control, thus less autonomic dysfunction and more hypoglycaemic awareness. In patients with poor glycaemic control, autonomic dysfunction and hypoglycaemic unawareness may result in an inability to detect and correct mild hypoglycaemia early, leading to severe hypoglycaemic episodes.

The ADA recommend that all people with diabetes participate in diabetes self-management education and receive the support needed to facilitate the knowledge, decision-making, and skills mastery for diabetes self-care.(16) Patient support programmes have been shown to improve patient outcomes and reduce costs by improving adherence and persistence.(19–21) Group-centred patient education within the resource-constrained setting of sub-Saharan Africa has been shown to result in significant improvements in HbA1c. In patients with T1DM or T2DM in Rwanda, those assigned to the interventional treatment group achieved a reduction in HbA1c of 1.7%, compared to 0.53% in the non-interventional arm. Hence, improvements in glycaemic control within a resource-constrained setting are possible without significant financial implications.(22) Ideally, the aforementioned practices should be adopted in the South African public sector health centres managing patients with DM.

LIMITATIONS

There are several limitations of this study. Firstly, this was a retrospective study design and patient selection was only from tertiary health facilities. Data was reliant on a chart review and hence entries from the treating healthcare worker. There is a potential limitation of underreporting and lack of diagnosis standardization when relying on a chart review. Recruitment occurred during the COVID-19 pandemic which may have influenced the patient population enrolled. Despite the limitations, the study provides important insights into the lack of glycaemic control in people living with T1DM.

CONCLUSION

The majority of patients with T1DM managed in two of the largest public sector hospitals in South Africa, did not achieve their target HbA1c, which places them at high risk of developing micro- and macrovascular complications. Furthermore, poor glycaemic control predisposed the uncontrolled group to diabetic ketoacidosis, which creates further strain on an already overburdened public health sector in South Africa. Also, lack of insulin analogues predisposes these patients to more hypoglycaemic events. Patient support programmes and group-centred patient education which have shown significant improvements in HbA1c should be implemented as a matter of urgency in the public health sector in South Africa.

CONFLICTS OF INTEREST

The research costs for this study were funded by Sanofi. KN and LS are employees of Sanofi and PN is a former employee of Sanofi.

AUTHOR CONTRIBUTION

SB, BP, PN and EV contributed to the study design. SB, BP and EV contributed to the data collection. All authors were involved in the writing of the paper and proofreading.

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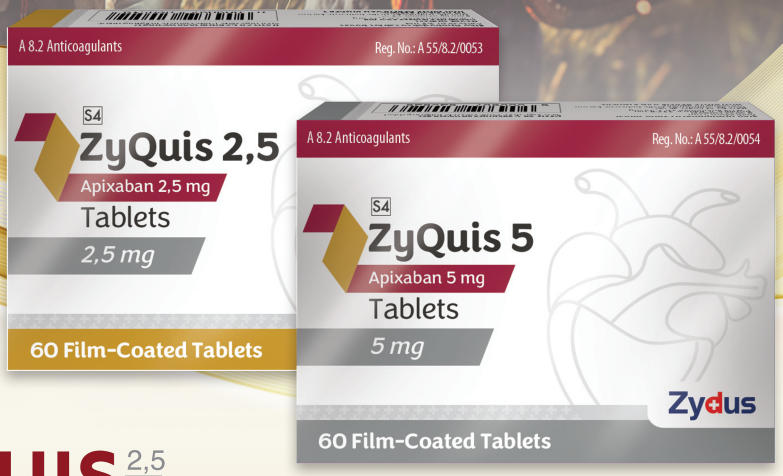

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