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High frequency of hypoglycaemia in patients with type 1 diabetes mellitus attending a tertiary diabetes clinic in Durban, South Africa ☆

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ABSTRACT

Aim: The study aimed to assess the prevalence of hypoglycaemia in subjects with type 1 diabetes (T1D) attending a public health tertiary diabetes clinic in Durban, South Africa.
Methods: Patients with T1D were enrolled at the time of clinic attendance. Data on hypoglycaemia over the previous 12 weeks were obtained from glucose meter downloads as well as diary records. Each patient completed the Hypoglycaemia Fear Survey questionnaire as well as an in-house questionnaire on hypoglycaemic episodes in the previous 12 months.
Results: A total of 151 subjects (58% female, 54% black African) were enrolled. "Any" hypoglycaemia occurred in 144 (95.4%) in the 12 months prior to clinic attendance. Of these, "severe" hypoglycaemia occurred in 107 (74.3%) and 22 (20.6%) had five or more severe episodes. The most frequent behavioural change in response to hypoglycaemia was insulin dose self-adjustment and the commonest worry was the possibility of becoming emotionally upset during hypoglycaemia.
Conclusions: In a tertiary diabetes clinic in Durban, South Africa, there was a high frequency of hypoglycaemia in patients with T1D and in the majority, at least one severe episode occurred in the 12 months prior to clinic attendance. The results indicate a need for further study and strategies to reduce the frequency and severity of hypoglycaemia.

1. Introduction

Current management strategies in patients with type 1 diabetes mellitus (T1D) aim to achieve near-normoglycaemia, with glycated haemoglobin (HbA1c) levels <7.0% (53 mmol/mol) [1]. This requires the use of insulin either in multiple daily doses, or in an infusion pump. Despite innovation in the design of new insulin analogues, patients using multiple daily doses still need to deal with some degree of unpredictability in the glycaemic response to an injected dose [2]. In addition, people with T1D are also required to estimate meal carbohydrates and use various methods to determine prandial insulin requirements. These estimates are imperfect and wide glycaemic fluctuations often occur after meals. Hypoglycaemia is a common adverse effect of insulin therapy

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and as glycaemic control improves, the risk increases. In the Diabetes Control and Complications Trial (DCCT), intensive insulin treatment was associated with a significantly increased risk of severe hypoglycaemia (relative risk 3.28) [3]. Severe hypoglycaemia, which requires a third party for treatment, is characterised by neuroglycopaenia and is reported to occur at a frequency of 0.70–1.59 episodes per patient per year in subjects with T1D [4]. Hypoglycaemia of any degree influences quality of life and may hinder attempts to tighten glycaemic control. Furthermore, recurrent hypoglycaemia may lead to loss of the counter-regulatory responses and unawareness of falling glucose levels. The symptoms generated during episodes of hypoglycaemia are unpleasant and individuals may devise strategies to avoid hypoglycaemia, with the inevitable consequence of poorer overall glucose control. Fear of hypoglycaemia has been evaluated using structured patient questionnaires and hypoglycaemia has been shown to be accompanied by substantial psychologic distress [5].

The prevalence of hypoglycaemia and associated risk factors in patients with T1D in Africa is not well described. A study from Kenya reported that severe hypoglycaemia occurred in 53.5% of children over a 6-month period [6]. This study, however, did not focus specifically on hypoglycaemia, but rather provided an overall review of glycaemic control in Kenyan children and adolescents in three outpatient clinics. A survey of acute and chronic complications in 99 Tanzanian children reported a 6-month frequency of hypoglycaemia of 55.6% [7]. In this study, however, hypoglycaemia was recorded only by self-reported presence of symptoms, with no capillary glucose confirmation. By contrast, severe hypoglycaemia was uncommon in a group of 80 South African children, primarily from private medical facilities, attending diabetes camps and a 20-year follow up study of 88 patients with T1D in Soweto, South Africa, reported six deaths due to hypoglycaemia [8,9]. The public health care sector in South Africa provides for 84% of the population, with an annual per capita health expenditure that is 10-fold lower than the 16% of the population cared for by the private sector [10]. Factors such as access to care, medication and support are vastly different between public and private sectors in South Africa and would be anticipated to impact on multiple aspects of management in a condition such as T1D. There are no studies on the prevalence of hypoglycaemia in the public sector in South Africa and this lack of clear data on the prevalence of hypoglycaemia in subjects with T1D in Africa as well as limited information on risk factors for hypoglycaemia prompted the current study.

2. Methods

The study was a cross-sectional survey of patients with T1D attending a tertiary diabetes clinic at Inkosi Albert Luthuli Central Hospital (IALCH) in Durban, KwaZulu-Natal, South Africa. Adult patients were invited to participate at the time of routine, scheduled clinic review. Subjects were 18 years or older and had a diagnosis of T1D based on clinical and laboratory criteria. Demographic, anthropometric, clinical and laboratory data were collected from each patient's electronic medical record. Each patient completed two questionnaires: a structured in-house questionnaire to determine the frequency and severity of hypoglycaemic episodes and the standard Hypoglycaemia Fear Survey [11]. The in-house questionnaire collected data on the frequency and severity of hypoglycaemic episodes in the previous 12 months, by patient recall. The questionnaires were translated into isiZulu for Zulu-speaking patients. In addition, the data stored in each patient's glucose meter were downloaded for analysis. All patients used Accuchek® glucose meters and Smartpix® (Roche) software was used for data extraction. The software was able to extract meter data for the 3 months prior to clinic attendance. Hand-written glucose diaries were collected for comparison with the glucose meter data and episodes of hypoglycaemia recorded in the meter memory were correlated with diary entries. The prevalence of hypoglycaemia was therefore derived from both patient recall as well as data from meter downloads.

2.1. *Definitions*

Hypoglycaemia was defined as finger prick (capillary) glucose <4.0 mmol/l [12]. "Severe" hypoglycaemia was that which required a third party for treatment. "Frequent" severe hypoglycaemia was defined as more than two episodes per year and "less frequent" severe as two or fewer severe episodes per year.

2.2. *Data collection*

Patient data included age, gender, and duration of T1D, ethnic group, employment status, number of clinic visits and number of defaulted visits. Clinical data included height, weight, waist and hip circumference, blood pressure, presence of retinopathy (using non-mydriatic fundal photography), neuropathy (clinical assessment) and nephropathy (presence of microalbuminuria (spot urine albumin-creatinine ratio >3.0 mg/mmol) or proteinuria) and isotope glomerular filtration rate. Laboratory data included the most recent glycated haemoglobin (HbA1c), fructosamine, creatinine, lipid levels, presence of anti-glutamic acid decarboxylase (GAD) antibodies and fasting c-peptide levels. In addition, details of insulin type, number of injections and daily dose were collected. The availability of glucagon for emergency home management of hypoglycaemia was recorded.

2.3. *Hypoglycaemia Fear Survey*

This has been widely used to evaluate fear of hypoglycaemia in patients with diabetes [11]. The questionnaire is in two parts: the first part consists of 18 questions relating to concern for hypoglycaemia (the "worry" sub-scale) and the second consists of 15 questions relating to behavioural responses to hypoglycaemia (the "behaviour" sub-scale). Responses require selection of a rating on a 5-point Likert scale, ranging from 0 (never) to 4 (almost always). The scores range from 0 to 72 for the worry sub-scale, 0 to 60 for the behaviour sub-scale and the total scores from 0 to 132. Higher scores indicate greater fear of hypoglycaemia.

2.4. Laboratory methods

All laboratory tests were performed in the IALCH Chemical Pathology laboratory. Glucose was measured with the hexokinase method and serum lipids with an enzymatic assay (Siemens Advia 1800, Germany). Low density lipoprotein cholesterol was calculated with the Friedewald formula. HbA1c was measured with high performance liquid chromatography (Tosoh, Japan), fructosamine with an enzymatic spectrophotometric method (Siemens Dimensions EXL, Germany), urine albumin with an immunoturbidometric assay (Siemens Advia 1800, Germany) and anti-GAD with enzyme-linked immunosorbent assay (Euroimmune AG, Lübeck Germany). C-peptide was measured with a chemiluminescent immunoassay (Siemens Centaur, Germany). Proteinuria was defined as dipstick positivity for three consecutive visits.

Glomerular filtration rate was measured with the Perkin Elmer Wizard^2 2470 Multi-Channel Well Counter (Waltham, Massachusetts, USA) after injection of 500 μCi ^{99m}Tc-DTPA (diethylenetriamine penta acetate) and sampling at 2 and 3 h post-injection.

2.5. Statistical methods

Data were analysed with STATA v13.1 (StataCorp 2013, College Station, TX). Results are expressed as mean ± SD, or median ± inter-quartile range (IQR) for continuous variables and as percentage for categorical variables. Fisher's exact test, chi square and Mann Whitney tests were used for group comparisons. A p value <0.05 was regarded as significant.

2.6. Ethics and approvals

The Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal (Reference BE304/13) and the KwaZulu-Natal Department of Health approved the study. Professor Linda Gonder-Frederick, Health Sciences Center, University of Virginia, Charlottesville, Virginia, USA kindly provided permission for the use of the Hypoglycaemia Fear Survey.

3. Results

3.1. Participant characteristics

The total study group included 151 patients of whom 88 (58%) were women. The median age was 25 (IQR 2331) years, median age at diagnosis 16 (IQR 11–21) years and median duration of T1D 11.5 (IQR 6–18) years. The majority of participants, 82 (54%), were African (black); 55 (36%) were Asian Indian, 10 (7%) White and 4 (3%) Mixed Race subjects. Seventy-six (50%) subjects were either employed or students. Clinical and laboratory results are shown in Tables 1 and 2. No patient eligible for the study declined participation.

3.2. Insulin therapy

All study subjects were treated with insulin and the majority with basal-bolus therapy. Bolus insulin was regular soluble human insulin in 66 (44%) and ultra-rapid acting analogue insulin (lispro) in 82 (54%). The majority (91%) of subjects used human isophane basal insulin, with only 14 (9%) using an analogue basal insulin (detemir). The median total daily insulin dose was 1.0 (IQR 0.8–1.4) units/kg; the median basal

Table 1 – Demographic and clinical characteristics of subjects with Type 1 diabetes (n = 151).

	N = 151
Ethnic group	
African	82 (54.3)
Indian	55 (36.4)
White	10 (6.6)
Mixed race	4 (2.7)
Gender	
Male	64 (42.4)
Female	87 (57.6)
Age (yr.)	25 (21–36)
Age at diagnosis (yr.)	15 (11–22)
Diabetes duration (yr.)	12.0 (6–18)
Body mass index (kg/m^2)	26.4 ± 5.2
Waist circumference (cm)	83 (76–92)
Systolic BP (mmHg)	129.5 ± 16.1
Diastolic BP (mmHg)	73.1 ± 10.8
Retinopathy	21 (13.9)
Background	9 (6.0)
Proliferative	15 (9.9)
Peripheral neuropathy	7 (4.6)
Macrovascular disease (any)	15 (9.9)
Insulin therapy	
Basal-bolus therapy	149 (98.7)
Pre-mix therapy	1 (0.7)
Insulin pump	1 (0.7)
Total dose (units/kg/day)	1.0 (0.8–1.4)
Basal dose (units/kg/day)	0.34 (0.3–0.5)
Bolus dose (units/kg/day)	0.63 (0.5–0.8)

Data shown as n (%), mean ± SD, or median (IQR).

Table 2 – Laboratory characteristics of 151 subjects with Type 1 diabetes.

	N = 151
HbA1c (%)	9.3 (8.1–10.9)
HbA1c (mmol/mol)	78 (65–96)
Fructosamine (μmol/l)	378 (318–465)
Creatinine (μmol/l)	60 (48–74)
Microalbuminuria	28 (18.5)
Proteinuria	27 (17.9)
GFR (ml/min/m^2)	112.0 ± 33.7
Total cholesterol (mmol/l)	4.3 (3.7–5.1)
Triglycerides (mmol/l)	1.1 (0.7–1.6)
HDL cholesterol (mmol/l)	1.5 (1.2–1.8)
LDL cholesterol (mmol/l)	2.2 (1.8–2.9)
Anti-GAD positive*	99 (66)
Fasting c-peptide (ng/ml)**	0.1 (0.0–0.5)

Data shown as n (%), mean ± SD or median (IQR).
GFR: Glomerular filtration rate; HDL: High density lipoprotein; LDL: Low density lipoprotein.
GAD: Glutamic acid decarboxylase.
* Anti-GAD available for 150 subjects.
** Fasting c-peptide available for 107 subjects.

insulin dose was 0.3 (IQR 0.3–0.5) units/kg per day (35% of the total daily dose) and the median bolus insulin dose 0.6 (IQR 0.5–0.8) units/kg per day (65% of the total daily dose) (Table 1). One hundred (66%) study subjects reported having been issued with glucagon for emergency use, at previous clinic visits.

3.3. *Glucose monitoring*

The study subjects performed a median of 1.0 (IQR 0.5–1.7) tests per day. Of these, day-time tests were more frequent than night-time tests (1.06 ± 0.92 vs. 0.15 ± 0.24, $p < 0.0001$).

3.4. *Hypoglycaemia*

3.4.1. *Overall prevalence*

In the total study group (n = 151), hypoglycaemia of any severity was recorded in 144 (95.4%) (Table 3). A median of 10 hypoglycaemic events per patient occurred in the 3 months prior to the enrolment clinic visit (3.3 events/patient/month).

3.4.2. *Severe hypoglycaemia*

Of the 144 subjects that reported any hypoglycaemia, 107 (74.3%) had at least one severe episode in the preceding year and 29 (20.1%) reported that hospitalisation for hypoglycaemia had been required on at least one occasion; "frequent severe" hypoglycaemia occurred in 65 (60.7%) and 22 (20.6%) reported five or more severe episodes per year. Overall, "severe" hypoglycaemia occurred at a rate of 2.36 episodes/patient/year. Subjects in whom "severe" hypoglycaemic episodes occurred experienced more nocturnal hypoglycaemia (31 vs 15%, p = 0.04) than those who had either none or mild to moderate hypoglycaemia. No significant differences were found between these groups for other clinical and laboratory parameters (Table 3).

Subjects who experienced "frequent" severe hypoglycaemic episodes were more often female (63 vs. 43%, p = 0.044) and had a higher prevalence of peripheral neuropathy (27.7 vs. 9.5%, p = 0.03) than those who had "less frequent" severe hypoglycaemia. Frequency of severe hypoglycaemia was not associated with other clinical and laboratory parameters (Table 3).

3.4.3. *Factors associated with hypoglycaemia*

Of 144 respondents, the majority (n = 130; 90.3%) identified a probable cause of any hypoglycaemia. Amongst these, 110 (76.4%) reported that missing a meal accounted for a documented episode, 96 (66.7%) due to exercise, 80 (55.6%) due to intercurrent illness, 67 (46.5%) due to insulin dose error and 15 (10.4%) related to consumption of alcohol. Thirteen subjects (9.0%) reported the absence of symptoms at the time of documented hypoglycaemia. By contrast, symptoms suggestive of hypoglycaemia, with a documented capillary glucose >4.0 mmol/l, occurred in 97 (67.4%).

Table 3 – Hypoglycaemia according to severity and frequency in subjects with Type 1 diabetes (n = 144) over 12 months.

	Any hypoglycaemia N = 144	All severe N = 107	Frequent severe N = 65	Less frequent severe N = 42	P value
Male	61 (42)	48 (45)	24 (37)	24 (57)	
Female	83 (58)	59 (55)	41 (63)	18 (43)*	0.044
Age (yrs.)	25 (21–36)	27 (22–37)	29 (22–38)	25 (22–36)	NS
BMI (kg/m^2)	26.4 ± 5.2	26.3 ± 5.0	26.2 ± 4.9	26.3 ± 4.8	NS
Diabetes duration (yrs.)	11.5 (6–18)	12 (6–19)	12 (6–21)	12 (7–17)	NS
Defaulted clinic visits	1 (0–2)	1 (0–2)	1 (0–2)	1 (0–2)	NS
Glucose tests per day	1.0 (0.5–1.7)	0.9 (0.5–1.7)	0.9 (0.4–2.1)	1.0 (0.5–1.5)	NS
Total insulin dose (u/kg/day)	1.04 (0.8–1.4)	1.1 (0.8–1.4)	1.0 (0.8–1.4)	1.1 (0.9–1.4)	NS
Basal insulin dose (u/kg/day)	0.35 (0.3–0.5)	0.35 (0.3–0.5)	0.34 (0.3–0.5)	0.36 (0.3–0.5)	NS
Bolus insulin dose (u/kg/day)	0.64 (0.5–0.8)	0.65 (0.5–0.9)	0.64 (0.5–0.9)	0.70 (0.5–0.9)	NS
Systolic BP (mmHg)	130 ± 16	129 ± 15	128 ± 16	131 ± 13	NS
Diastolic BP (mmHg)	73 ± 11	73 ± 10	73 ± 12	73 ± 8	NS
HbA1c (%)	9.3 (8.1–10.9)	9.4 (8.1–10.9)	9.5 (8.0–10.8)	9.0 (8.2–11.0)	NS
HbA1c (mmol/mol)	78 (65–96)	79 (65–96)	75 (66–97)	80 (64–95)	NS
Fructosamine (μmol/l)	378 (319–465)	378 (314–459)	376 (327–469)	378 (305–457)	NS
Creatinine (μmol/l)	61 (48–75)	63 (46–77)	60 (45–82)	65 (53–76)	NS
Microalbuminuria	27 (18.8)	21 (19.6)	12 (18.5)	9 (21.4)	NS
Proteinuria	27 (18.8)	27 (25.2)	19 (29.2)	8 (19.1)	NS
GFR (ml/min/m^2)	112 ± 33	111 ± 34	108 ± 36	115 ± 30	NS
Retinopathy	30 (20.8)	24 (22.4)	16 (24.6)	7 (16.7)	NS
Peripheral neuropathy	15 (10.4)**	22 (20.6)	18 (27.7)	4 (9.5)*	0.03
Anti-GAD positive	97 (67.4)	69 (64.5)	42 (64.6)	27 (64.3)	NS
Fasting c-peptide (ng/ml)	0.1 (0.0–0.5)	0.1 (0.0–0.4)	0.1 (0.0–0.5)	0.1 (0.0–0.3)	NS

Data shown as n (%), mean ± SD, or median (IQR).

GAD: Glutamic acid decarboxylase; Frequent severe hypoglycaemia: more than two episodes per year; Less frequent severe hypoglycaemia: two or fewer episodes per year.

* Frequent severe vs. less frequent severe.

** Any hypoglycaemia vs. All severe; Any hypoglycaemia vs. frequent severe.

Table 4 – Hypoglycaemia Fear Survey scores in subjects with Type 1 diabetes.

	Total score	Worry sub-scale	Behaviour sub-scale
All subjects	50 (37–67)	25 (17–39)	24 (18–30)
Severe hypoglycaemia	52 (39–68)	27 (18–42)	25 (19–31)
Non-severe hypoglycaemia	41 (30–60)	20 (10–35)	23 (16–27)
Frequent severe hypoglycaemia	54 (40–76)*	29 (19–45)	27 (19–32)
Less frequent severe hypoglycaemia	45 (38–62)	21 (18–31)	24 (20–29)

Data shown as median (IQR).
* p = 0.04 frequent severe vs. less frequent severe hypoglycaemia.

3.5. *Hypoglycaemia Fear Survey*

Scores for the HFS questionnaire are shown in Table 4. The median total score for the entire study group was 50 (IQR 37–67, range 5–111). The scores did not differ between the group of subjects who experienced severe hypoglycaemia and those in whom severe hypoglycaemic episodes did not occur, either for the total score or for each of the sub-scales (behaviour and worry). Patients who experienced "frequent severe" hypoglycaemia had a higher total score compared to those who had "less frequent severe" hypoglycaemia (54 (IQR 40–76) vs. 45 (IQR 38–62), p = 0.04). No other differences were found between the sub-groups of patients. The most frequent behavioural responses to hypoglycaemia were insulin dose reduction, followed by ensuring that people were around and the most frequent concerns expressed in response to hypoglycaemia were becoming emotionally upset and difficult to deal with, as well as hypoglycaemia occurring during sleep.

4. Discussion

The current study shows that hypoglycaemia occurs in almost all (95.4%) subjects with type 1 diabetes, attending a tertiary diabetes clinic in KwaZulu-Natal, South Africa. In addition, 74.3% reported at least one severe hypoglycaemic episode in the 12 months prior to enrolment in the study and of these, hospitalisation was required in 20.1%. Furthermore, the majority (60.7%) of those with severe hypoglycaemia experienced "frequent" severe hypoglycaemia. Missing a meal, exercise, intercurrent illness and insulin dose error were the commonest reasons identified as precipitants of a hypoglycaemic episode.

The United States T1D Exchange Clinic Registry reported on factors associated with severe hypoglycaemia and diabetic ketoacidosis in 7 012 adult subjects with T1D [13]. In this study, severe hypoglycaemia occurred in at a lower rate (11.8%) than in the current study and both longer disease duration and lower socio-economic status were associated with severe hypoglycaemia [13]. The global HAT study reported on rates of hypoglycaemia in 27 585 patients with type 1 and insulin-treated type 2 diabetes from 24 countries [14]. Although no African centres were included in this study, a high rate of any hypoglycaemia (83%), similar to the current study, was recorded in the 8 022 subjects with T1D. However, in contrast to the current study, only 14.4% experienced severe hypoglycaemia. In the global HAT study, factors associated with severe hypoglycaemia included longer duration of insulin therapy and fear of hypoglycaemia. More recently, The International Operations HAT (IO HAT) study retrospectively and prospectively assessed the incidence of hypoglycaemia in 7 289 subjects with insulin-treated diabetes in Bangladesh, Colombia, Egypt, Indonesia, Philippines, Singapore, South Africa, Turkey, and United Arab Emirates [15]. In IO HAT study, the South African patients were enrolled from a private practice, whereas the patients in the current study were all part of the public health sector; there are vast disparities in the resources provided by the private and public sectors in South Africa and this limits comparisons with the IO HAT and the current study [10]. In the IO HAT study any hypoglycaemia occurred in 97.4% of the 1 016 subjects with T1D and severe hypoglycaemia occurred from 48.6 to 50.6% of subjects, depending on the method of data collection (prospective or retrospective). Hospitalisation for hypoglycaemia occurred in 9.6% (retrospective recall) and 3.1% (prospective ascertainment). The current study only collected retrospective data and showed a similar rate of any hypoglycaemia, but a higher rate of severe hypoglycaemia as well as hospitalisation for severe hypoglycaemia. The IO HAT study showed differences in prevalence rates depending on the method of data collection, possibly accounting for some of the differences between the studies.

A questionnaire-based study in 99 children and adolescents with T1D aged 5–18 years in Tanzania found that 55.6% of patients experienced symptomatic hypoglycaemia in the previous six months [7]. The lower rate of hypoglycaemia in the Tanzanian study, as compared to the current study, may be due to the fact that none of the patients in Tanzania performed home glucose monitoring and it is possible that a number of episodes were therefore not recorded. Furthermore, the Tanzanian study did not specifically report on severe hypoglycaemia. A report on 82 children and adolescents with T1D, aged 3–19 years, attending three clinics in Nairobi, Kenya found that 53.6% of subjects experienced severe hypoglycaemia [6]. The data were also collected by questionnaire and, as with the Tanzanian study, very little self-monitoring of glucose was performed suggesting that less severe episodes of hypoglycaemia may not have been recognised. All patients included in the current study performed self-monitoring of glucose, but the severe episodes were also determined retrospectively, as in the Tanzanian and Kenyan studies, and are therefore also subject to recall bias. A study of 230 Danish subjects with T1D compared retrospective recall and prospective recording of severe hypoglycaemic episodes and found a 15% discrepancy, with under-reporting of retrospective episodes [16]. Therefore, the

rate of hypoglycaemia in the current study population may be under-estimated due to a similar influence of recall bias.

The median HbA1c in the current study was 9.3 (IQR 8.1–10.9) % (78 (IQR 65–96) mmol/mol), indicative of poor overall glycaemic control. Furthermore, the majority of subjects tested their glucose less than twice daily. The high frequency of hypoglycaemia in the current study is at variance with the overall poor glycaemic control and with the results of the DCCT study, which showed a higher frequency of severe hypoglycaemia with lower HbA1c levels [3]. Whilst there is a clear relationship between the frequency of glucose self-tests and HbA1c, recent studies have shown a weakening relationship between HbA1c and severe hypoglycaemia at least in those reported from Europe [17]. This may reflect increasing use of new technology in these countries and is not likely to be similar to the situation in the public health sector in South Africa.

The predominant bolus insulin used by the study group was ultra-rapid analogue insulin. Although the longer duration of action of regular insulin compared to rapid-acting analogue bolus insulin may theoretically lead to glucose-insulin mismatches more often in the group treated with regular insulin, no difference in hypoglycaemic rates between regular and analogue bolus insulin in adults with T1D was shown in a recent Cochrane review [18]. An additional possible explanation for the pre-meal susceptibility to hypoglycaemia in the current study may be the observation that patients used proportionately more bolus insulin (65% of the total daily dose) than basal and thus may have been over-treated with prandial doses.

Apart from the relation to meals and time of day, patients reported exercise and illness as other factors associated with hypoglycaemia. Managing glycaemia during physical exercise poses well-established challenges and it is not unexpected that this was one of the factors reported in the current study [19]. Although data on exercise habits were not collected, many of the young people in the study engage in informal exercise activities, such as football, and it is probable that education on the importance of specific insulin dose adjustments prior to exercise or augmenting carbohydrate intake during exercise is sub-optimal in these patients.

The Hypoglycaemia Fear Survey (HFS) was initially developed to assess concerns and behavioural strategies related to hypoglycaemic episodes in adults with type 1 diabetes [11]. In the current study, patients who experienced episodes of “severe” hypoglycaemia had similar responses, for the composite of both scales as well as for each sub-scale, to the subjects in whom “severe” hypoglycaemia did not occur. The large number of subjects in the group who experienced “severe” hypoglycaemia (107 of 151) may have skewed these results as, intuitively, severe hypoglycaemia would instil fear of future episodes, as reported in other studies [20,21]. The HFS identified an overall difference between subjects with “frequent severe” hypoglycaemia and “less frequent severe” hypoglycaemia, although none of the sub-scales were significantly different. The higher total score in those with “frequent severe” hypoglycaemia probably reflects the overall sense of vulnerability in subjects who have repeated severe episodes of hypoglycaemia.

Limitations of the study include the retrospective nature and the limitations imposed by recall bias. In addition, reliance was placed on self-recording of hypoglycaemic episodes and it is possible that a number of episodes were unrecorded, either in the diary or the glucose meter. Despite these shortcomings, it is clear that hypoglycaemia is a significant clinical problem in patients with type 1 diabetes in KwaZulu-Natal and there is an urgent need to devise strategies to limit the frequency and severity of hypoglycaemia, implemented concurrently with strategies to improve glycaemic control. The basis of these efforts must focus on better education of patients in terms of self-management, insulin dose selection and improved dietary management where this is practically possible. In addition, a prospective study would add important information on the prevalence and risk factors for hypoglycaemia in patients with T1D cared for in the public sector in South Africa.

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Declaration of Competing Interest

None.

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