

Obesity and hypoglycaemia in type 2 diabetes mellitus outpatients on insulin therapy in Nigeria—data from the multicentre evaluation of type 2 diabetes mellitus outpatients patients on insulin therapy (METOIN) study.

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Abstract

Background and Objective: Despite the obvious benefits of early insulin use in achieving good glycaemic control, insulin linked overweight/obesity and hypoglycaemia are sources of concern and worry. Burden of these side effects among type 2 diabetes mellitus (T2DM) outpatients on insulin therapy in Nigeria is unknown.

Subjects and Methods: This was a prospective, cross sectional and observational study in which consenting T2DM outpatients that meet the inclusion criteria for the study in five tertiary health facilities were simultaneously recruited and relevant data obtained via investigator-administered questionnaire. Data obtained which included gender, anthropometric measures, hypoglycaemia and where it was treated were analyzed using Statistical Package for Social Sciences (SPSS) version 23.0 software.

Results: A total of 245 T2DM outpatients were recruited into the study, made up of 107 (43.7%) male and 138 (56.3%) female. Of this, 121 (49.8%) patients were overweight while 70 (28.7%) were obese. Among the patients, 104 (42.4%) T2DM outpatients on insulin therapy reported hypoglycaemia which was mild in 83 (79.8%) of the patients

Conclusion: A significant number of the type 2 DM outpatients on insulin therapy were overweight/obese with mild hypoglycaemia in a majority of them.

Obésité et hypoglycémie chez les patients ambulatoires atteints de diabète sucré de type 2 sous insulinothérapie au Nigéria – données de l'évaluation multicentrique des patients ambulatoires atteints de diabète sucré de type 2 sous insulinothérapie (étude METOIN)

Résumé

Contexte et objectif de l'étude : Malgré les avantages évidents de l'utilisation précoce de l'insuline pour obtenir un bon contrôle glycémique, le surpoids/l'obésité et l'hypoglycémie liés à l'insuline sont des sources de préoccupation et d'inquiétude. La charge de ces effets secondaires chez les patients ambulatoires atteints de diabète sucré de type 2 (DT2) sous insulinothérapie au Nigéria est inconnue.

Sujets et méthodes de l'étude : Il s'agissait d'une étude prospective, transversale et observationnelle dans laquelle des patients ambulatoires consentants atteints de DT2 et répondant aux critères d'inclusion de l'étude dans cinq établissements de santé tertiaires ont été simultanément recrutés et des données pertinentes obtenues via un questionnaire administré par l'investigateur. Les données obtenues comprenant le sexe, les mesures anthropométriques, l'hypoglycémie et l'endroit où elle a été traitée ont été analysées à l'aide du logiciel Statistics Package for Social Sciences (SPSS) version 23.0.

Résultats de l'étude: Au total, 245 patients ambulatoires atteints de DT2 ont été recrutés dans l'étude, composés de 107 (43,7 %) hommes et 138 (56,3 %) femmes. Parmi eux, 121 (49,8 %) patients étaient en surpoids tandis que 70 (28,7 %) étaient obèses. Parmi les patients, 104 (42,4 %) patients ambulatoires atteints de DT2 sous insulinothérapie ont signalé une hypoglycémie légère chez 83 (79,8 %) des patients.

Conclusion : Un nombre significatif de patients ambulatoires atteints de diabète de type 2 sous insulinothérapie étaient en surpoids/obèses avec une légère hypoglycémie chez la majorité d'entre eux.

INTRODUCTION

Glycaemic control in patients with T2DM not only reduces the macrovascular and microvascular complications but also improves the cardiovascular profile (1), reduces glucotoxicity, decreases morbidity, mortality and healthcare costs and improves quality of life (2). In the USA, glycaemic control is not achieved in more than 60% of patients with T2DM (3). This is because one barrier to insulin use among these patients is patient's apprehension over the possibility of insulin related weight gain (4). Getting this insulin related weight gain under check is relevant to the prevention of metabolic and cardiovascular consequences in T2DM (5). It has been shown that early insulin therapy helps preserve and maintain pancreatic islet beta cell function in patients with T2DM (6). Insulin related weight gain in patients with T2DM frequently leads to delays in the initiation of insulin therapy and poses challenges when treatment is intensified (7). Despite the obvious benefits of early insulin initiation in patients with T2DM, delays in insulin initiation is common even when glycaemic control is poor (2). Concern regarding the possibility of insulin related weight gain is a major barrier to insulin use by patients and health care professionals (8,9).

Hypoglycaemia militates against safe achievement of optimal glycemia (10). The benefits of tight glycaemic control in reducing microvascular diabetes complications are known but contentious for macrovascular complications (10). In a bid to decrease the risk of microvascular complications through intensive glycaemic control, one is faced with a 3-fold increased risk of severe hypoglycaemia with severe consequences to the brain and the heart (10). Optimal glycemic goals must be personalized but may be generally defined as haemoglobin A1c (HbA1c) of less than 7% as generally recommended by the American Diabetes Association, ADA (11). In general, hypoglycaemia is believed to be less severe and frequent in type 2 DM (12) than in type 1 diabetes mellitus, T1DM.

Type 2 diabetes mellitus outpatients on insulin therapy in Nigeria are prone to hypoglycaemia and overweight/obesity. Hypoglycaemia is fatal if severe, is scary to the patients if he/she survives it but overweight/obesity with diabetes mellitus, hypertension, dyslipidaemia, among others constitute cardiovascular risk factors. There is very scanty information on the burden of hypoglycaemia and overweight/obesity in type 2

diabetes mellitus outpatients on insulin therapy in Nigeria. This study, therefore, is aimed to document the impact of overweight/obesity and hypoglycaemia in type 2 diabetes mellitus outpatients on insulin therapy. Data generated from this study will be useful to clinicians, policy makers, government and managers of health institutions to guide practice and appropriate healthcare budgeting leading to appropriate allocation of healthcare resources and services.

SUBJECTS AND METHODS

Study design and Setting

This was a prospective, cross sectional observational study which took place simultaneously in five tertiary health facilities in Nigeria. The centres were Federal Medical Centre, Umuahia, Nnamdi Azikiwe University Teaching hospital, Nnewi, Obafemi Awolowo University, Ile Ife, University of Port Harcourt Teaching hospital and Federal Medical centre, Yenogua, Bayelsa state. The principal investigator in each of the health institution was a Consultant endocrinologist assisted by medical residents. It was a tertiary hospital based study in which consecutive consenting T2DM outpatients on insulin therapy who meet the inclusion criteria for the study were recruited. An investigator administered questionnaire was used to generate data for the study; data collection was concluded within 24 months. The participant's gender, history of hypoglycaemia and anthropometric data were obtained.

Inclusion criteria

All T2DM outpatients on insulin therapy including all women of child-bearing ages who were on insulin therapy to achieve a better control in an effort to achieve pregnancy were included in the study.

Exclusion criteria

All type 1 diabetes mellitus (T1DM) patients, pregnant women/gestational diabetes mellitus (GDM) patients, post operative T2DM patients or patients recovering from diabetic foot ulcer were excluded from the study.

Recruitment and Data Collection

From January 1, 2020 to December 31, 2021, all consenting T2DM outpatients who met the inclusion criteria for the study were consecutively recruited. Data for the study were extracted from patients using the investigator-administered questionnaire which consisted of their gender, anthropometric indices (such as weight, height and body mass index), history of hypoglycaemia and their treatment. Participants

with a BMI of 25 – 29.9kg/m² were overweight while participants with BMI of = or >30kg/m² were classified into various stages of obesity. Hypoglycaemia was defined by having adrenergic symptoms when the blood glucose was less than 45mmol/l and when glucose is given orally in form of drinks or as infusion led to the relief of symptoms.

Ethical consideration

Ethical approval was obtained from the Institution's Health Research Ethics Committee of each health facility participating in the study before commencing the study.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS Inc. Chicago IL. USA) version 23.0 statistical software was used for data analysis. For continuous variables such as the ages of the study subjects, mean values and standard deviations (SD) were calculated and the means compared using independent two samples t-test. Categorical variables such as the gender, level of obesity etc were summarized using proportions expressed in percentages. The categorical variables were compared using the non-parametric test, chi square test. Level of statistical significance was set at $p < 0.05$.

RESULTS

A total of 245 T2DM outpatients on insulin therapy participated in the study; made up of 107 (43.7%) men and 138 (56.3%) women. While mean age of the participants was 56.93±12.98; the age range of the participants was 23-81 years. The socio-demographic characteristics of the study participants are shown in Table 1.

The mean body mass index (BMI) of the male participants was 27.28 ±3.72kg while that of the female participants was 28.66±4.23kg. The difference between the mean BMI of the male and female participants was statistically not significant ($t=2.675$, $p=0.08$). Majority of the study participants 121 (49.4%) were overweight while 70 (28.6%) were obese (Table 2)

Of the 125 study subjects who had university and postgraduate education, 103 (82.4%) were overweight and obese (Table 3). The study subjects highest level of education and the tendency towards overweight and obesity was not statistically significant ($X^2 = 21.822$, $p = 0.35$).

Majority of the study participants, 141 (57.6%) have never had hypoglycaemia (Figure 1) but out of the 104 study participants who had

hypoglycaemia, 83 (79.8%) were treated at home and it was severe in 21 (20.2%) participants who needed hospital admission (Table 4).

DISCUSSION

The main findings of this study were that majority of the study participants were overweight and obese; overweight and obesity was reported mainly among those who had university and postgraduate education. Again, majority of the study participants have never reported hypoglycaemia and predominant number of those who experienced hypoglycaemia did not need hospital admission.

Majority of the type 2 DM outpatients on insulin therapy in this report were either obese (28.6%) or overweight (49.4%) and this is comparable to the 83% of T2D patients in Ibadan (13) who were either obese or overweight, 27.4% of T2DM patients who were obese in the Kano (14) report and the 24.5% and 39.9% diabetic patients who were obese and overweight respectively in Sudan (15). Because the burden of obesity on type 2 DM outpatients on insulin therapy is comparable to that of the general population of T2DM patients, it is possible that being on insulin therapy may not have contributed considerably to T2DM patients being obese or overweight. The implication of this conclusion is that obesity as a complication of insulin therapy may not be enough reason for not accepting insulin as a treatment modality.

The findings of obesity and overweight predominantly in those who had university and postgraduate education in this report cannot easily be explained except to say that they may be prone to sedentary lifestyle and over eating because of their probable positions as bosses in various fields of life. This is worrisome as this negates the benefits and advantages of higher education. Overweight and obesity was least in those without any formal education at 4.1%; this is probably the population who are subsistence farmers and petty traders.

Majority of the study participants (57.6%) have not reported hypoglycaemia ever since they were on insulin therapy and this is heartwarming to know that hypoglycaemia in T2DM outpatients on insulin therapy was mild and occurred in a minority of the type 2 DM outpatients. Even at that, 79.8% of the T2DM outpatients that suffered hypoglycaemia were treated at home probably because it was mild and, because majority of them were well grounded on diabetes self management education (DSME), they didn't have a need for hospitalization. This

underscores the importance of diabetes self management education in the care and treatment of diabetes complications. It is worrisome to note that more than 20% of those who had hypoglycaemia were admitted and treated in hospital. The experience of severe hypoglycaemia by a patient leaves a soar taste in the patient's mouth. Severe hypoglycaemia is a strong enough reason not to accept insulin therapy.

In conclusion, obesity and hypoglycaemia are complications of insulin therapy in T2DM outpatients which the patients can live with. They are not enough reasons not to accept insulin as a treatment modality. Insulin related weight gain and hypoglycaemia are side effects which cannot outweigh the glycaemic control benefits of insulin.

A limitation of this study included that the weight of the study participants were not captured prior to the commencement of insulin initiation so that insulin related weight gain could not be documented. Overweight and obesity due to T2DM per se could not be differentiated from that due to insulin therapy.

CONCLUSION/RECOMMENDATIONS

This study has shown that the majority of T2DM outpatients on insulin therapy were overweight or obese and this insulin related weight gain was predominantly among those that had university and postgraduate education. Again, hypoglycaemia was reported by a minority of the T2DM outpatients on insulin therapy majority of whom did not need hospital treatment. It is, therefore, recommended that all T2DM outpatients on insulin therapy should have dietary manipulations, lifestyles changes and diabetes self management education.

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Author;s contribution: Dr Marcellinus O. Nkpozi - Conception and design of the research with drafting of the manuscript. He, also, takes overall responsibility for the study. Dr Bozimo EB, Dr Akhidue K, Dr Ezeude CM,

Dr Ogbonna SU and Dr Owolabi FA - Collection of the data; analysis, interpretation of the data and statistical analysis

Dr Ike O Mbah- Final approval and critical revision of the manuscript

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Table 1: Socio-demographic characteristics of the study participants

Characteristics		Frequency	(n = 245) (%)
Gender:	Male	107	43.7
	Female	138	56.3
Marital status:	Married	197	73.5
	Single	23	8.6
	Widow/widower	47	15.3
	Separated	1	2.6
Highest level of education:	No formal education	14	5.2
	Primary education	57	21.3
	Secondary education	60	22.4
	University education	113	42.2
	Postgraduate education	24	9.0
Occupation:	Civil servant	71	26.5
	Trader	61	22.8
	Self employed	43	16.0
	Unemployed	16	6.0
	Retired	68	25.4
	Clergy	9	3.4

Table 2: Frequency of overweight/obesity among the participants

BMI	Frequency (%)
Underweight (weight<18.5kg)	1 (0.41%)
Normal weight (18.5-24.9kg)	53 (21.6%)
Overweight (25-29.9kg)	121 (49.4%)
Obesity stage 1 (30-34.9)	56 (22.9%)
Obesity stage 2 (35-39.9kg)	12 (4.9)
Morbid obesity (40kg and above)	2 (0.82%)

Table 3: Distribution of the weight according to level of education

HLE	underweight	Normal	overweight	Obesity 1	Obesity 2	Morbid obesity
Nil	0	2	6	3	1	0
Primary	0	12	26	11	2	2
Secondary	1	17	18	16	3	0
University	0	18	57	22	8	0
Postgraduate	0	4	14	4	0	0

Key: HLE = highest level of education, Obesity 1 and 2 = obesity stages 1 and 2, normal = normal weight, nil = no formal education

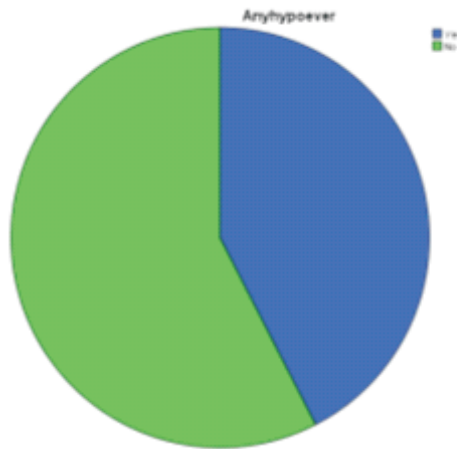


Figure 1: A pie chart showing a larger portion of 141 (57.6%) participants that have not ever had hypoglycaemia.

Table 4: Distribution of participants who had hypoglycaemia and their treatment

Hypoglycaemia	Frequency (%)
No hypoglycaemia	141 (57.6%)
Hypoglycaemia mild, treatment at home	83 (79.8%)
Hypoglycaemia severe, treatment at hospital	19 (7.8)
Hypoglycaemia, treatment at home and hospital	2 (0.82%)
Total	245 (100%)

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