

## Research

### **The association of polypharmacy to diabetes distress among patients with type 2 diabetes mellitus attending an outpatient clinic in Omdurman-Sudan**



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#### **Abstract**

**Introduction:** Diabetes distress and polypharmacy are causes of concern among diabetic patients. The present study assessed the association of polypharmacy to diabetes distress among patients with type 2 diabetes mellitus. **Methods:** A cross-sectional descriptive study conducted among 103 consecutive patients with type 2 diabetes at an outpatient clinic in Omdurman, Sudan during the period from June 2016 to September 2016. Participants signed a written informed consent, then interviewed to collect demographic data, number and type of drugs taken to assess the polypharmacy and the duration of diabetes mellitus. A blood sample was taken for fasting plasma sugar and the HbA1c. The 17-items diabetes distress scale was used to assess diabetes distress. The ethical committee of Omdurman Teaching Hospital approved the research and the Statistical Package for Social Sciences was used for data analysis. **Results:** They were 103 patients with type 2 diabetes, their age mean  $\pm$  SD (59.64  $\pm$  9.6), the mean HbA1c was 9.91  $\pm$  2.65, the majority (70.9%) had poor glycemic control (HbA1c > 7) and the fasting plasma sugar was above the goal recommended by the American Diabetes Association in 82.4% of the participants. Polypharmacy was observed in 31.1% of patients. No differences were found between patients on polypharmacy and those without regarding age, diabetes duration, the glycosylated hemoglobin and diabetes distress. **Conclusion:** No significant statistical difference was found between polypharmacy patients and their counterparts regarding diabetes distress score.

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## Introduction

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Worldwide 6% of the population are affected by diabetes mellitus and the projection for the year 2030 is 438 million [1, 2]. Diabetes mellitus is emerging as a significant health problem in Sudan due to the adoption of obesogenic diet and work involving physical inactivity; this chronic morbid disease is on the rise in Sudan. By the year 2000, half million people were affected by diabetes mellitus and expected to reach one million in the year 2030 according to the World Health Organization. Diabetes mellitus is a significant burden both emotionally and financially to the affected person and the whole community [3, 4]. Diabetes mellitus affects the vascular system leading to macrovascular (myocardial infarction, stroke and peripheral arterial disease) and microvascular complications (nephropathy, neuropathy and retinopathy). The American Diabetes Association recommended a glycated hemoglobin of < 7 in both type 1 and type 2 diabetes mellitus to reduce or prevent the microvascular complication [5]. The hyperglycemic complication of diabetes mellitus can be avoided by the rational use of antidiabetic medications and insulin. The sound use of drugs is defined as: the patients receive medications appropriate to their clinical needs, in doses that meet their individual requirements for an adequate period and at the lowest cost to them and their community [6, 7].

Diabetes distress is the reaction (it captures concerns, worries and fear, not necessarily a co-morbid) to a demanding chronic disease like diabetes mellitus; it is content related, imply etiology and distinguish between different causes [8, 9]. The 2050 projection for people aged  $\geq 65$  years worldwide is 1.5 billion (nearly triple the number in 2010), the increasing number of aging population coupled with chronic diseases and polypharmacy is a global health burden physically, mentally and financially [10, 11]. Polypharmacy which is defined as administration of five or more drugs had been linked to unfavorable health outcomes including unwanted medications side effects, falls, increasing hospitalization, dementia and death [12-14] with deleterious consequences on health authorities, the patients and the community as a whole. Previous literature showed that a greater proportion (15.6%) of the glycated hemoglobin variance was related to medication, while diabetes distress and socio-demographic factors accounted for 14% [15]. Sudan is a vast country taking about 2% of the earth and due to war and instability the health resources are lacking (diabetes mellitus could account for 25% of health expenditure). Given all of the above, an optimal prescription to patients and particularly

patients with diabetes is of paramount importance. To our best of knowledge, this is the first survey to study the relation of polypharmacy to diabetes distress among patient with type 2 diabetes mellitus in Sudan. Thus we conducted this research to assess the polypharmacy among diabetic patients and its relation to diabetes distress.

## Methods

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This cross-sectional study carried out at a diabetic center in Omdurman City, Sudan during the period from June 2016 to September 2016. One hundred and three patients with the diagnosis of type 2 diabetes mellitus and presented for regular follow-up were approached. Participants were asked to sign a written informed consent then interviewed using a structured questionnaire to collect the demographic data, the duration since the diabetes diagnosis, the number and type of drugs used by the patient to calculate the polypharmacy (hyperglycemic medications, statins, aspirin, and hypertension drugs). A blood sample was taken to measure the fasting blood sugar (in 84 patients), for those who were not fasted (14 participants) the random plasma sugar was estimated. The glycated hemoglobin was measured for all the participants to assess the glycemic control. The glycol hemoglobin reagent set from HB1C Siemens Healthcare Diagnostics Newark, DE 19714, USA was used. The American Diabetes Association targets [5] for HbA1c were followed. The diabetes distress scale, a 17-choice scale was used to measure diabetes distress, each component with six choices with zero = not a problem and 6 = a severe problem. The questionnaire is further divided into four domains: emotional burden, physician-related, regimen-related and interpersonal domain (questions (1, 3, 8, 11, 14), (2, 4, 9, 15), (5, 6, 10, 12, 16) and (7, 13, 17) respectively. The questionnaire had been previously validated [16] and a cut-off value of  $\geq 3$  is considered significant [17]. The ethical committee of Omdurman Teaching Hospital, Omdurman, Sudan approved the research and the Statistical Package for Social Sciences (SPSS version 16) was used for data analysis. The T-Test was used to compare those on polypharmacy and their counterparts, data were presented as means  $\pm$  SD or percentages unless otherwise specified with a P-value < 0.05 considered significant.

## Results

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Out of 103 patients with type 2 diabetes mellitus, 59.6% were females, their ages ranged from 38-82 years. Nearly one-third of patients were above 65 years, only 29.1% targeted the ADA guidelines of fasting plasma glucose <130mg/dl, and 17.4% approached the target of HbA1c of  $\leq 7$ . (Table 1). The mean age of the participants was ( $59.64 \pm 9.6$ ) years, the duration since the diagnosis of diabetes was ( $9.14 \pm 8.1$ )years and the mean glycated hemoglobin was ( $9.91 \pm 2.65$ ). The mean fasting plasma glucose was ( $161 \pm 51.97$ ) mg/dl. Some of the participants already took their meal( $n = 14$ ), thus, random blood sugar was checked and found to be ( $326 \pm 27.66$ ) mg/dl. The average drug intake was ( $3.24 \pm 1.85$ ) drugs (Table 2). In the present study, 72.4% of diabetic patients were taking metformin tablets and 59.1% were on sulphonylureas. It is interesting to note that 8% of patients were on Pionorm, while 8.9% were on NPH insulin. The current data showed that 54.1% were taking Statins, Aspirin was prescribed in 47.7% of patients, 52.4% of patients were taking antihypertensive medications, while polypharmacy was reported in 31.1% of patients (Table 3). Table 4, illustrated a comparison between patients with and without polypharmacy in which: No significant statistical difference was evident between polypharmacy and non-polypharmacy patients regarding age ( $62.33 \pm 9.4$  vs.  $58.45 \pm 9.67$ , P-value = 0.081), the duration since diabetes diagnosis ( $10.18 \pm 5.37$  vs.  $8.68 \pm 9.04$ , P-value = 0.427), the glycated hemoglobin ( $10.54 \pm 2.51$  vs.  $9.63 \pm 2.68$ , P-value = 0.139) and the overall diabetes distress score ( $3.81 \pm 0.62$  vs.  $3.61 \pm 0.62$ , P-value = 0.210).

## Discussion

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The present study showed that the polypharmacy was present in nearly one-third of patients and not correlated with the HbA1c, age and duration of diabetes mellitus. The most common used antidiabetic medications were Metformin and Glimepiride, the treating physicians have a tendency to prescribe metformin as the first antidiabetic medications following the ADA guidelines but still the long-acting sulphonylureas (Glibenclamide) were on the list despite the old age of the participants and hence the high risk of hypoglycemia. Clinical inertia to insulin was evident (only 8.9% were on insulin despite the polypharmacy and the poor control in the majority of patients). The use of brand name in the prescription

could be due to the pharmaceutical influence. Polypharmacy is the natural consequence in patients with type 2 diabetes mellitus where multi-drug regimen is needed to approach the glycemic targets and to control the associated vascular risk factors including dyslipidemia and hypertension [18]. In the present study, the average prescribed medication was  $3.24 \pm 0.85$  and lower than an average observed among uncontrolled diabetic patients in Singapore [19]. A similar survey conducted in India [1] reported a mean of  $5.56 \pm 2.52$  and is higher than the mean observed in the current study. The differences could be explained by the fact that the study group from Singapore were high-risk uncontrolled polypharmacy patients, further plausible explanations could be the medication cost and the specialties of the treating physician. In the present diabetes center, the patients are seen by an internist in comparison to other areas in which the general practitioners are the doctors in charge. In the Indian study, metformin and glimepiride were the most common used antidiabetic combination, in similarity to the current research in which metformin and glimepiride were the most prescribed drugs at a rate of 72.4% and 43.2% respectively. A higher number of patients were using metformin compared to their Indian counterparts. The explanation could be to the cost and the awareness of the favorable effects of metformin on lipids and its euglycemic effects [20].

Acharya et al [1] conducted a study on pattern of prescription and found that the most commonly prescribed medications other than the antidiabetic drugs were Aspirin (18.9%) and Atorvastatin (15.4%) in agreement with the current study in which 47.7% and 54.1% of patients were taking Aspirin and Statins. The insurance coverage or a higher rate of the coronary syndrome could explain the higher rate of Aspirin and Statins in the current center. A study conducted in Spain [21] concluded the use of Insulin in 25.3% of type 2 diabetic patients and is higher than the present observation. The current findings are in accordance with Acharya et al [1] who observed Insulin use in 12% of patients. The slight takeover of Insulin despite the high degree of poor control of hyperglycemia (82.6% of patients had HbA1c more than seven and 70.9% had their fasting plasma sugar above 130mg/dl) could be due to needle phobia, fearing of hypoglycemia, the propensity to gain weight and cost. The current data showed that 52.4% of patients were on hypertension medications, comparable percentages were on Aspirin and lipid-lowering drugs. These trends point to the association of other vascular morbidities like dyslipidemias, hypertension and myocardial ischemia among patients with type 2 diabetes. It is interesting to note the higher tendency towards brand rather than

generic names in the prescription, the influence of pharmaceutical companies on doctors prescribing could be significant. The small order of gliclazide (4.3%) despite the higher rate of elderly patients and hence the fear of hypoglycemia, the show-up of Pionorm (8%) despite the black box warning in many countries [22], the absence of Dipeptidyl-Peptidase-4 Inhibitors (DPP-4 Inhibitors) and different Insulin analogues in our study call for an urgent need to improve the prescription. Including the newer highly effective drugs with low rates of hypoglycemia, weight loss and cardiovascular benefits under the medical insurance are highly recommended. In the present study, no significant differences were found between patients with polypharmacy and those without regarding diabetes distress, age, the duration since diabetes diagnosis and the glycated hemoglobin. Adherence to medications, treatment complexity, diet and exercise rather than the number of drugs could explain the diabetes distress in the present study. Limitations of the study were the small size of the survey sample and the study was conducted at a single diabetes center so generalization cannot be insured. Also, the cost of the medications and medication adherence were not investigated.

## Conclusion

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In the present study no difference was found between patients on  $\geq$  five drugs (polypharmacy) and their counterparts (those on four or less medications) regarding diabetes distress.

### What is known about this topic

- Polypharmacy is prevalent among patients with type 2 diabetes;
- Polypharmacy is associated with more side effects and non-adherence to medications.

### What this study adds

- Polypharmacy may not be associated to diabetes distress.

## Competing interests

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The authors declare no conflicts of interests.

## Authors' contributions

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Hyder Mirghani is corresponding author: the concept and design, data acquisition and interpretation, data analysis, writing of the manuscript and revising it critically before submission for review. The author approved the final version before submission.

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## Tables

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**Table 1:** Basic characteristics of the study group

**Table 2:** The characteristics of the study group (mean  $\pm$  SD)

**Table 3:** The pattern of prescription among the study group

**Table 4:** Comparison between patients with polypharmacy and their counterparts T-test

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**Table 1:** Shows the basic characteristics of the study group

Character	No%
Sex	
Females	61 (59.2%)
Males	42 (40.8%)
Age range (38-82)	
≥65 years	27 (26.2%)
Fasting plasma sugar ≤ 130 mg/dl	30 (29.1%)
HbA1c ≤ 7	18 (17.4%)

**Table 2:** Shows the characteristics of the study group (mean ± SD)

Character	Mean ± SD
Age	59.64 ± 9.6
Duration of diabetes	9.14 ± 8.1
HbA1c	9.91 ± 2.65
Fasting blood glucose (N=89)	161 ± 51.97
Random blood glucose (N=14)	326 ± 27.66
Average medication	3.24 ± 1.85

<b>Table 3:</b> Shows the pattern of prescription among the study group	
<b>Drug</b>	<b>%</b>
Sulphonylureas	59.1%
Glibenclamide (Doanil Brand)	11.4%
Gliclazide (Diamicon Brand)	4.5%
Metformin (Xmet and Formit Brand)	72.4%
Pioglitazone (Pionorm Brand)	8%
Insulin (Mixtard Brand)	8.9%
Statins	54.1%
Aspirin (Aspicot Brand)	47.7%
Amlodipine (Amilo)	21.8%
Losartan	26.1%
Bisoprolol (Bizocore)	4.5%
Number of medications used by patient with type 2 diabetes	
≥ five drugs (Poly-pharmacy)	32 (31.1%)
Four drugs	20 (19.4%)
Three drugs	13 (12.6%)
Two drugs	16 (15.5%)
One drug	16 (15.5%)
Lifestyles	6 (5.8%)

<b>Table 4:</b> Shows a comparison between patients with polypharmacy and their counterparts*			
<b>Character</b>	<b>Polypharmacy present n=31</b>	<b>No polypharmacy n=72</b>	<b>P-value</b>
Age	62.33±9.4	58.45±9.67	0.081
Duration of diabetes	10.18±5.37	8.68±9.04	0.427
Glycated hemoglobin	10.54±2.51	9.63±2.68	0.139
Diabetes distress score	3.81±0.62	3.61±0.62	0.210
T-test			