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POOR ADHERENCE TO ANTIDIABETIC MEDICATIONS IN PATIENTS WITH DIABETES AT MADINA, SAUDI ARABIA: THE ROLL OF DIABETES RELATED EMOTIONAL DISTRESS

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ABSTRACT

Background: Diabetes mellitus is a chronic disease that significantly grows globally. It is a major cause of mortality and morbidity and so, excellent control for diabetes by medication is strictly advised. Patients may have terrible adherence to drugs, and sometimes they do not take their medication. Several factors affect the adherence of diabetic patients. Distress among diabetic patients was reported, and it negatively impact on the patient's life. **Objective:** To determine the prevalence of diabetes related emotional distress in patients with diabetes at Madina, Saudi Arabia, assess their adherence to antidiabetic medications, and to examine the influence of diabetes related emotional distress on adherence to the antidiabetic medications. **Material and methods:** This is a cross sectional study conducted in Madina, Saudi Arabia between November 2016 and April 2017. Patients with diabetes were recruited from Prince Majed bin Abdul-Aziz Diabetes Center and two primary care centers. Inclusion criteria include patients 14 years and older with type 1 or type 2 diabetes mellitus. Exclusion criteria include patients with gestational diabetes and patients with mental retardation or Alzheimer disease. The study was approved by the research and human ethics committee of Taibah University. After taking patients 'consents, data was collected through interviews using a questionnaire that consists of 3 parts: first, demographic data which includes age, type of DM, duration of DM, number and type of hypoglycaemic medications and the presence of diabetic complications. Second, problem areas in diabetes (PAID) questionnaire which was used to assess for diabetes-related emotional distress and third, the eight-item Morisky Medication Adherence Scale (MMAS) which was used to assess for adherence to hypoglycemic medications. On the same day of the interviews, medical records were

reviewed for most recent hemoglobin A1C (HbA1c) levels. **Results:** A total of 403patients were included in the study. Approximately 60% of the patients were men. The mean age of the study population was 48.17±15.01years (14–88 years). Most of the participants were Saudi 343(85.1%) More than two thirds of the patients were having T2DM 252 (62.5%) and 87 (21.6%) were having T1DM. The mean HbA1c was 8.05±1.68, and the mean duration of diabetes was 12.37±8.81. In the present study, we found 30.3% of the patients were having diabetes related emotional distress and 65.8% were having poor adherence to the diabetes medications. 32.2% had medium adherence, 2% patients had high adherence. Diabetes related emotional distress was significantly associated with poor adherence, P 0.001. Factors contributing to the increased risk of diabetes related emotional distress were duration of diabetes. Factors contributing to the increased risk of poor adherence to antidiabetic medications were: emotion stress (P 0.001), male sex. **Conclusions:** Our study demonstrated a substantial poor antidiabetic medications adherence in patients with diabetes at Madina, Saudi Arabia. There was a significant relationship between diabetes related emotional distress and non-adherence. even though The distress was low in prevalence among patients. This stresses the need for continuous education and motivation to patients with diabetes at follow up visits. Early screening for diabetes related emotional stress in patients with poor drug adherence is recommended.

KEYWORDS: Compliance, Depression, Diabetes, Distress, Medication adherence, MMAS.

INTRODUCTION

Diabetes mellitus (DM) is raising health problem with high levels of morbidity and mortality. 6.6% of the population is now living with diabetes mellitus, and the study's predict it will raise to 7.8% by 2030; most of them living in developing countries in according to the international diabetes federation.[1] In a population based cohort of 18034 candidates aged ≥30 years in Saudi Arabia a nationwide, household study found that the prevalence of DM is 25.4%.[2]

The association between diabetes and depression have been noticed in plenty of studies several studies showed the prevalence of depression in a population with diabetes is high compared to non-diabetics[3-4] In another study, depression affected 20 - 25% of patient with diabetes; 12% was major depressive disorder and 15%-35% were depressive symptoms[5] The development of depression among diabetics is related to different factors. Including the physiological and psychological effect of the disease. furthermore, the genetics and abnormal

pathophysiology which are attributed to neuroimmunolgicaland neuroendocrinal pathways. In addition to injury of micro vessels in the brain as a result of longstanding diabetes mellitus., Anyhow, the exact reason and relation of diabetes and depression not fully understood.

The effect of depression on diabetic patients is correlated with symptoms such as: self-careless, decrease physical activity, bad lifestyle and lower adherence to hypoglycemic medication[6-7] consequently, it lead to poor glycemic control and increase the risk of macro and micro vascular complications.[8]

As we Know, Adherence to DM medication is known to improve glycemic control. However, the efficacy of the treatment is limited by lack of adherence. Various studies regarding medication compliance have shown unsatisfactory adherence among diabetics by 36-93%.[9-10] In one systemic review, a lot of patients with diabetes mellitus were not Regular on their medications and taking less of prescribed amount.[8] Subsequently, it's leading to increased mortality and morbidity with considerable costs to the healthcare system.[11-12]

There is limited information on the rate of depression in patients with diabetes in Saudi Arabia and the association between depression and adherence to hypoglycemic medications needs to be explored. For this reason, we will conduct this study at Madina, Saudi Arabia.

OBJECTIVE

1- To look at prevalence of diabetes related emotional distress in patients with diabetes at Madina, Saudi Arabia.
2- To look at the effect of diabetes related emotional distress on adherence to hypoglycemic medications in patients with diabetes at Madina, Saudi Arabia.

MATERIAL AND METHODS

A cross sectional study will be conducted at Prince Majed bin AbdulAziz Diabetes Center and some of the primary care clinics at Madina, Saudi Arabia between November, 2016 and June, 2017. four hundred patients with diabetes; of both types type 1 and type 2, 15 years and older will be included in the study. Exclusion criteria include; patients with history of depressive disorders diagnosed before onset of diabetes, or those receiving psychotropic drugs before diagnosis of diabetes, mentally retarded patients and patients with Alzheimer disease.

After taking patients' consents, a self-administered questionnaire distributed. The questionnaire consists of 3 parts: first, demographic data which includes age, type of DM, duration of DM, number and type of hypoglycaemic medications, and the presence of diabetic complications such as neuropathy, retinopathy, nephropathy, or cardiovascular disease. Second, problem areas in diabetes (PAID) questionnaire which will be used to assess for diabetes-related emotional distress. and third, the eight-item Morisky Medication Adherence Scale (MMAS) which will be used to assess for adherence to hypoglycemic medications.

PAID contains 20 items that describe negative emotions related to diabetes (e.g. fear, anger, frustration) commonly experienced by patients with diabetes. Completion takes approximately five minutes. It has high acceptability and scientific validity.[13-14] The PAID measure of diabetes related emotional distress correlates with measures of related concepts such as depression, social support, health beliefs, and coping style, as well as predicts future blood glucose control of the patient. Each question has five possible answers with a value from 0 to 4, with 0 representing "no problem" and 4 "a serious problem". The scores are added up and multiplied by 1.25, generating a total score between 0 – 100. Patients scoring 40 or higher may be at the level of "emotional burnout" and warrant special attention. An extremely low score (0-10) combined with poor glycaemic control may be indicative for denial. Standardized self-reported questionnaires to estimate medication adherence have been used frequently because they are low in both cost and time expenditure.[15-16] Among structured self-reported scales, a four-item self-reported questionnaire to assess medication adherence was developed by Morisky et al.[17] and recently, an eight- item self-reported scale by Morisky has been updated and called the Morisky Medication Adherence Scale (MMAS).[18] Patients scoring 0 are considered highly adherent, 1-2 are medium adherent and 3-8 are low adherent. On the same day of the interviews, records reviewed for hemoglobin A1C (HbA1c) levels.

The data entered into the computer and analyzed by using SPSS version 20 (Statistical Package for Social Science). Descriptive statistics used to describe demographic and disease characteristics of the patients and their diabetes related emotional distress and medication adherences scores. Percentages and frequencies used for the categorical variables, while means and standard deviations calculated for the continuous variables. The characteristics of the whole sample and of the group of emotional distress and normal emotions presented. The

Chi square ($\chi 2$) test employed for categorical variables and t test used to evaluate the differences between the group of emotional distress and normal emotions.

RESULTS

A cross-sectional study of 403 adult patients data who met the inclusion criteria were analyzed in this study. Data were collected in 8 months (from November 2016 to June 2017). 242 (60%) of them were males and 161 (40%) females responded to the questionnaires. it included Saudi individuals represented 343 (85.1%) of participants, while non-Saudi represented 51 (12.7%) and 9(2.2%) didn't mention their nationalities. The duration of disease ranged from months to 55 years with a mean± SD of 12.37±8.81. The clinical characteristics of the study group are shown in table1. There were 87 (21.6%) had type I diabetes, 252 (62.5%) had type II, while 64 (15.9%) didn't report the type of diabetes. There were 79 (19.6%) individuals reported that they suffered depression before and 324(80.4%) didn't. Most individuals did not take antidepressant 363(90.1%), whereas 29(7.2%) only administrated it and 11(2.7%) didn't report any answer. The large majority of participants 213(52.9%) had hypertension, whereas 190 (47.1%) didn't. Lower percents of participants suffered hyperlipidemia, CHD and neuropathy; 188(46.7%), 64(15.9%) and 155(38.5%) respectively than those who didn't suffer any of the previous diseases; 215(53.3%), 339(84.1%) and 248(61.5%) respectively for hyperlipidemia, CHD and neuropathy. The range of Hb1AC for participants was 4-15 with a mean± SD of 8.05±1.68. 236(58.6%) of the individuals administrated oral hypoglycemic and 242 (60%) were insulin injection regimen.

Table 1: Clinical characteristic of the individuals of the study.

Characters		N	%
Type of DM	Type I	87	21.6
	Type II	252	62.5
	DM	64	15.9
Suffereing depression before	Yes	79	19.6
	No	324	80.4
Taking antidepressant	yes	29	7.2
	No	363	90.1
	DM	11	2.7
Hypertension	Yes	213	52.9
	No	190	47.1
Hyperlipidemia	Yes	188	46.7
	No	215	53.3
CHD	Yes	64	15.9
	No	339	84.1
Neuropathy	Yes	155	38.5

	No	248	61.5
Oral hypogycaemic	Yes	236	58.6
	No	164	40.7
	DM	3	.7
Insulin	Yes	242	60.0
	No	157	39.0
	DM	4	1.0
HBAC	Mean ±SD	8.05±1.68	
	Range	4-15	

DM: Data missed.

Assessing of the adherence of patients to drugs was performed for 395 patients and 8 of patients their data were missed, there were 260(65.8%) had low adherence, 127(32.2%) had medium adherence and 8 (2%) only had high adherence, figure1.

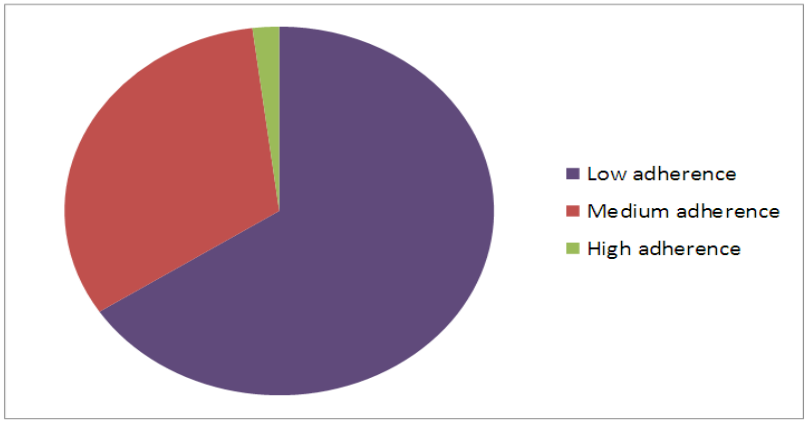

Fig 1: Adherence of patients to drugs.

The prevalence of distress among patients was evaluated for 390 patients, where 13 were missed. There were 272 (69.7%) suffer no distress (scale≤40), while 118 (30.3%) had emotional burnout (scale ≥40), figure2.

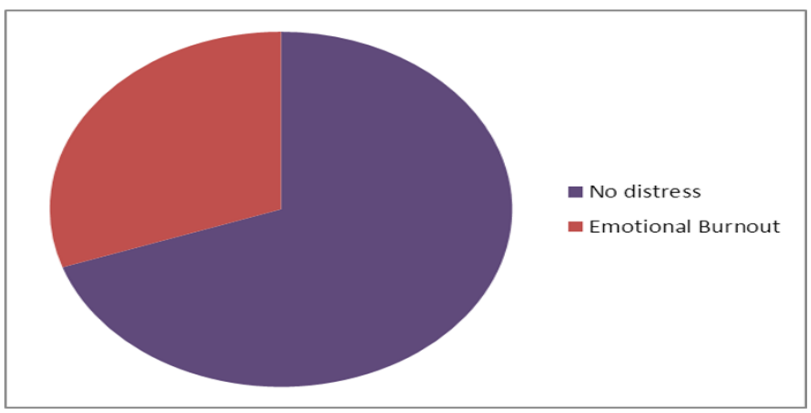

Figure 2: The prevalence of distress among patients.

The predictors of distress among study group was duration of disease only (P-value=0.01), while regarding other factors no significances were found, where P-value was >0.05 of all factors, table2.

Table 2: Predictor of distress among study group.

Distress		High adherence	Medium adherence	Low adherence	P value
No	N	6	112	150	<0.001
	%	85.7%	89.6%	59.8%	
Yes	N	1	13	101	
	%	14.3%	10.4%	40.2%	

There was a significant difference between different adherence levels to drugs and distress (P-value=0.001), low adherence was more prevalent in those with or without distress, table3.

Table 3: Association between distress and drug compliance.

Predictors	P value	OR	95.0% C.I.OR	
			Lower	Upper
Duration of diseases	.019	.945	.900	.991
Female versus male	.174	1.577	.818	3.039
Suffering from depression before D x	.164	.605	.298	1.227
Neuropathy	.369	.735	.375	1.440
retinopathy	.131	.584	.290	1.174
nephropathy	.472	.679	.237	1.950
insuline1)	.332	.709	.355	1.419
Nationality (Saudi versus non Saudi	.123	2.248	.803	6.295

The predictors of low adherence between patients were distress of patients and male sex, while type of diabetes, duration of disease, insulin injection, Hb1AC level and age were not significant factors to affect adherence to drugs, table4.

Table 4: Predictors of low adherence between patients.

Predictors	P value	OR	95.0% C.I. for OR	
			Lower	Upper
Distress (yes Versus No)	.000*	1.051	1.022	1.081
Type of diabetes (Type II Versus type I)	.510	.606	.136	2.691
Duration	.267	.962	.898	1.030
Insulin (no versus yes)	.655	1.284	.428	3.846
HB AC	.786	1.038	.795	1.355
Age	.437	1.020	.970	1.072
Gender (Male Vs female)	.023*	3.084	1.166	8.157

DISCUSSION

It was found previously that patients had difficulty in following a diet, changing their lifestyle and adhere to their medications.[19] Adherence to medication in chronic diseases were reported by several studies and it was found that patients didn't complete their medication course and sometimes didn't take them at all[20-22] Low adherence to medication for diabetes management is critical matter as the disease develops, where diabetes is a progressive silent disease, also chronic complications to increase with time as a result of poor glucose control.[23] The present study showed that there was low adherence between diabetic patients to drugs, where 65.8% had low adherence and 32.2% and 2% had medium and high adherence respectively. Similar to our results, in a previous Saudi study[24] it was reported that 54.8% of diabetic patients had low adherence, 34.5% had medium adherence and 10.7% had high adherence. A study by Shaimol et al[25] revealed that 43% of patients had low adherence, 35.3% had medium adherence and 21.8% only had high adherence. Another study reported that treatment adherence was high in 26.1%, faire in 47.9% and poor in 26%.[26] Other studies[27,28] reported better adherence levels, where in one study[27] it was found that 38.5% of patients had high adherence, 44.6% had medium adherence and 16.9% had low adherence. The other study[28] reported that good adherence was in 40.6% of patients and medium was in 32.8% of patients, while 26.6% of patients had poor adherence. A study by Gimenes HT et al[23] showed that patient adherence to drug therapy was 78.3%, another study was performed on diabetes patients showed that the prevalence was 79.7%.[29] Higher rate of prevalence was reported by a study performed on type2 diabetic patients and it was 95.7%.[22] The current study revealed that distress (emotional burnout) between patients was low in prevalence, 30.3% of patients had distress. It was reported that depressive symptoms were more common in type2 diabetic patients.[30,31] Also it was reported that almost a quarter of patients with type 2 diabetes suffer from emotional stress or depressive symptoms, and 18-45% of patients with type 2 diabetes were diagnosed with diabetes-related distress.[32-34] There were studies showed that diabetic patients were more prone to suffer depression twice than those without diabetes.[35,36] There are several factors that can influence the adherence to medication. The predictors of low adherence to drugs in this study were found to be distress of patients and male sex. In this study women were more adhere to medication than men, however in a previous study on adherence to anti- diabetic drugs[23] it was found that male sex was associated with higher adherence to therapy than female, another study showed that female gender was a threshold risk factor for non-adhering to drug when compared to male and gender was a significant factor to influence adherence to drugs.[37] In agreement with our

study, a study from Tanzania demonstrated that gender was not associated with adherence.[38] The current study revealed that there was a significant difference between those with distress and without distress regarding different levels of adherence to drugs (P-value=0.001), however low adherence was prevalent in both group of patients, this can attributed to the low adherence was the most prevalent, but patients who didn't suffer distress were more prone to had medium and high adherence than those with distress. We found that lower adherence was associated with presence of distress, also other studies reported that there was association between poor adherence to anti-diabetic medication and depression.[35,36] It was reported that chronic patients' age influence adherence to medication, as lower adherence was seen among younger patients[39], however in the present study age was not a significant factor. In a study conducted in Mulago hospital in Uganda to assess adherence to diabetes medication it was found that 31.3% in the age group 36 to 50 years didn't adhere to their medication, however overall age was not a significant factor affecting adherence.[37] Also, there was a study reported that patients in the age range of 41-50 years had the least adherence, while good adherence was observed in elderly patients.[38] The current study showed that Hb1AC was not a significant factor that influence adherence to therapy, while it was found in a literature that there was a significant association between adherence to therapy for diabetes management and Hb1Ac levels.[29] Diagnosis duration in this study was not a significant factor for drug adherence, however Organização Mundial de Saúde (OMS)[40] and another study[23] showed that there was negative association between adherence to drug therapy and diabetes duration, while another two studies[37,38] showed that duration of diabetes was not significantly associated with non-adherence. Limitation of this study include the presence of missed data and investigating the distress and adherence between all patients without categorizing patients with type 1 and 2 diabetes.

CONCLUSION

In summary The present study revealed that adherence to medications was low among diabetics, this low adherence was associated with presence of Diabetes –related distress, male gender. However, distress prevalence was low among patients. in general we recommend early screening for depression in patients with persistent poor HbA1C and on repeated indication of low self-care regarding the disease as it may have the potential to prevent long-term complications and guide these patients toward better treatment outcome.

Limitations of the study

Some of the limitations of the study were the unavoidable low reliability in any self-reported questionnaire. potential inaccuracies in answering the questions may related to different educational level among the sample which might create misconception in certain questions. complete access to patients data at the centers has not taken place. living with diabetes for different length of time might have decreased reliability toward the perception of medication adherence. furthermore, encountered elderly patients who were unable to remember the exact duration of their diabetes.

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REFERENCES

1. International Diabetes Federation. Diabetes Atlas. 4th edition. 2009. Available from: http://www.worlddiabetesfoundation.org/composite-35.htm.[cited 2015Jun].
2. Al-Rubeaan K, Al-Manaa H, Khoja T, Ahmad N, Al-Sharqawi A, Siddiqui K etal.Epidemiology of abnormal glucose metabolism in a country facing its epidemic: SAUDI-DM study. Journal of Diabetes, 2014; 7(5): 622-632.
3. Goldney R, Phillips P, Fisher L, Wilson D. Diabetes, Depression, and Quality of Life: A population study. Diabetes Care, 2004; 27(5): 1066-1070.
4. Lin E, Rutter C, Katon W, Heckbert S, Ciechanowski P, Oliver M et al. Depression and Advanced Complications of Diabetes: A prospective cohort study. Diabetes Care, 2009; 33(2): 264-269.
5. Fischer L, Skaff MM, Mullan JT, Areant P, Glasgow R, Masharani U. A longitudinal study of affective and anxiety disorders, depressive affect and diabetes distress in adults with type 2 diabetes. Diabet Med, 2008; 25: 1096–1101.[PMC free article] [PubMed]
6. Gonzalez J, Peyrot M, McCarl L, Collins E, SerpaL, Mimiaga M et al. Depression and Diabetes TreatmentNonadherence: A Meta-Analysis. Diabetes Care, 2008; 31(12): 2398-2403.

7. Lin E, Katon W, Von Korff M, Rutter C, Simon G, Oliver M et al. Relationship of Depression and Diabetes Self-Care, Medication Adherence, and Preventive Care. Diabetes Care, 2004; 27(9): 2154-2160.
8. Adisa R, Fakeye T, Fasanmade A. Medication Adherence among Ambulatory Patients with Type 2 Diabetes in a tertiary healthcare setting In southwestern Nigeria, Pharmacy Practice, 2011; 9: 72-81.
9. Krapek K, King K, Warren SS, George KG, Caputo DA, Mihelich K, etal. Medication adherence and associated hemoglobin A1C in type 2 diabetes. Ann Pharmacother, 2004; 38: 1357–62. [PubMed: 15238621]
10. Cramer Joyce A. A systematic review of adherence with medications fordiabetes.Diabetes Care, 2004; 27: 1218–24. [PubMed: 15111553].
11. Liebl A, Neiss A, Spannheimer A, Reitberger U, Wagner T, Gortz A. Costs of type 2 diabetes in Germany. Results of the CODE-2 study. Dtsch Med Wochenschr, 2001; 18: 585–9. [PubMed:11402924].
12. Hermanns N, Kulzer B, Krichbaum M, Kubiak T, Haak T. How to screen for depression and emotional problems in patients with diabetes: comparison of screening characteristics of depression questionnaires, measurement of diabetes-specific emotional problems and standard clinical assessment. Diabetologia, 2006; 49(3): 469- 477.
13. Snoek FJ, Pouwer F, Welch GW, Polonsky WH. Diabetes-related emotional distress in Dutch and U.S. diabetic patients: cross-cultural validity of the problem areas in diabetes scale. Diabetes care, 2000; 23(9): 1305–9. PMID:10977023.
14. Craig HM. Accuracy of indirect measures of medication compliance inhypertension. Res Nurs Health, 1985; 8: 61–6. [PubMed: 3846318].
15. Grymonpre RE, Didur CD, Montgomery PR, Sitar DS. Pill count, self-report, and pharmacy claims data to measure medication adherence in the elderly. Ann Pharmacother, 1998; 32: 749–54.[PubMed:9681089].
16. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measurement of medication adherence and long-term predictive validity of blood pressure control. Med Care, 1986; 24: 67–74. [PubMed:3945130].
17. Morisky DE, Ang A, Krousel-Wood M, Ward H. Predictive validity of a medication adherence measure for hypertension control. J Clin Hypertens, 2008; 10: 348–54.
18. Chew, Boon-How, Noor-Hasliza Hassan, and Mohd-Sidik Sherina. "Determinants of medication adherence among adults with type 2 diabetes mellitus in three Malaysian public health clinics: a cross-sectional study." Patient preference and adherence, 2015; 9:

639.

19. Valle EA, Viegas EC, Castro CAC, Toledo and Jr AC. A adesãoaotratamento. Rev Bras Clín Ter, 2000; 26(3): 83-6.
20. -Donnan PT, Macdonald TM and Morris AD. Adherence to prescribed oral hypoglycemic medication in a population of patients with type 2 diabetes: a retrospective cohort study. Diabet Med, 2002; 19(4): 279-84.
21. Leite SN and Vasconcellos MPC. Adesão à terapêutica medicamentosa: elementos para a discussão de conceitos e pressupostos adotados na literatura. Ciênc Saúde Coletiva, 2003: 8(3): 775-82.
22. Grant RW, Devita NG, Singer DE and Meigs JB. Polypharmacy and medication adherence in patients with type 2 diabetes. Diabetes Care, 2003; 26(5): 1408-12.
23. Gimenes HT, Zanetti ML and Haas VJ. Factors related to patient adherence to antidiabetic drug therapy. Rev Latinoam Enfermagem 2009 janeiro-fevereiro, 17(1): 46-51.
24. Ahmed NO, Abugalambo S and Almethen GH. Adherence to oral hypoglycemic medication among patients with diabetes in Saudi Arabia. International Journal of Health Sciences, 2017; 11(3): 45-49.
25. Shaimol T, Biju C, Anilasree B, Jayakrishnan S and Babu G. Medication adherence to oral hypoglycemic agents in Type 2 diabetic patients. J Pharm Res Clin Pract, 2014; 4: 8-12.
26. Heissam K, Abuamer Z and El-Dahshan N. Patterns and obstacles to oral antidiabetic medications adherence among Type 2 diabetics in Ismailia, Egypt: A cross section study. Pan Afr Med J, 2015: 20: 177.
27. Jamous RM, Sweileh WM, Abu-Taha AS, Sawalha AF, Zyoud SH and Morisky DE. Adherence and satisfaction with oral hypoglycemic medications: A pilot study in Palestine. Int J Clin Pharm, 2011; 33: 942-8.
28. Fadare J, Olamoyegun M and Gbadegesin BA. Medication adherence and direct treatment cost among diabetes patients attending a tertiary healthcare facility in Ogbomosho, Nigeria. Malawi Med J, 2015; 27: 65-70.
29. Schectman JM, Nadkarni MM and Voss JD. The association between diabetes metabolic control and drug adherence in a indigent population. Diabetes Care, 2002; 25(6): 1015-21.
30. Nouwen A, Winkley K, Twisk J, et al.; European Depression in Diabetes (EDID) Research Consortium. Type 2 diabetes mellitus as a risk factor for the onset of

depression: a systematic review and metaanalysis. Diabetologia, 2010; 53: 2480–2486.

31. Campayo A, Gómez-Biel CH and Lobo A. Diabetes and depression. Curr Psychiatry Rep, 2011; 13: 26–30.
32. American Diabetes Association. Standards of medical care in diabetes--2014. Diabetes Care, 2014; 37(1): S14-80.
33. Snoek FJ, Kersch NY, Eldrup E, Harman-Boehm I, Hermanns N, Kokoszka A, et al. Monitoring of Individual Needs in Diabetes (MIND): baseline data from the Cross-National Diabetes Attitudes, Wishes, and Needs (DAWN) MIND study. Diabetes Care; 2011; 34(3): 601-3.
34. Pouwer F, Wijnhoven HA, Ujcic-Voortman JK, de Wit M, Schram MT, Baan CA, et al. Ethnic aspects of emotional distress in patients with diabetes—the Amsterdam Health Monitor Study. Diabet Med, 2013; 30(1): e25-31.
35. Goldman Dana, Joyce GF, Escarce JJ, Pace JE, Solomon MD, Laouri Marianne, et al. Pharmacy benefits and the use of drugs by chronically ill. JAMA, 2004; 291(19): 2344-2350.
36. Lin Elizabeth, Katon W, Von Korff Ml, Rutter C, Simon GE, Oliver Malia, et al. Relationship of Depression and Diabetes Self-care, Medication Adherence and Preventive Care. Diabetes Care, 2004; 27(9): 2154-2160.
37. Kalyango Joan, Owino E and Nambuya Agatha. Non-adherence to diabetes treatment at Mulago hospital in Uganda: prevalence and associated factors. Afr Health Sci, 2008; 8(2): 67-73.
38. Rwegerera GM. Adherence to anti-diabetic drugs among patients with Type 2 diabetes mellitus at Muhimbili National Hospital, Dar es Salaam, Tanzania- A cross-sectional study. Pan African Medical Journal, 2014; 17: 252.
39. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. J Psychosom Res, 1999; 47(6): 555-67.
40. Organização Mundial de Saúde (OMS). Cuidados inovadores para as condições crônicas: components.