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Anti-diabetic Medication Use, Glycaemic Control and Sexual Function: A Cross Sectional Study Among Men with Type-2 Diabetes Mellitus in Nigeria

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Abstract

**Introduction:** Drug utilization studies are usually aimed at promoting rational use of medicines, improving therapeutic outcomes and enhancing patients' quality of life. Studies on anti-diabetic drugs generally focus on the pattern of prescription and use without necessary assessing the association between drug use and glycemic control. _**Objectives:**_ This study was aimed at evaluating the association between anti-diabetic medication use, glycemic control and sexual function in men with type-2 diabetes mellitus. _**Materials and Methods:**_ It was cross sectional, descriptive, hospital-based study conducted among persons with type 2 diabetes mellitus receiving care at two selected healthcare facilities in Nigeria. Data on the socio-demographic details of the participants was collected using a semi-structured questionnaire. The clinical, biochemical and anthropometric characteristics of the patients were also obtained. Furthermore, data on sexual function was obtained using the International Index of Erectile Function Questionnaire (IIEF). Data on the prescribed antidiabetic drugs were obtained and reviewed. Data analysis was carried out using the IBM SPSS programme. Descriptive and inferential statistics were used as applicable with p < 0.05 considered statistically significant. _**Results:**_ A total of 213 male patients with type-2 diabetes mellitus were recruited into the study. About 71.8% (n = 153) of the participants were identified as having sexual dysfunction (SD). Erectile dysfunction was the most frequently reported form of sexual dysfunction [97.4% (95% CI = 93.4 - 99.3%)]. Fasting blood sugar ($\chi2 = 4.73$; p = 0.03) and glycosylated hemoglobin ($\chi2 = 5.13$; p = 0.04) were significantly associated with the presence of sexual dysfunction among the patients. The biguanides (36.67%; n = 510) were the most frequently prescribed class of antidiabetic drug. Only pioglitazone was significantly associated with glycemic control [OR (95% CI) = 0.40(0.19-0.85); p = 0.02]. There was no statistically significant association (p > 0.05) between the prescribed antidiabetic drugs and the occurrence of sexual dysfunction. _**Conclusion:**_ The occurrence of sexual dysfunction was high in the patient population studied. It was significantly associated with the level of glycemic control. There was no statistically significant association between antidiabetic drug use and the occurrence of sexual dysfunction in this patient population.

**Keywords:** *Antidiabetic drugs, Sexual dysfunction, Glycaemic control.*

Introduction

The prevalence of diabetes mellitus is increasing worldwide with an estimated prevalence of 8.3% in the world and a predicted rise to 10.4% (642 million adults) in 2040. Therefore, the complications of diabetes mellitus including sexual dysfunction and its attendant problems are expected to increase [1].

In order to maintain adequate glycemic control and prevent its debilitating complications, patients with diabetes are expected to take an increased number of medications thereby exposing them to drug therapy problems. This is compounded by the fact that diabetes mellitus is a chronic disease with co-morbidities such as hypertension, dyslipidemia and other vascular complications that may require additional medications for their effective management [2,3]. Hence, there is a need to evaluate drug therapy among diabetic patients to encourage rational prescribing and use [4].

Drug utilization studies are geared towards enhancing the rational use of medicines for improving patients' quality of life [5]. Several studies have been carried out to review and study the prescription pattern of drugs among diabetic patients [6-8]. Many of such studies that focus on prescription and drug use pattern of antidiabetic drugs are also common in Nigeria [1,9-11]. However, only few of these studies on diabetic men have linked prescribed antidiabetic drugs with glycemic control and sexual dysfunction [3,12]. This study which was aimed at evaluating the association between anti-diabetic medication use, glycemic control and sexual function in men with type-2 diabetes mellitus receiving care in Nigerian hospitals seeks to provide more scientific information in this regard.

Materials and Methods

Study design

It was a cross sectional, descriptive, hospital-based study conducted among persons with type 2 diabetes mellitus receiving care at two healthcare facilities selected for the study.

Study sites

The study was carried out at the outpatient clinic of two (2) healthcare facilities. The selected healthcare facilities were University of Uyo Teaching Hospital (UUTH) and University of Uyo Health Centre (UUHC), both located in Uyo, Akwa Ibom State, Nigeria.

UUTH is a 500-bed capacity hospital that offers specialized tertiary healthcare services to a population of over three million people in the south-south geopolitical zone of Nigeria.

UUHC is a secondary health care facility with 21 beds. It is located within the main campus of the University of Uyo, Nigeria. It operates as a comprehensive health centre and serves a population of over 15,000 students and 5,000 members of staff of the University. It also caters for the health care needs of its immediate host community.

Study population

The population used for this study was adult male type 2 diabetes mellitus patients aged between 30 and 75 years, who attended the diabetic outpatient clinic of UUTH, and the general outpatient clinic of UUHC over a twelve-month period (January 2016 to January 2017).

The monthly attendance at the UUTH diabetic clinic is about 240 patients. Out of this number about 80 are male patients. This includes both new male patients and those who return for follow up care. The monthly attendance of male type 2 diabetes mellitus patients at UUHC is six (6). This data was obtained from available records on previous diabetic clinic attendance at the department of medical records of both study sites.

Sample Size determination

The sample size for this study was determined using the formula described by Araoye [13];

$$N = \frac{Z^2 \, P \, (1-P)}{d^2}$$

Where:

N = Minimum sample size,

Z = standard normal deviates set at 95% confidence level which correspond to 1.96,

P = Prevalence of sexual dysfunction among diabetic patients in Nigeria -74% [14] and

d = precision at 95% confidence interval is 5%.

Patient recruitment

Diabetic patients in UUTH and UUHC, who met the inclusion criteria for the study, were recruited consecutively until the required number of study participants was obtained. The study inclusion criteria were male type 2 diabetes mellitus patients aged between 30 and 75 years who willingly provided consent to participate in the study. Critically ill diabetic patients were excluded from the study.

Data collection instrument

Socio-demographic, clinical, biochemical and anthropometric characteristics of the patients were obtained. Data on the socio-demographic details of the participants was collected using a semi-structured questionnaire.

Data on sexual function was obtained using the International Index of Erectile Function Questionnaire (IIEF). The IIEF is a multi-dimensional instrument that has been widely used to evaluate male sexual functions. The initial version of the IIEF questionnaire was developed by Pfizer Incorporated in conjunction with clinical trial programme for Sildenafil. The final version of the instrument was generated and validated in 1996-1997 after further refinement and validation [15].

The IIEF is adopted as the gold standard treatment outcome measure for clinical trials on erectile dysfunction, regardless of the type of treatment intervention or study population under investigation. It is a 15-item questionnaire that assesses five domains of male sexual function: using 0 to 6point Likert scales, with 0 or 1 signifying a low frequency or ability and 5 or 6 signifying a high frequency or ability. These domains include erectile function (items 1,2,3,4,5,15), orgasmic function, (items 9,10), sexual desire, (items 11,12), intercourse satisfaction, (items 6,7,8) and overall satisfaction (items 13,14). The IIEF is a multi-dimensional self-report instrument that has been widely used to evaluate male sexual function. All items were scored in five domains according to the method used by Rosen *et al*. [15].

Data on the level of glycemic control among the study participants was obtained by evaluating their glycosylated hemoglobin and fasting blood sugar values using appropriate sample collection and analysis procedures. These investigations were carried out in the medical laboratory Department of UUTH.

Review of antidiabetic drug therapy

A review was carried out on all antidiabetic drug prescriptions that were issued to the study participants at each clinic visit during the period of the study. The review was aimed at determining the prescription pattern of antidiabetic drugs and evaluating the effectiveness of the prescribed drugs on glycaemic control and the occurrence of sexual dysfunction. Data on the prescribed drugs were obtained from the patients' case notes and recorded in a pre-designed data collection form.

Data analysis

Data analysis was conducted using the IBM Statistical Products and Services Solution (SPSS) version-25.0 software. The obtained data were summarized using descriptive statistics as appropriate. Inferential statistics such as the Pearson's Chi-square test were used to determine associations where applicable. For all inferential statistical analysis, p-values less than 0.05 were considered to be significant.

Ethical consideration

Approval for the study was obtained from the Health Research and Ethics Committee (HREC) of UUTH. Signed informed consent was obtained from each respondent. Participation in the study was voluntary and confidentiality was upheld.

Results

Socio-demographic characteristics of respondents

A total of 213 male patients with type-2 diabetes mellitus were recruited into the study. Their ages ranged from 30-75 years with a mean age of 56.7 (SD±9.8 years). Majority (n = 112; 52.6%) of the respondents had attained tertiary level of education. The socio-demographic characteristics of the study participants is presented in Table 1.

Prevalence of domains of sexual dysfunction among the respondents

Using the IIEF questionnaire, about 71.8% (153) of the participants were identified as having sexual dysfunction. A further evaluation of

these respondents with sexual dysfunction (n=153), based on the 5 domains of sexual function in the IIEF questionnaire, revealed that dysfunction was high in all the domains of sexual function with erectile dysfunction accounting for the most frequent domain of sexual dysfunction: 97.4% (95% CI = 93.4 - 99.3%). The prevalence of domains of sexual dysfunction among the respondents who were identified as having sexual dysfunction (n = 153) is presented in Table 2.

Relationship between blood glucose levels and the occurrence of sexual dysfunction among the study participants

Our results (see **Table 3**) indicated that fasting blood sugar (FBS) and glycosylated haemoglobin were significantly associated with the presence of sexual dysfunction among the diabetic patients.

Antidiabetic drug therapy evaluation and prescription pattern

A total of 1, 391 antidiabetic drug prescriptions were encountered in this study. The biguanides were the most prescribed class of antidiabetic drug in this study population. Table 4 shows the drug prescription pattern by antidiabetic drug classification.

Association between antidiabetic drug therapy and sexual dysfunction

We found no statistically significant association between the prescribed antidiabetic drugs and the occurrence of sexual dysfunction among the patient population studied (**Table 5**).

Table 6 presents the association between antidiabetic medications used and glycaemic control in the population studied. The total number of patients that achieved glycaemic control was 93 [43.7% (95% CI = 36.9-50.6%)]. Only pioglitazone was significantly associated with glycaemic control (p = 0.02).

Table 1: Socio-demographic characteristics of respondents (N= 213)

Characteristics	Frequency	Percentage (%)
Age (in years)		
30 – 39	8	3.8
40 – 49	36	16.9
50 – 59	88	41.3
60 – 69	65	30.5
≥70	16	7.5
Marital status		
Single	16	7.5
Married	181	85.0
Divorced/Separated	1	0.5
Widowed	15	7.0
Highest Educational level attained		
No formal education	15	7.0
Primary education	36	16.9
Technical/Vocational	23	10.8
Secondary education	27	12.7
Tertiary	112	52.6
Work Status		
Unskilled	29	13.6
Semiskilled	29	13.6
Unemployed	51	23.9
Professional	104	48.9
Ethnic Group		
Yoruba	1	0.5
Others	9	4.3
Igbo	10	4.7
Oron	15	7.0
Annang	35	16.4
Ibibio	143	67.1
Income Level		
Lower Level (0–7)	74	34.7
Middle Level (8-15)	113	53.1
Higher Level (16–17)	26	12.2

Table 2: Prevalence of domains of sexual dysfunction (SD) among respondents (N=153)

Prevalence of SD	Frequency (n)	Percentage (%)	95% CI
Erectile Function	149	97.4	93.4 – 99.3
Orgasmic Function	126	82.4	75.4 – 88.0
Sexual Desire	142	92.8	87.5 – 96.4
Intercourse Satisfaction	138	90.2	84.3 – 94.4
Overall Satisfaction	137	89.5	83.6 – 93.9

Table 3: Presence of SD based on blood glucose levels of respondents

Variables	Sexual Dysfunction – Yes (%) (N=153)	Sexual Dysfunction – No (%) (N=60)	X²	p-Value
Fasting Blood Sugar (FBS) (mmol/L)				
3.0 – 5.5	59 (64.1)	33 (35.9)	4.73	0.03*
>5.5	94 (77.7)	27 (22.3)		
Glycosylated Hemoglobin (%)				
<6.5	34 (64.2)	19 (35.8)	5.13	0.04*
6.5 – 7.0	34 (65.4)	18 (34.6)		
>7.0	85 (78.7)	23 (21.3)		

Table 4: Medication prescription pattern by antidiabetic drug classification

Drug group	Frequency	Percentage
Biguanide- (*Metformin*)	510	36.67
Sulfonylurea	415	29.83
Glimepiride	*285*	
Glibenclamide	*130*	
Thiazolidinedione (*Pioglitazone*)	143	10.28
Insulin	235	16.89
Dipeptidylpeptidase 4 inhibitors (DPP4i) – (*Vildagliptin*)	2	0.14
Combination-1 (Biguanide + DPP4i)	5	0.36
Combination-2 (Biguanide + Sulfonylurea)	81	5.82

Table 5: Association between prescribed antidiabetic drug and SD

Prescribed Antidiabetic Drugs	χ²	p-value
Metformin	0.05	0.83
Sulfonylureas	0.47	0.49
Pioglitazone	0.36	0.55
Insulin Therapy	0.002	0.97
Metformin + Sulfonylurea	0.97	0.33
Metformin + DPP4 Inhibitor	0.96	0.33

Table 6: Association between antidiabetic medications used and glycaemic control

Drugs	OR (95% CI)	p-value
Anti-diabetic drugs		
Metformin	1.26 (0.39–3.98)	0.70
Sulfonylurea	1.32 (0.25–2.31)	0.34
Pioglitazone	0.40 (0.19–0.85)	0.02*
Insulin Therapy	0.67 (0.37–1.19)	0.17
Metformin + Sulfonylurea	0.89 (0.45–1.78)	0.75
Metformin + DPP4 Inhibitor	1.30 (0.18–9.38)	0.80

Discussion

We noted an average rate of 1.9 antidiabetic drug per prescription in this study. This is similar to the rate of 1.7 per prescription reported in earlier antidiabetic drug utilization studies in Nigeria and Southern India [1,16]. The biguanide, Metformin, was found to be the most frequently prescribed antidiabetic drug. Although some previous studies have reported the sulfonylurea group of anti-diabetic drugs to be the most commonly prescribed drug class [7,17], our finding is in consonance with other previous findings in Nigeria and Nepal [11,18]. Upadhyay *et al.* had reported that Metformin accounted for more than fifty-percent of the antidiabetic drugs prescribed in their study [18]. The high utilization of Metformin is probably due to its recommendation as the first-line antidiabetic agent by some clinical guidelines [19,20]. Metformin has been shown to reduce diabetes mellitus related complications and mortality in randomized controlled trials and its use has been associated with a lower risk of hypoglycemia. Furthermore, the drug has been reported to demonstrate greater tolerability among diabetic patients [4,21].

Combination anti-diabetic drug therapy was more frequently utilized than monotherapy, a finding also reported by other investigators within and outside Nigeria [1,22].

The Metformin-glimepiride combination was the most frequently prescribed antidiabetic drug combination in our study. Although similar to the findings of Achyra *et al.* in their study in a hospital in Gujarat [23], it appears to be at variance with previous reports from Nigeria which show the Metformin-glibenclamide combination as the most frequently prescribed antidiabetic drug combination [1,12].

We found no significant association between the prescribed and utilized antidiabetic drugs and the occurrence of sexual dysfunction among the diabetic patients used in this study. Diabetes mellitus has been identified as a risk factor for sexual dysfunction. The use of antidiabetic drugs and the occurrence of sexual dysfunction has been of significant interest to clinicians providing care to patients with diabetes mellitus [24]. A study by Feng *et al.*[24] using a two-sample Mendelian randomization revealed that the use of insulin, though suitable for controlling blood glucose levels and

has no causal relationship with erectile dysfunction, may increase the risk of erectile dysfunction in patients with diabetes mellitus. The use of metformin in combination with the sulphonyl urea-glibenclamide has also been reported to increase the risk of erectile dysfunction in diabetic patients [24].

On the contrary, a randomized double-blinded, placebo-controlled clinical trial by Rey-valzacchi et al.[25] to evaluate the effect of the use of metformin in non-diabetic erectile dysfunction patients with insulin resistance who responded poorly to sildenafil therapy had significant improvement in their erectile function after a 4-month combined treatment with metformin. The findings by Rey-valzacchi et al. is inconsistent with the conclusion of two studies by Al-kura et al. and Abdul-Hadi et al.[26,27] which reported an association between the use of metformin and decreased libido, low testosterone levels and the occurrence of erectile dysfunction in patients with diabetes mellitus.

The effect of the sulphonyl urea class of oral hypoglycemic agents on sexual function has been investigated using animal models [24]. Glyburide was found to increase the sexual behavior of male rats when administered by intra-peritoneal injection [24]. Insuk in his study on the sulphonyl ureas [28] found that this class of antidiabetic drug can inhibit smooth muscle relaxation and thereby aggravate erectile dysfunction.

Our results showed that less than one-half of the patients attained glycemic control. Only the thiazolidinedione - pioglitazone was significantly associated with glycemic control. There is limited data from studies that focus on the evaluation of hypoglycemic agents and its efficacy in achieving and maintaining adequate glycaemic control in diabetic patients. However, Agarwal et al. [7] had reported a statistically significant association between anti-diabetic therapy along with lifestyle modifications and glycaemic control. Although the effect of lifestyle modification on glycaemic control was not investigated in this study, available data suggest that lifestyle modification along with anti-diabetic drug treatment has the potential to improve glycaemic control in diabetic patients [4,7]. Prescription for pioglitazone accounted for about one-tenth of the total anti-diabetic drug prescription and it was only prescribed in combination with other anti-diabetic drugs to effect glycaemic control. Pioglitazone is a known insulin sensitizer with ability to reduce insulin resistance in type 2 diabetes mellitus patients [29]. The use of pioglitazone in combination with either metformin, sulfonylurea or insulin is recommended because of the synergistic effect of the combinations and the fact that pioglitazone is weight neutral and is associated with a low risk of hypoglycaemia [30].

Conclusion

The occurrence of sexual dysfunction was high in the patient population studied. It was significantly associated with the level of glycemic control among the patients. There was no statistically significant association between antidiabetic drug use and the occurrence of sexual dysfunction. Periodic evaluation of male diabetes mellitus patients for sexual dysfunction should form part of routine clinical care as this is an important clinical outcome of treatment.

Declarations

Ethics approval and consent to participate

The Helsinki declaration was adhered to in this study. Ethical approval for the study was obtained from the Health Research Ethics Committees of UUTH and UUMC. In addition, informed consent was obtained from the respondents.

Conflict of interest

The authors declare no competing interest.

Authors' contributions

UO and PN conceived and designed the study; UO, UE and PN contributed to development and selection of data collection instruments, data collection, analysis and interpretation. UO and UE wrote the manuscript. UE critically reviewed it for important intellectual content. All authors read and approved the submitted manuscript.

Availability of data

The datasets used and analysed during this study are available from the principal author on reasonable request.

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References

[1] Okoro, R.N., Nmeka, C. and Erah, P.O. (2017). Utilization study of anti-diabetes medicines in tertiary care hospital in Nigeria. Future Journal of Pharmaceutical Services, 1-7.

[2] Stratton, I. M., Adler, A. I., and Neil, H. A. (2000). Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS-35): prospective observational study. British Medical Journal, (7258): 405-412.

[3] Rana, B., Bukhsh, A., Khan, T.M., Sarwar, A., Omer, M.O., Jamshed, S.Q. (2017). Evaluation of therapeutic effectiveness of prescribed medications in patients with type 2 diabetes mellitus: findings from tertiary care hospital, Lahore Pakistan. Journal of Pharmacy and Bio-allied Sciences, 9 (2): 121-125.

[4] United Kingdom Prospective Diabetes Study (UKPDS) Group (1998) Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type diabetes (UKPDS 33). Lancet, 353 (9131): 837-53.

[5] World Health Organization (WHO), (2003). Introduction to drug utilization research/statistics methodology, WHO collaborating center for drugs statistics methodology, centre for drugs utilization and research and clinical pharmacological services.

[6] Patel, B., Oza, B., Patel, K. P., Malhotra, S. D., Patel, V. J. (2013). Pattern of anti-diabetic drugs use in type-2 diabetic patients in a medicine outpatient clinic of a tertiary care teaching hospital. International Journal of Basic and Clinical Pharmacology, 2 (4): 485-491.

[7] Agarwal, A.A., Jadhav, P.R.. and Deshmukh, Y.A. (2014). Prescribing pattern and Efficacy of anti-diabetic drugs in maintaining optimal glycaemic levels in diabetic patients. Journal of Basic and Clinical Pharmacy, 5(3):79-83.

[8] Ahmed, Z., Hafzer, M. A., Bari, M. A., Akhter, J. (2016). Pattern of anti-diabetic drugs prescribed in a tertiary care hospital in Bangladesh. International Journal of Basic Clinical Pharmacology, 5 (1): 6-12.

[9] Uwakwe JN, Agboghoroma OF, Akanbi FO, Odoh G, Puepet FH. Pattern of anti diabetic drug prescription at a health facility in Jos, North-Central Nigeria. Jos Journal of Medicine. 9(1):59–62.

[10] Usman, H.M., Medinat, K.O., and Rashida, A. (2014). Medication adherence evaluation among diabetic patients attending a secondary health facility in northern Nigeria. International Journal of Pharmacy teaching and Practices, 5(4):1561-1565.

[11] Ogbonna, B.O., Ezenduka, C.C., Opara, C.A., Ahara, L.G. (2014). Drug therapy problems in patients with type 2 diabetes in a tertiary hospital in Nigeria. International Journal of Innovative Research and Development, 3(1): 494-502.

[12] Olurishe, C.O., Gyang, S.O., Olurishe, T.O., Shekarau, T.T. (2012). Drug utilization review of anti-diabetic medications and therapeutic outcome in type 2 diabetes in a tertiary hospital in northern Nigeria.West African Journal of Pharmacy, 23 (2): 58-64.

[13] Araoye, M.O. (2004) Sample Size Determination in Research Methodology with Statistics for Health and Social Sciences. Nathadex Publishers, Ilorin, 115-121.

[14] Unadike, B. C., Eregie, A. and Ohwovoriole, A. E., (2008). Prevalence and types of sexual dysfunction among males with diabetes mellitus in Nigeria. Mera Diabetes International 18-20.

[15] Rosen, R. C., Riley, A., Wagner, G., Osterioh, I.H., KirkPatrick, J., Mishra, A. (1997). The International Index of Erectile Function (IIEF): a multidimensional scale for assessment of erectile dysfunction, Urology, 6:822-830.

[16] Haghighat Panah, M., Thunga G., Jha, A., Mallayasamy, S. (2016). Study on prescribing pattern of anti-diabetic drugs among type 2 diabetes patients with complications in south Indian Teaching Hospital. Asian Journal of Pharmaceutical and Clinical Research, 9(1): 194-197.

[17] Alkhaja, K.A., Sequeira, R.P. and Mathur, V.S. (2001). Prescribing patterns and therapeutic implications for diabetic hypertension in Bharain. Annals of Pharmacotherapy. 35: 1350-1359.

[18] Upadhyay DK, Palaian S, Ravi Shankar P, Mishra P, Shah K. Prescribing pattern in diabetic outpatients in a tertiary care teaching hospital in Nepal. J Clin Diag Res. 2007;1:248–55.

[19] George, C. M., Bruun, L. L., Will, K., Howard-Thompson, A. (2015). Non-insulin therapies for type 2 diabetes. American Association of Family Physicians, 92(1): 100-112.

[20] Khardori, R. (2017). Type 2 Diabetes mellitus treatment and management. Drugs and diseases-Endocrinology e-Medicine Medscape.com

[21] Qaseem, A., Barry, M. J., Humphrey, L. L., Forciea, M. A. (2017). Clinical guidelines committee of the American College of Physicians. Oral pharmacological treatment of type 2 diabetes mellitus: a clinical practice guideline update from the American college of physician. American journal of Internal Medicine, 100: 207-220.

[22] Satpathy, S.V., Datta, S. and Upreti, B. (2016). Utilization study of anti-diabetic agents in a teaching hospital of Sikkim and adherence to current standard treatment guidelines. Journal of Pharmacy and Bio-allied Sciences, 8(3): 223-238.

[23] Acharya, K.G., Shah, K.N., Solanki, N.O., Rana, D.A. (2013). Evaluation of anti-diabetic prescription, cost and adherence to treatment guidelines: a prospective, cross sectional study at a tertiary care teaching hospital. Journal of Basic Clinical Pharmacy, 3: 82-87.

[24] Feng L, Jinhua W, Shulin G, Jiangping X, Zhongxiang L and Xiaohong L (2024) Causal association between antidiabetic drugs and erectile dysfunction: evidence from Mendelian randomization. Front. Endocrinol. 15:1414958. doi: 10.3389/fendo.2024.1414958

[25] Rey-Valzacchi GJ, Costanzo PR, Finger LA, Layus AO, Gueglio GM, Litwek LE et.al. Addition of Metformin to Sildenafil treatment for erectile dysfunction in eugonodal non-diabetic men with insulin resistance. A prospective, randomized, double-blind pilot study. JAndrol. (2012) 33 (4):608-14. Doi: 10.2164/jandrol.111.013714.

[26] Al-Kuraishy HM, Al-Gareeb AI. Erectile dysfunctionand low sex drive in men with type 2 DM: the potential role of diabetic pharmacotherapy. J Clin Diagn Research: JCDR (2016) 10: FC21-6. Doi: 10.7860/JCDR/2-16/19971.8996.

[27] Abul-Hadi MH, Naji MT, Shams HA, Sami OM, Al-Kuraishy HM, Al-Garreb AI. Erectile dysfunction and type 2 diabetes mellitus: A new twist. Int J Nutrition Pharmacology Neurological Dis (2020) 10:43-9. Doi:10.4103/ijnpnd.ijnpnd_83_19.

[28] Insuk SO, Chae MR, Choi JW, Yang DK, Sim JH, Lee SW. Molecular basis and characteristics of KATP channel in human corporal smooth muscle cells. Int J Impotence Res (2003) 15:258-66. Doi: 10.1038/sj.ijir.3901013.

[29] Yki-Järvinen H. Thiazolidinediones. N Engl J Med. 2004 Sep 9;351(11):1106-18. doi: 10.1056/NEJMra041001. PMID: 15356308

[30] Phung, O.J., Sood, N.A., Sill, B.E., Coleman, C.L. (2011). Oral anti-diabetic drugs for the prevention of type 2 diabetes. Diabetic Medicines, 8: 948-964.