

Risk of Diabetes and Renal Dysfunctions in Postmenopausal Women using Antidepressants for Short Term

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Abstract

Objective: To study the use of antidepressants for a short period and the risk of diabetes and kidney functions in postmenopausal women of Peshawar city Khyber Pakhtunkhwa.

Material and Methods: The patient group (PG) consisted of 140 postmenopausal women taking various antidepressants drugs for ≥ 3 and < 6 months, and 140 postmenopausal women from the Khyber Pakhtunkhwa general population as controls. Serum urea was measured using the UV kinetic method, serum creatinine was measured using the modified Jaffe method, and glycated hemoglobin (HbA1c) was measured using the rapid ion-exchange resin separation method.

Results: Mean age was 51.65 ± 5.81 years in the control group (CG), 43.09 ± 6.28 years in the selective serotonin reuptake inhibitor (SSRI) group, and 45.33 ± 5.15 years in the PG tricyclic antidepressant (TCA) group. Mean BMI for the CG, SSRI, and TCA groups was 25.42 ± 5.04 , 30.49 ± 7.25 , and 28.71 ± 7.78 kg/m², respectively. Mean serum urea in the CG, SSRI and TCA groups was 27.07 ± 7.78 , 30.17 ± 30.39 and 21.40 ± 3.56 mg/dl, respectively. Mean serum creatinine in the CG, SSRI and TCA groups was 0.85 ± 0.21 , 0.70 ± 0.28 and 0.67 ± 0.09 mg/dl, respectively. Mean HbA1c in the CG, SSRI, and TCA groups were 6.06 ± 0.59 , 5.67 ± 0.56 , and $5.45 \pm 0.49\%$, respectively. Mean fasting blood glucose levels in the CG, SSRI, and TCA groups was 85.37 ± 8.34 , 79.96 ± 7.85 , and 76.96 ± 7.04 mg/dl., respectively.

Conclusion: The result of this study showed that short term use of SSRIs, and TCAs may lower the risk of diabetes and renal dysfunctions in postmenopausal women

Keywords: Urea, Creatinine, Anti-depressant, post-menopausal.

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Introduction

Antidepressants are used to treat various manifestations of depressive syndrome by correcting imbalances in chemical messengers in the brain. Chemical disorders can also cause mood and behavior changes.¹ For the treatment of patients with mild or simple depre-

ssion, the major antidepressants given to patients in the early stages of treatment are intended to cure the symptoms of the disorder, but they can cause a range of side effects in patients if they do not alleviate the symptoms of depression.² There is a need that while prescribing an antidepressant health condition of the patient should be taken into consideration to avoid the unwanted side effects.³ Antidepressants can have a variety of adverse effects in certain people.⁶ Recognition of the side effects profile of advanced antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs), compared to older drugs such as tricyclic antidepressants (TCAs), has increased awareness among prescribers and patients. It may have contributed to its popularity.⁷ A number of recent publications indicate that antidepressants are not safe for long-term use and may increase the risk of

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diabetes.⁸ Longer durations of 24 months or more increase the risk of diabetes⁹. Other studies found a less significant and a weaker link between risk of diabetes and antidepressant use. In 2012, the National Center for Health Statistics found that adults taking antidepressants for depressive symptoms were not at risk of diabetes. In addition, this study used improved blood test frequency variability in the general population to assess blood glucose levels in antidepressant users who had not recently a blood glucose test and thus could not have been detected.¹⁰ Kivimaki and Batty proposed two approaches to address the limitations of the previous studies, first to look for the potential risk of diabetes in antidepressant users; and Second, to study the association between antidepressant use and blood glucose levels in normal subjects.¹¹ Shulman KI et al observed the adverse effect of lithium therapy on renal functions. Rej S et al reported a very little evidence to support the risk of renal dysfunctions in elderly patients using antidepressant lithium.¹² This bio analytical cross sectional study was conducted to study the effects of the use of various antidepressants on HbA1c levels and biochemical serum markers of renal functions in postmenopausal women in Peshawar city from Khyber Pakhtunkhwa Province of Pakistan.

Materials and Methods

The study was conducted in Khyber Teaching Hospital (KTH) and Shafique psychiatric clinic Peshawar from February 19, 2016 to May 15, 2019. Approval of the study was given by the ethical committee of KTH vid no 766/KTH/E-111. Data of 140 patients (PG) fulfilling the inclusion criteria of the study and age matched control group (CG) was collected using random sampling technique on informed consent. The patient in the PG were further divided into SSRIs and TCAs groups. Anthropometric data was collected from the study population on their well keeping the human dignity in accordance with standard protocol. Exclusion criteria were followed in letter and spirit. Fasting blood samples

were taken from all patients and were analyzed for the required bio chemical markers using standard kits and protocols. Kinetic UV method 13 was used for the determination of serum urea while modified Jaffe method 14 was used for the quantification of serum creatinine on Autoanalyser (Erbamannhein chemistry autoanalyser, Germany) using standard Erba kits. Normal serum levels for Urea = 05-45 mg/dl and Creatinine= 0.5-1.5 mg/dl HbA1c test. Fast ion-exchange resin separation method was used for the determination of HbA1c.¹⁵ SPSS windows 21.0 software (SPSS Inc. Chicago, IL, USA) was used for Statistical analysis. The obtained values were reported as Mean ± Standard Deviation (SD). Pearson's bivariate correlation analysis was used for variable of interest. A two-tailed p value<0.05 was considered statistically significant.

Results

The mean age of CG, SSR and TCA groups was 51.65 ±5.81, 43.09±6.28 and 45.33± 5.15 years respectively. The mean BMI of CG, SSR and TCA group was 25.42 ± 5.04, 30.49±7.25 and 28.71±7.78 Kg/m² respectively. The serum urea of SSRI group (30.17±30.39mg/dL) was higher than both the TCA (21.40±3.56mg/dL) and CG (27.07±7.78mg/dL) The serum Creatinine of SSRI group (0.70±0.28 mg/dL) was higher than the TCA (0.67±0.09 mg/dL) and lower than CG (0.85±0.21 mg/dL).The mean HbA1c level of SSRI was higher (5.67 ± 0.56) than TCA (5.45 ± 0.49 %), while lower than CG (6.06 ± 0.59%). The mean fasting glucose level of SSRI (79.96 ± 7.85 mg/dl) was higher than TCA (76.97± 7.04 mg/dl) while lower than control

Table 1: Base line characteristics of control and patient groups

S.No	Group ID	Age(years)		BMI(Kg/m ²)	
		Mean	S.D	Mean	S.D
1	CG (n= 140)	51.65	5.81	25.42	5.04
2	PG (n= 140) SSRI n=71 TCA n=69	43.09	6.28	30.49	7.25
		45.33	5.15	28.71	7.78

Table 2: Comparison biochemical markers in the study population

S.No	Group ID	S.U (mg/dL)		S.Cr (mg/dL)		HbA1c %		Average Glucose Level (mg/dL)	
		Mean	S.D	Mean	S.D	Mean	S.D	Mean	S.D
1	CG (n= 140)	27.07	7.78	0.85	0.21	6.06	0.59	85.37	8.34
2	PG (n=140) SSRI n= 71 TCA n=69	30.17	30.39	0.70	0.28	5.67	0.56	79.96	7.85
		21.40	3.56	0.67	0.09	5.45	0.49	76.97	7.04

Serum Urea (mg/dL): S.U: Serum Creatinine (mg/dL): S.Cr

group (85.37 ± 8.34 mg/dl). The results of Pearson bivariate correlation analysis of both SSRI and TCS group of patients is shown in the table 3. A highly significant correlation of serum urea ($p=0.001$) and creatinine ($p=0.01$) was found with age in SSRI group while no significant

relation was found in TCA group for urea. A negative significant correlation was found for Serum creatinine ($p=0.03$) in TCA group. No association of HbA1C and mean glucose level was observed in any of the patients group.

Table 3: Pearson's bivariate correlation analysis of renal and diabetic markers in PG

S. No	Group ID PG n =140	Parameters	Renal Markers		Diabetic Markers	
			S. U r (p)	S.Cret r (p)	HbA1c % r(p)	Average Glucose Level (mg/dl) r(p)
1	SSRI group n= 71	Age	0.86** (0.001)	0.73*(0.01)	-0.02(0.94)	-0.02(0.94)
		BMI	-0.25 (0.45)	-0.04 (0.90)	0.25(0.42)	0.25(0.42)
		Duration in months	-0.25 (0.46)	-0.34 (0.31)	0.34(0.25)	-0.34(0.25)
		Dosage in mg	-0.13 (0.71)	-0.01 (0.98)	-0.21(0.49)	-0.21(0.49)
2	TCA group n= 69	Age	0.02 (0.95)	-0.72* (0.03)	-0.56(0.19)	-0.56(0.19)
		BMI	-0.01 (0.98)	0.33 (0.39)	0.70(0.08)	0.70(0.08)
		Duration in months	-0.34 (0.38)	-0.14 (0.71)	-0.20(0.66)	-0.20(0.66)
		Dosage in mg	0.17 (0.66)	0.48 (0.20)	0.10(0.83)	0.10(0.82)

Discussion

Pakistani society is facing many problems due to a number of factors including social, economic, political, law and order situation due to which a large no of people are suffering from mental health issues and are rising day by day.^{16,17} WHO report show that almost 20% of the world population are suffering from mental health issues and is believed to be the main cause of disability in future.¹⁸ In Pakistan according to some reports the prevalence rate of mental disorder is from 10 to 50 %.¹⁹ The health care providers prescribe various medications for the treatment of mental illness in Pakistan. It is reported that 1/3 of the total patients are taking Monoamine Oxidase Inhibitors (MAOIs) SSRI and TCAs.²⁰ A number of research publications show that the long term use of these drugs may have a role in the onset of diabetes and may cause renal dysfunctions in certain patients.²¹ We conducted this cross sectional study in postmenopausal women of Peshawar city in Khyber Pakhtunkhwa whose population is more affected by terrorism than the other regions of Pakistan on the hypothesis whether the use of these drugs may affect the sugar metabolism or have effect on renal health in our study population or otherwise. We found that the level of HbA1c is lower in the PG as compared to CG which is in agreement with the finding of Lust man et al. 2006.²² A study conducted by Pyykkonen et al found no effects of antidepressants medications on glucose level in adults.²³ A UK General Practice Research Database study reported that long

term use of more than 24 months increase the risk of diabetes.²⁴ The serum urea in SSRI group was found higher than both the TCA and CG. The serum Creatinine of SSRI group was higher than the TCA and lower than CG group. Al Jurdi et al, Rej S et al, Hendrie H et al¹² found no effect of antidepressants medication on renal health in elderly patients while Van Wyck Fleet J et al reported polyuria (2-5%), urinary urgency (< 2%), urinary incontinence (< 1%) and urinary retention (< 1%)²⁵ in his study subjects. The limitations of the study include small sample size (280), short period and lack of finance. Thus it will not be sufficient for a megacity like Peshawar. Moreover the population of the city is heterogeneous in nature being the capital of the province and the influx of Afghan refugees. For better results large population size is required.

Conclusion

The result of this study showed that short term use of SSRIs and TCAs may lower the risk of diabetes and renal dysfunctions in postmenopausal women.

Conflict of Interest: None

Funding Source: None

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Authors Contribution

MY: Conceptualization of Project

LA: Data Collection

AY: Literature Search

AY: Statistical Analysis

Jl: Drafting, Revision

MY: Writing of Manuscript