Original Article

Use of Antidepressant Drugs for Medium or Long Term May Cause Obesity, Diabetes or Renal dysfunction in Women of Reproductive Age Group

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ABSTRACT

Objective: To assess the use of Anti-depressant drugs are supposed to cause obesity, diabetes or renal dysfunction.
Study Design: Cross sectional study.
Place and Duration of the Study: The study was conducted in two tertiary care hospitals of Peshawar City of Khyber Pakhtunkhawa in Pakistan i.e. Khyber Teaching Hospital (A public sector health care facility) and Shafique psychiatric clinic (A Private health care facility) Peshawar from February 19, 2016 to May 15; 2016.
Materials and Methods: This cross sectional analytical study was carried out in Khyber Pakhtunkhawa in Pakistan to study the side effects of medium term use (03- 36 months) of anti-depressant drugs on the metabolism of glucose and renal functions in women of reproductive age. The study population consists of 165 female (18-45 years). Five ml of fresh fasting venous blood was collected from each subject and was analyzed for HbA1c and renal markers using standard methods & kits.
Results: The average serum urea level for both the patients group (SSRI: 22.65 ± 6.41mg/dl and TCA: 18.33 ± 4.53mg/dl) was lower than the control group (24.50 ±5. 14 mg/dl).
Similarly the creatinine level of the control group (1.10±0.23 mg/dl) was also higher than both the patients group (for SSRI group was 0.62 ± 0.19 and for TCA was 0.53 ±0.20 mg/dl).
The average value of HbA1c was 5.94 ± 0.39, 4.84 ± 0.89, 4.91 ± 0.70 (%) for control, SSRI and TCA groups respectively. Positive correlation was observed between serum urea and drug dosage in mg/day in TCA group (p= 0.01). No significant correlation was found for serum creatinine HbA1c and average glucose level in the patients group (SSRI, TCA) for other variables of interest.
Conclusion: Anti-depressant drugs may induce obesity in women of reproductive age if used for medium term, while it may not cause diabetes or renal damage. The effect on the HbA1c level is still not fully understood where as some studies reports its elevation in long term use.

Key Words: Anti-depressant, Urea, Creatinnie, Serum

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INTRODUCTION

The spills of current wave of violence in Pakistan and disruption in social structure in the society are the leading causes of mental and psychological problems in our country[1, 2]. The exact prevalence rate of mental disorders in Pakistan is not known, as there is no authentic data available. A few studies report a prevalence rate to be between 10% and 50%[3,4].

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Worldwide studies revealed that women live longer than men but they do not live healthier and better lives than their male counterparts. The women are exposed to greater risk for the onset of anxiety, depression and eating disorders[5]. The prevalence rate of depressive disorders among women is stated to be higher (41.9%) than men (29.3%). The main causes of anxiety and depression in women are their gender specific roles and responsibilities, cultural and social factors prevalent in Pakistani society. Other causes responsible for stress are gender based discrimination, poverty, hunger, malnutrition, family preference for a male child, lack of support from in-laws and domestic violence[5-7]. The prevalence rate of depression and anxiety in Pakistan is about 34% and is mainly due to social problems.
About 33% depressed patients are taking various anti-depressant drugs like Selective Serotonin Reuptake Inhibitors (SSRIs) and Tricyclic Anti-depressants (TCAs) [8,9].

These drugs when used for longer time, causes damage to kidneys and may disturb glucose metabolism [10].

One study carried out by UK General Practice Research has reported that those patients who had taken antidepressants drugs for more than two years had a higher risk of diabetes [11].

Ryan MC, et al also found that more than 50% of non-diabetic patients who were using anti-depressant drugs had higher level of HbA1c levels (> 7.0) [12].

Van Wyck et al. observed in their study that Bupropion use (Antidepressant drug) can cause polyuria (2-5 %), [13] while Turpeinen, et al reported that it may elevate serum creatinine level [14].

Weinstein JR et al observed in their study that long term therapy with Lithium may be linked with CKD in some patients [15].

The aim of the present cross sectional analytical study was to investigate the effects of the medium term use of antidepressant drugs on glucose metabolism and renal functions in women population in the reproductive age in northern Pakistan in the province of Khyber Pakhtunkhawa.

MATERIALS AND METHODS

Study population/ study site: The present cross sectional analytical study was conducted from February 19, 2016 to May 15; 2016 in two tertiary care hospitals of Peshawar Cit**y** of Khyber Pakhtunkhawa in Pakistan i.e. Khyber Teaching Hospital (A public sector health care facility) and Shafique psychiatric clinic (A Private health care facility) Peshawar. Approval letter no 766/KTH/E-111of the present study was given by the ethical committee of Khyber teaching hospital (KTH) in Peshawar Khyber Pakhtunkhawa, Pakistan. The target patients were women of reproductive age (18-45 years) visiting the above hospitals.

The exclusion criteria for the study population were diabetes, hypertension, renal disorders and use of antidepressant drugs for short term (<02 months) and long term (> 03 years).

Informed consent was taken from each patient personally or through her attendant and the data was collected from the target patients on well-designed pro-forma using purposive sampling method. The study population consists of 165 female in the reproductive age (18 45- years). Five ml of fresh fasting venous blood was collected from each subject and was then analysed in the central Pathology laboratory of KTH for the required biochemical tests using standard methods and kits.

Determination of Renal Markers: Kinetic UV method was used for the determination of Serum urea[16] while serum creatinine was determined by Jaffe method[17] on chemistry auto analyser (Erbamannhein chemistry auto analyser, Germany). The normal range for urea was 05-45 mg/dl and for Creatinine was 0.5-1.5 mg/dl respectively.

HbA1c Determination: HbA1c was tested by Fast ion-exchange resin separation method[18].

Statistical Analysis: The data of the study group was statistically analysed on SPSS for windows 21.0 software (SPSS Inc. Chicago, IL, USA) and Microsoft Excel. The values were reported as Mean ± Standard Deviation (SD). Pearson's correlation analysis for the required parameters was also done to determine the kind of association between these parameters. A two-tailed p value<0.05 was considered statistically significant.

RESULTS

The study population consists of 165 women in reproductive age (18 to 45 years) were divided into two groups, the Control Group (CG), using not any ant-depressant drugs and the Patient Group (PG), using various antidepressant drugs for various duration and in different dosages. The results are given below.

Baseline Characteristics of CG and PG

Age: The average age of CG was 29.10 ±7.52 years, for PG in SSRI & TCA group was 27.92 ±7.90 and 29.63 ±10.64 years respectively.

BMI: The mean BMI of CG was 24.54 ± 2.01Kg/m^2 for PG in SSRI & TCA group was 25.35 ± 6.86 Kg/m^2 and 30.76 ± 4.66 Kg/m^2 respectively.

Comparison serum urea, creatinine & HbA1c of Control & Patients

The average serum urea of CG was 24.50±5.14 mg/dl, for PG in SSRI &TCA group was 22.65 ± 6.41mg/dl and 18.33 ± 4.53mg/dl respectively.

Similarly the mean values of serum creatinine of CG was 1.10 ± 0.23 mg/dl, for PG in SSRI &TCA group were 0.62 ±0.19 mg/dl and 0.53 ±0.20 mg/dl respectively. The mean value of HbA1c was higher in CG (5.94 ± 0.39%) than PG (SSRI: 4.84 ± 0.89, and for TCA: 4.91 ± 0.70 %).

Table No.1: Baseline characteristics of CG &PG

S. No	Group ID		Age (years)				BMI (Kg/m^2)			
	CG		Max	Min	Mean	S.D	Max	Min	Mean	S.D
1	n= 80		40.0	18.00	29.10	7.52	28.00	20.20	24.54	2.01
	PG	SSRI n= 50	40.0	18.00	27.92	7.90	44.50	17.00	25.35	6.86
2	n= 85	TCA n= 35	43.00	18.00	29.63	10.64	39.40	24.20	30.76	4.66

CG: Control Group**, PG:** Patient Group, **TCA**: Tricyclic Antidepressant, **SSRI**: Selective Serotonin Reuptake Inhibitor

Table No. 2: Comparison of serum urea creatinine & HbA1c of CG and PG

S.no	Group ID		Serum Urea (mg/dl)		Serum Creatinine (mg/dl)		HbA1c (%)	
1	CG n= 80		Mean	S.D	Mean	S.D	Mean	S.D
			24.50	5.14	1.10	0.23	5.94	0.39
	PG	SSRI n=50	22.65	6.41	0.62	0.19	4.84	0.89
2	n=85	TCA n=35	18.33	4.53	0.53	0.20	4.91	0.70

TCA= Tricyclic Antidepressant SSRI= Selective Serotonin Reuptake Inhibitor

Table No.3: Correlation Analysis of Serum urea & Creatinine in PG

S.no	Group ID PG n= 85	Parameters	Renal Markers		Diabetic marker
			Serum Urea r (p)	Serum Creatinine r (p)	HbA1c(%) r(p)
1	SSRI group n= 50	Age (Years)	-0.04 (0.90)	0.27 (0.40)	-0.539(0.09)
		BMI (Kg/m^2)	-0.23 (0.48)	-0.13 (0.68)	-0.446(0.17)
		Duration in months	-0.06 (0.85)	0.50 (0.19)	-0.05(0.89)
		Dosage in mg/day	-0.21 (0.52)	-0.02 (0.96)	-0.26(0.43)
2	TCA group n= 35	Age (Years)	0.27 (0.52)	-0.50 (0.21)	0.40(.30)
		BMI (Kg/m^2)	0.40 (0.32)	0.34 (0.42)	0.35(.36)
		Duration in months	-0.51 (0.21)	-0.13 (0.77)	-0.25(0.52)
		Dosage in mg/day	0.87** (0.01)	-0.14 (0.74)	0.62(0.08)

TCA= Tricyclic Antidepressant SSRI= Selective Serotonin Reuptake Inhibitor

Correlation analysis of renal& diabetic markers in PG: Pearson's correlation analysis of serum creatinine, urea and HbA1c was carried out with all the require variables. The results of the analysis are presented in table 3.

Insignificant negative correlation was found between serum Urea, BMI, age, Dosage in mg/day and duration of medication in months, while positive correlation was observed for urea in TCA group with drug dosage in mg/day (p= 0.01). For serum creatinine no significant correlation was observed.

Negative insignificant correlation for HbA1c with age, BMI, dosage in mg/day, duration in months was found for PG in SSRI group.

The HbA1c for TCA group was negatively correlated with duration in month and positive correlation was found with Age, BMI; Dosage in mg/day.

DISCUSSION

Diabetes and renal impairment are co-morbid with anxiety and depression. This relationship has been confirmed by a number of epidemiological studies.

The present cross sectional study was carried to look for the association between anti-depressants use, HbA1c and renal markers level in women of reproductive age having depressive illness.

The study population includes 165 female aging 18-45 year, 85 of them were patients (PG) using various antidepressant drugs and 80 were normal (CG), who were not user of drugs. The prevalence rate of obesity was higher in PG (44.50 Kg/m2for SSRI &39.40 Kg/m^2 for TCA) than the CG (28.00 Kg/m^2) [17-19]. This finding is in consistence with other similar studies which reported an increase in BMI in the patients treated with anti-depressant drugs [20].The HbA1c level of CG was found to be higher than PG. Similar results have been reported by Lust man et al. 2006, who observed lower level of HbA1c in patients irrespective of the type of antidepressant used [21]. Pyykkonen et al. 2011 found mixed results between antidepressant use and glycemic control in adults. Researchers had also found an association between antidepressants use and increased insulin resistance as evaluated by Homeostasis Model Assessment of Insulin Resistance (HOMAIR) [22].

Renal function the study population was evaluated by determining Serum urea and creatinine.

Our results revealed that subjects who were using SSRIs and TCAs have lower level of urea and creatinine as compared to subjects in CG. Different results have been reported for other similar studies where an association has been established between ant-depressant use and renal damage and elevation in serum cretinine level [23]. Our results suggest that antidepressants users may not be at risk of developing kidney diseases.

The period of medication with the anti-depressant drugs is also important in the onset of dubieties and consequently on the renal damage. In this study an insignificant negative correlation was found between Serum urea, age, BMI, dosage in mg/day and duration in months.

A very significant positive correlation was observed between serum urea and drug dosage in mg/day in TCA group (p= 0.01), while no significant correlation was found between serum creatinine and other parameters in PG (SSRI, TCA). Positive correlations of HbA1c with age and BMI, while negative correlations with duration in month and dosage in mg per day in SSRI (PG) were observed.

The study of Diabetes Prevention Program reports that long term use of the antidepressants can increase the risk of diabetes twice [24].

Some surveys have found a very weak association between the antidepressants drug use and the risk of diabetes [25].

Lust man et al. 2000, hypothesized that change in hormones level caused by depression can stimulate the cortisol level in the body to increase and weakens the insulin tolerance [26].

The important aspects of this study are that we have focused on a segment of our society who is facing enormous health issues due to poverty and other social factors. The limitations of the study are small sample size of 165 women in a certain age group, data collection from only two centers, lack of finances and time limitation.

Further studies are required involving larger population for better results.

CONCLUSION

The medium term use of antidepressant drugs may induce obesity in women of reproductive age but may not impair glucose metabolism and renal function.

Author's Contribution:

Concept & Design of Study:	MM Yousaf
Drafting:	Mehr Liqa Khattak
Data Analysis:	Faryal Tayyiba
Revisiting Critically:	Samiullah
Final Approval of version:	MM Yousaf

Conflict of Interest: The study has no conflict of interest to declare by any author.

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