

Glucose Level and Body Mass Index (BMI) Among Chronic Psychotic Patients Treated with A Typical Antipsychotic (Olanzapine) or Traditional Antipsychotic or Both of Them. In Nasiriya City \ Iraq.

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Abstract--- Background: Schizophrenic and manic depressive patients treated with olanzapine have 1.5-2 times more rate of diabetes mellitus and obesity in comparism with normal population (1), it was observed that traditional antipsychotic associated with hyperglycemia in uncontrolled study (2), this study facilitate a chance to study the side effect of both typical and atypical antipsychotic drugs on glucose during prospective trial (3), probable explanation related to increase body weight due to atypical antipsychotic blockage of hypothalamic H1 receptor or serotonergic 5-HT receptorantagonism.(4)

Aims of Study: Study assessed the glucose level, BMI, through period of treatment with olanzapine, traditional antipsychotic or both dugs on studysample. Also, tudyng of the effect of various risk factors like socio_ demographic variables, type of treatment (TOT), duration of disease (DOD), random blood sugar (RBS).

Methods: Seventy patients (20males and 50 females) with chronic psychotic disorder, manic depressive psychoses were out patients studied in cross- sectional approach established evaluation consist patients treated for many years with atypical, traditional antipsychotic or both drugs, involving RBS, glycated hemoglobine HbA1c and BMI for the period march,1 to Sep,1 2019 DSMIV criteria was used for diagnosis of mental disorders

Ethics: Verbal and written consent was taken from patients and their relatives

Result: Most of patients were diagnosed as chronic psychotic or manic depressive psychoses or other psychiatric disorders treated from one year and above. 70 patients of study sample (20male,50females), (48.6%) were on olanzapine,(20%) Were treated with traditional antipsychotics,(31.4%) were on both drugs, most of patients were obese (35.7%)and over weight (37.1%),(14.3%)of study sample were diabetic,(85.7%)were with normal HbA1C, other correlated variables to diabetes mellitus were studied in various statistcal approaches

Conclusion: Cross sectional study of sample treated with olanzapine, traditional antipsychotics or both to reveal level of HbA1c,BMI and other relevant variables

Keywords--- Glucose Level, BMI, Olanzapine, Traditional Antipsychotic, Nassirya City, Iraq.

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I. INTRODUCTION

Antipsychotic drugs are commonly applied in treatment of schizophrenia or bipolar disorders and other psychiatric diseases like dementia, major depressive episode(5) traditional antipsychotics like fluphenazine decanoate and chlorpromazine were used for six decades ago. Their mechanism of action is dopamine antagonism(6), the real reason for increase serum glucose is not obvious, how over 5-HT₁ blockage decrease the response of Beta cell which decrease in production(7) olanzapine also disturb of glycogen production which may lead to resistance of insulin(8), other pathological factors of hyperglycemia is autoimmune damage of pancreatic B-cell(9) BMI increase by many etiological factors like increase leptin level in treated patients produce new-onset diabetes, though it is believed that adipocytes release leptin which may also reduce appetite and increase catabolism of fat but high serum level in obese person refers to leptin resistant(10) drugs also have high tendency to block (5-HT) and histamine(H) receptor which lead to excessive body weight (11) and BMI due to change in eating habit like increased excessive food intake due to stimulated appetite(12) elevated baseline BMI referred to adverse serum glucose after one year of treatment with olanzapine(13). Neuroendocrine disturbance may concerned with increased BMI, this change is hyperprolactinemia increased with BMI, limited studies exposed for antipsychotic-induced hyperprolactinemia in females and it concerned to BMI(14)

II. PATIENT AND METHODS

Seventy patients with chronic schizophrenia or bipolar disorder visiting private clinic(20males, 50females), study sample population had regular consulting of the clinic for many years, psychiatric diagnosis was established by DSMIV criteria. Cross sectional study of sample was achieved, it extended from first of March- first September 2019. After getting patients and his relative written and verbal consent, well organized forum was arranged involving all essential information to achieved the research data including identity information, duration of disease (dod), type of treatment (TOT), body weight and length of patient to find out BMI, at same time patients were sent for random blood sugar(RBS) and glycaled Haemoglobin(HbA1C), for documentation mellitus. Of diagnosis of diabetes

III. STATISTICAL ANALYSIS

Data were analyzed with the use of commercially available software (spss) to reveal χ^2 , p-value, ANOVA test, t test, F E, logistic regressions, correlation regression to show the correlation between various variables and comparison of HbA1C according to category variables, BMI. p-value less than 0.5 indicate non-significant, correlation regression is significant at 0.05 level (2-tailed) and at 0.01 level(2-tailed), clarification figures were used to reveal the frequency and percentage of distribution of study sample, according to their treatment, HbA1C to show diabetic or normal percentage of study sample.

IV. RESULTS

Most of our studied population were on Olanzapine (48.6%), only 20% on traditional antipsychotic treatment, while for those on both types constitute(31.4%) as shown in figure 1.

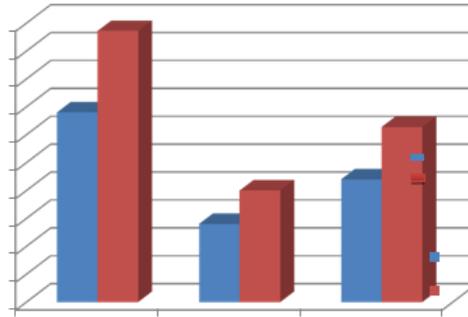


Figure 1: Distribution of Study According to their (Treatment)

Regarding the distribution according to Body Mass Index, most of population were with overweight followed by obese, the normal weight, lastly the underweight,(35.7, 37.1, 22.9 and 4.3%) respectively as shown in figure 2.

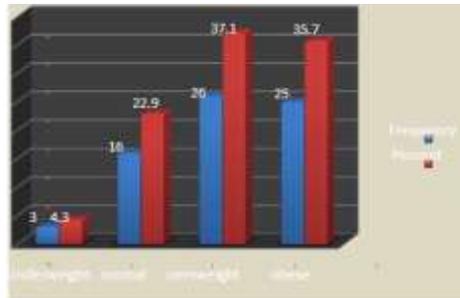


Figure 2: Distribution of Study According to their Body Mass Index (BMI)

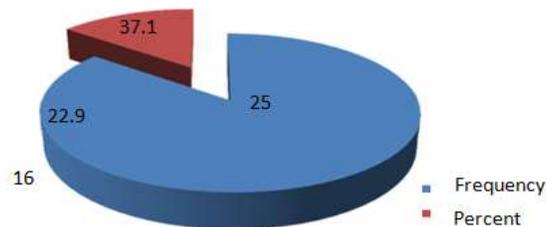


Figure 3: Showing Only 14.3% (10 patients) develop DM according to HbA1C.

Table 1: Distribution According to Gender

Variables	Sex	N	Mean	S. D	ANOVA	P value
Age	Male	20	38.0000	9.717	9.453	0.003
	Female	50	42.5200	16.332		
Duration Of Disease	Male	20	10.1500	5.244	1.033	0.313
	Female	50	9.8000	7.183		
BMI	Male	20	26.1195	7.284	.453	0.503
	Female	50	30.2890	7.934		
Random Blood Sugar	Male	20	133.6500	47.558	1.830	0.181
	Female	50	147.0000	64.852		
HBA1C	Male	20	5.3680	.703	5.629	0.021
	Female	50	5.9156	1.392		

There was significant statistical association between age and gender and HbA1c with gender, where P value <0.05, while other character dose not showing such association where P value >0.05.

Table 2: Group Statistics according to HbA1 C subtypes and levels

	HBA1CN	Mean	S. D	t Test	Sig2 tailed)	HBA1C level	ANOVA	P
age	Normal	6039.9	14.32	1.772	.081	Betw. Groups	1.236	.265
	DM	1048.8	16.28	1.614	.134	Within Groups		
BMI	Normal	6028.4	6.631	1.791	.078	Bet Groups	1.926	.027
	DM	1033.1	13.12	1.127	.287	Within Groups		
DOD	Normal	609.2	6.578	2.104	.039	Bet Groups	1.725	.055
	DM	1013.9	5.89	2.278	.040	Within Groups		
RBS	Normal	60129.6	40.72	5.464	.000	Bet Groups	10.11	.0001
	DM	10224.3	92.49	3.184	.010	Within Groups		

According to HbA1c as a categorical variables, There was significant statistical association between HbA1c with duration of the diseases and surely with Random blood sugar where P value <0.05, while other character such age and BMI dosnot showing such association where P value

>0.05, but in a quantative term the HbA1C values show significant difference with duration of diseases and BMI and also with RBS, when assessed as between and with- in group analysis by ANOVA test.

Table 3: Relationship between Gender and DM Development

sex	DM development		Total	χ ²	
	No	Yes			
Male	Count	20	0	20	4.661
	% within sex	100.0%	0.0%	100.0%	
Female	Count	40	10	50	0.031
	% within sex	80.0%	20.0%	100.0%	
Total	Count	60	10	70	
	% within sex	85.7%	14.3%	100.0%	

There was significant statistical association between gender and development of DM in form HbA1c, where P value <0.05.

Table 4: Types of Treatment According to Development of DM

Type Of Treatment	HBA1C		Total	X ² , P
	Normal	DM		
Olan	27	7	34	1.770
	79.4%	20.6%	100.0%	
Traditional anti-psychotic	13	1	14	0.142
	92.9%	7.1%	100.0%	
Both	20	2	22	
	90.9%	9.1%	100.0%	
Total	60	10	70	
	85.7%	14.3%	100.0%	

There was no significant statistical association between development of DM inform of HbA1c with type of antipsychotic drug , where P value >0.05.

Table 5: Body Mass Indices According to Development of DM

		HBA1C		Total	F.E
BMI		NORMAL	HIGH		
Under Weight	Count	1	2	3	10.166
	%	33.3%	66.7%	100.0%	0.008
Normal	Count	16	0	16	
	%	100.0%	0.0%	100.0%	
Over wt.	Count	24	2	26	
	%	92.3%	7.7%	100.0%	
Obese	Count	19	6	25	
	%	76.0%	24.0%	100.0%	
Total	Count	60	10	70	
	%	85.7%	14.3%	100.0%	

There was no significant statistical association between development of DM inform of HbA1c with BMI, where most of the affected individuals where obese(60%)

Table 6: Logistic Regression Analysis of Determinants of Development of DM

	B	S.E.	Sig.	Exponential (B)
Sex	-53.200-	12012.101	.996	.000
TOT	17.452	5588.876	.998	37946957.045
BMI2	-18.388-	24140.222	.999	.000
Diagnosis	.779	2.159	.718	2.178
age	15.498	25527.490	1.000	5381164.567
Constant	-18.036-	5588.877	.997	.000

Multi variant analysis of independent factor are seem to be non-significantly associated with some variables of interest.

Table 7: Correlations regression analysis for determinants of DM developments

		HBA1C	age	DOD	TOT	RBS	BMI
age	Pearson Correlation	.240*	1				
	Sig. (2-tailed)	.045					
	N	70	70				
DOD	Pearson Correlation	.190	.681**	1			
	Sig. (2-tailed)	.115	.000				
	N	70	70	70			
TOT	Pearson Correlation	-.262*	.084	-.008-	1		
	Sig. (2-tailed)	.029	.491	.948			
	N	70	70	70	70		
RBS	Pearson Correlation	.727**	.284*	.173	-.074-	1	
	Sig. (2-tailed)	.000	.017	.152	.544		
	N	70	70	70	70	70	
BMI	Pearson Correlation	.100	.272*	.170	.132	.041	1
	Sig. (2-tailed)	.412	.023	.160	.276	.738	
	N	70	70	70	70	70	70

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

There was significant statistical association between HbA1c level with some expected as determinants (type of treatment, and the age), while BMI does not show such association., while univariate analysis show some difference.

V. DISCUSSION

SEVENTY patients (20) males and (50) females with chronic psychotic disorder, manic depressive psychoses and other chronic psychoses were treated with atypical anti-psychotic olanzapine (48.6%), traditional antipsychotic (20%) or with both of them (31.4%). High percentage of second generation atypical antipsychotic olanzapine is related to its potency which is equal to traditional antipsychotic e.g. fluphenazine decanoate with less side effects extrapyramidal symptoms, tardive dyskinesia, neuroleptic malignant syndrome (15), however persistent use of traditional antipsychotic, specially decanoate type for their long term effect from 2-3 weekly injection that facilitate patient compliance to treatment, in addition to its low price and accessibility, combination of both olanzapine and traditional antipsychotic probably increase their therapeutic potency and efficacy, such combination were not suggested to increase risk of diabetes mellitus (16)

Figure 2 shows distribution of study sample according to their BMI, majority of patients 26 (37.1%) were overweight, 25 (35.7%) were obese collectively (72.8%) of study sample have increased body weight, which is higher than national survey in America, which revealed (34%) of patients on second generation antipsychotic report and (16%) on traditional antipsychotics (17), possibly related to the habit and nature of excessive calories food intake with poor exercise and ignorance of healthy behavior in study sample population. Over all, weight gain, and obesity are due to increase appetite and increase food intake, or it is probably due to, histaminergic, serotonergic, dopaminergic disturbance of these neurotransmitter with increase body weight with long term duration of drugs (18)

Figure 3 reveals (14.3%) of study sample were diabetic, (85.7%) were normal. Similar findings mentioned that less diabetes rate (6.3%) among patients treated with clozapine (19), which is probably related to long term of treatment and other related to long term of treatment and other risk factors like high percentage of BMI in this study, so patients used olanzapine are at higher risk of diabetes, than patients treated with traditional antipsychotic (20).

Statistical analysis shows significant association between age and gender and HbA1C with gender as seen in table- 1. comparable result in which glycated hemoglobin HbA1C increased gradually will increase risk of diabetes mellitus with age (21) disregard of family history of diabetes among patients with chronic psychoses (22).

HbA1C has significant association between HbA1C and duration of disease (dod) and random blood sugar (RBS). finding related to the chronicity course of psychotic disorders, which take a course of relapse and remission or finally end with chronic negative schizophrenia, really this study deals with chronic disease extended from one to more than twenty years. Sptewise increasing of glucose level according to HbA1C with duration of disease. Explorative sectional study of chronic psychotic patients express prevalence rate of diabetes mellitus type 2 diabetes was (9%), which is significantly higher than general population concerning high body weight. Random blood sugar logically increase with high level of HbA1C, because both measures are parameters of diagnosis of

diabetes, but glycated haemoglobin HbA1C refers to long duration of blood sugar level for last three months, so antipsychotic treatment measurement of (RBS) specially atypical group is correlated to increase glycated haemoglobin(23).

HbA1C high level associated with increased BMI, due to peripheral resistance to insulin among obese patient newly expected BMI change are in first (12) months of treatment among patients with normal baseline BMI condition attributed to hyperlipidosis (24). all these articles findings are comparable to this study result.

Table-3... refers to statistical significant association inform of HbA1C (p value < 0.05) among males compare to female, which comparable with result for gender group shows high HbA1C among males group than females group(24). this finding is contradictory with many other studies which shows female ratio higher than males, but open trial olanzapine treated subject express no, significant difference between males and females group(21) findings shows women more prone to diabetes mellitus, due to excessive weight gain during management with antipsychotic, in addition to hormonal adverse effect on dyslipidemia(25). these different association of males and females groups through various studies, probably related to more compliance of male than female to treatment in this study, due to family ignorance and stigmatization sense to word females with psychotic disease in primitive societies. No statistical association between HbA1C in from of HbA1C with type of antipsychotic treatments, because traditional antipsychotic was admitted for more than (6) decades ago, they were regularly used for psychotic patients, in spite of their side effects in this country for their low price and availability, however atypical antipsychotic are more accepted and patients well complaints for them.

Both traditional and atypical antipsychotic have diabetogenic but mild effect in traditional compare with atypical antipsychotic (26) so, incompatible finding explored from this study, probably due to different samples populations studied or due to criteria used for diagnosis of diabetes. In different study, furthermore, a lot of studies unable to restrict the exposure to mono therapy or switch in from one therapy to other without informing physician (27).

There is no significant association between developments of diabetes according to HbA1C with BMI; however most of patients were obese (60%). for the tendency of antipsychotic drugs for histamine-1, serotonin receptor (28). comparable results shows increase in BMI which is expected of long term treatment for many years (29). Olanzapine and other second generation drugs are concerned with higher weight gain than general population. International diabetes center advice for regular monitoring of HbA1C and habit of food intake and organized physical exercise(30).

Multivariate analysis of independent factors to non- significant association with some variables of interest. Some studies revealed poor explanation for increase rate of diabetes mellitus in psychotic patients(31), however antipsychotic-naïve schizophrenic patients shows high risk of diabetes in first year, this study sample shows (dod) was from one to many years(32). The mean duration of disease (dod) relatively higher than other studies, that was around mid-twenties (33), and persisting on first episode. in our study the mean age of diabetes onset was more than 50 years.

Female sex was consider as a risk factor for diabetes type2, but this sex variation was abolished in the end of last century(34). But this study reveals high risky male group than females.

Regarding type of treatment as risk factor for progression of diabetes mellitus in mild and high potency drugs (35), although separate atypical antipsychotics (olanzapine), traditional various types, but we also used both. Atypical and traditional as line of treatment, in addition to traditional antipsychotic was not assessed separately, the case that multivariate analysis showed no significant association with many variables as seen in table-6. RBS measurement and HbA1C without baseline level, due to limitation of facilities and acceptance of patients for excessive and long term investigations.

Correlation regression analysis for determinants of diabetes mellitus at level 0.05 and 0.01 level (2-tailed) between HbA1C level with some expected variables as (type of treatment and age). relatively olanzapine shows association with relative risk of development of diabetes (36), in addition to statistical significance with decrease in insulin peripheral resistance and significant increase in fasting blood sugar and increase BMI (37), significant association between HbA1C and the age of patients was revealed as natural progression of disease with increased BMI and deterioration of schizophrenia into negative course which associated with self-ignorance and poor hygienic state associated with poor monitoring and assessment of glucose level, however the relative contribution for enhancing metabolic risk with atypical antipsychotic may be due to accumulative effect of other factor that also have impact metabolic risk on long life (38), similar results was revealed on metabolic abnormalities after eight years, high percentage of patients treated with olanzapine showed metabolic disturbance like diabetes mellitus and or hyperlipidemia (39).

Body mass index (BMI) shows significant correlation with HbA1C with BMI, as obesity and increase body weight were high risk factors, as long as variability between different studies, multilevel regression was achieved, two level models with person within study were used to facilitate the simpler explanation of results, in addition to use binary logistic regression for overweight, blood sugar and other metabolic changes, they revealed increase in BMI in (50%) of study sample (40).

VI. CONCLUSION

There are high percentage (48.6%) of patients used olanzapine, less percentage on traditional antipsychotic and both. BMI showed high percentage of overweight and obese patient (60%) was diabetic, which is higher than normal population, significant association was seen in different variables (age, duration of disease, RBS, gender and HbA1C, BMI), difference in quantitative values of HbA1C, correlation regression analysis of determinant of diabetes mellitus show significant association between HbA1C with same determinant like (TOT, age).

VII. LIMITATIONS

- Variability of initial premedication monitoring of blood sugar, BMI, since study sample was chronic in duration (chronic psychotic) with cross-sectional assessment, so longitudinal study is suggested.
- Poor compliance and adhesion of patients to treatment Recommendations.
- Regular assessment of blood sugar, serum lipid BMI of patients treated with antipsychotic treatment.
- Precaution and alertness of physicians treating
- Psychotic patient with a typical antipsychotic

- Olanzapine, which shows pre-existential diabetes,
- Sudden withdrawal of drug and shifting to less diabetogenic drug like aripiprazole may have ceased progression of diabetes mellitus.

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