Metabolic Derangement in Schizophrenia: Relation To Antipsychotic Treatment

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ABSTRACT

Background: Patients with schizophrenia have high prevalence of over weight and related medical disorders when compared with the general population. **Objective:** We aimed at finding out the risk for metabolic disturbances among a group of drug naïve schizophrenics. Also we compared the metabolic effects of first, second generation and combined first and second generation antipsychotics. **Subjects and methods:** The study included 122 Egyptian schizophrenic patients. They were divided into four groups [36 patients on first generation antipsychotics (gp 1), 40 patients on atypical antipsychotics (gp 2), 16 patients on combined typical and atypical antipsychotics (gp 3), 30 neuroleptic naive patients(gp 4)]. Thirty healthy subjects matching age, sex and BMI were taken for the control group (gp 5). Anthropometric measures, fasting glucose, insulin and adiponectin, total cholesterol, TG, HDL, LDL, insulin resistance index (HOMA IR) and quantitative insulin sensitivity check index (QUICKI) were evaluated. **Results:** The prevalence of insulin resistance and atherogenic lipid profile are higher among gp4 *(86.7% and 60%, respectively)* compared to gp 5 *(0% and 6.7%, respectively, p<0.01)*. Patients in gp3 show the highest prevalence of insulin resistance *(100%, p<0.01)* and atherogenic lipid profile *(87.5%, p<0.01)*. Fasting insulin is highest among gp2 *(41.78±23.46µIU/ml, p<0.01)* with a positive significant correlation between fasting serum insulin level and duration of the treatment among patients of gp2 *(r=0.38, p <0.05)*. There is a significant negative correlation between QUICKI and duration of treatment *(r=-0.276, p<0.05)* among patients on atypical antipsychotics (gp2+gp3). Fasting adiponectin has a highly significant lower level among gp1,2,3 and 4 compared to gp5 *(p<0.01)*, gp2 show the lowest level *(1.73±0.58ng/ml)*. There is a highly significant negative correlation between BMI and fasting serum adiponectin levels *(r=0.48, p<0.01)* among gp2 patients. **Conclusion:** Schizophrenia puts the patient at a higher risk for insulin resistance even prior to antipsychotic treatment. Combined typical and atypical antipsychotic treatment showed the highest prevalence of insulin resistance and atherogenic lipid profile. Insulin resistance increases with increasing the duration of antipsychotic treatment among patients on atypical antipsychotics.

Key words: Metabolic syndrome, Schisophrenia, Antipsychotic drugs.

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INTRODUCTION

Insulin resistance plays an important role in the pathophysiology of diabetes and is associated with obesity and other cardiovascular risk factors[1-2]. Several studies showed a higher prevalence of diabetes or abnormal glucose metabolism in schizophrenic patients[3]. However, these studies, many of which have been retrospective and of variable size, have not always been controlled for potential confounders such as age, race, gender, family history and obesity. In addition, many studies have not been controlled for use of antipsychotic drugs[4]. Atypical antipsychotic (AAP) medications are of great benefit to a wide variety of people with psychiatric disorders, especially patients with schizophrenia[5]. Studies showed association of AAP with weight gain and alterations of lipid homeostasis[6]. Moreover, increasing numbers of reports concerning impaired glucose tolerance, diabetes, and ketoacidosis have raised concerns about a possible association between abnormal glucose metabolism and treatment with AAP, although the question is still debated because of the presence of many confounding factors. These adverse effects of atypical antipsychotic medications are not only the risk factors for cardiovascular disease, insulin resistance and diabetes mellitus leading to increased morbidity and mortality but may also impair the patient's adherence to treatment[7].

Race is strongly associated with risk for metabolic dysfunction. High prevalence of obesity and metabolic disturbances in patients with schizophrenia has been reported in western countries**.** However reports in the Middle East remain scanty. The present study was done in Egypt to find out the risk for metabolic disturbances among a group of drug naïve schizophrenics, to compare the metabolic effects of typical, atypical and combined typical and AAP and to detect factors associated with greatest risk for metabolic disturbances among the studied group. We also investigated possible role of adiponectin in such metabolic disturbance.

SUBJECTS AND METHOD

Before carrying out this study, written informed consent was obtained from each individual. The study included 122 patients with schizophrenia diagnosed according to *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition (DSM IV criteria), recruited from the Institute of Psychiatry, Ain Shams University, Cairo, Egypt. Patients were included if they were aged between 18 and 60 years, did not have diagnosis of type 2 diabetes and were not treated with other medications known to affect weight, such as sodium valproate. Hematological, renal and liver function tests were done to exclude the presence of other abnormality. Medicated patients were receiving treatment for at least 6 weeks. The patients were divided into Group 1 (on conventional antipsychotics n=36; 28 patients on haloperidol, 4 patients on haloperidol and trifluperazine and 4 patients on haloperidol and clopenthoixol), Group 2 (on AAP n=40; 14 patients on resperidone, 20 patients on clozapine, 2 on olanzpine, 2 on aripiprazole and 2 patients on quetiapine), Group 3 (on both typical and AAP n=16; 2 patients on resperidone and haloperidol, 6 patients on resperidone and clopenthixol, 2 patients on clozapine and haloperidol, 2 patients on clozapine and clopenthixol, 2 patients on olanzapine and

haloperidol and 2 patients on olanzapine and clopenthixol), Group 4 (drug naive patients n=30). Group 5: Thirty healthy subjects matching age, sex and BMI were the control group. Full medical history and clinical examination including measurement of waist circumference and calculation of the body mass index (weight in kilograms divided by the square of height in meters) were done. Fasting (12 hours) venous blood samples were collected at 8-10am to measure fasting insulin level, fasting blood sugar (FBS), adiponectin and lipid profile [total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL-C), and LDL-C. Insulin resistance was determined using the homeostasis model of assessment (HOMA) and also by QUICKI (quantitative insulin-sensitivity check index) which is among the most accurate and useful surrogate indexes for determining insulin sensitivity in humans[8].

Laboratory procedures: Plasma levels of glucose were measured enzymatically[9]: Stanbio Laboratory, Texas, USA), TC and TG were determined using an Aeroset analyzer (Abbott, North Chicago, IL). Determination of HDL-C and LDL-C: were according to the method of Lopes-Virella[10]: Stanbio Laboratory, Texas, USA. Serum adiponectin and insulin concentrations were measured by enzyme linked immunosorbant assay (ELISA) (Orgenium Laboratories, Helsiniki Finland and BioSource International, Inc USA), respectively.

Statistical analysis:

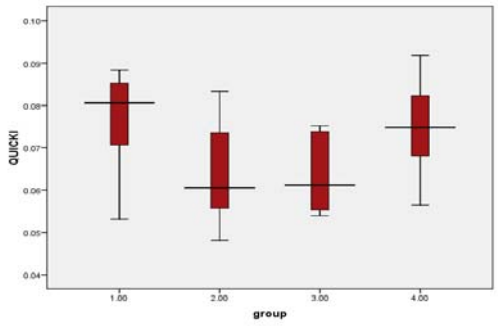
Analysis of data was done by IBM computer using SPSS (statistical program for social science version 16) as follows:- Description of quantitative variables as mean and standard deviation and qualitative data as number and percentage. One way ANOVA test was used to compare more than two groups as regards continuous variables with correction for multiple comparisons using Bonferroni. Kruskall Wallis test was used instead of ANOVA test in non parametric data. Mann Whitney test was used to compare two groups as regards quantitative non parametric data. Chi-square test was used to compare qualitative variables. Associations of continuous variables were estimated using Spearman's correlation coefficients for non parametric data and Pearson correlation coefficients for parametric data. Logistic regression model was used to find out the most important independent predictors of the presence of insulin resistance and also the atherogenic lipid profile. Linear regression analysis was used to determine the independent predictors of adiponectin. A $p<0.05$ was considered to be significant and <0.01 was highly significant.

RESULTS

The demographic and clinical data of the studied population is shown in table (1). There was insignificant difference in age, sex, BMI, family history of DM and cigarette smoking in between the studied groups. There was also insignificant difference in waist circumference except for group 3 *(patients on combined typical and AAP)* which was significantly higher than group *4 (neuroleptic naïve patients, p=0.002)* and group 5 (*control group, p=0.004*) (table 1). The patient groups *[whether medicated (group1, 2 and 3) or neuroleptic naïve (group4)]* had highly significant elevation of insulin level and HOMA IR while QUICKI was significantly lower compared to the controls (*p=0.0001)* (table 1). Insulin resistance was prevalent among the different patient groups with

patients on combined typical and AAP showing the highest prevalence *(100%, p=0.0001)* (table 2). Comparing the patient groups with each other, we found that patients on AAP whether alone *(group 2)* or combined with conventional antipsychotics *(group3)* had lower insulin sensitivity as evidenced by the significantly higher HOMA IR *(9.013±5.33 and 8.66±3.8, respectively)* and significantly lower QUICKI *(0.0645±0.01 and 0.0637±0.009, respectively)* compared to patients on conventional antipsychotics *(group 1; HOMA IR: 4.63±2.91, QUICKI: 0.0768±0.009, p=0.0001)* or neuroleptic naïve patients *(group 4; HOMA IR: 4.9±2.25, p=0.001, QUICKI: 0.0745±0.009, p=0.0001, 0.002, respectively) (*fig. 2). No significant difference was present between group 2 and 3 or between group 1 and 4.

Figure (1): Significantly lower QUICKI among gp2 & gp3 compared to gp1 & gp4



Duration of treatment showed a negative correlation with FBS and QUICKI and a positive correlation with fasting insulin level (fig. 3) among group 2*(r=-0.406, p=0.009, r=-0.341, p=0.03 and r=0.386, p=0.014, respectively)* and group 3 *(r=-0.228, p value 0.39 , r=-0.281, p value 0.2 and 0.442, p=0.087)*: statistically significant in group 2 only, this may be attributed to the small number of group 3 (16 patients). QUICKI showed a significantly negative correlation with duration of treatment among all patients on AAP (group 2+3) *r=-0.276, p=0.04* (fig. 4).

Figure (2): A positive significant correlation between fasting serum insulin level & duration of treatment among gp2

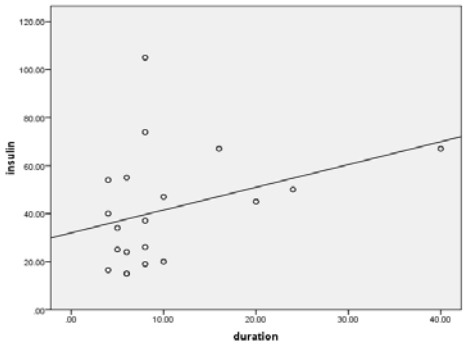
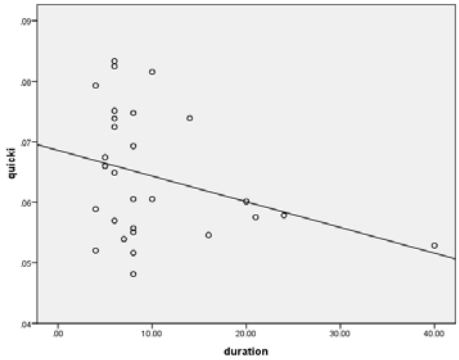


Figure (3): Negative significant correlation between QUICKI and duration of treatment among all patients on atypical antipsychotics (Gp 2+3)



Dyslipidemia is apparent in the patient groups (table 1); total cholesterol, triglycerides, LDL-C, LDL/HDL ratio showed highly significant elevation while HDL-C showed highly significant lower levels among the medicated and neuroleptic naïve patients compared to the controls

(p=0.0001). The prevalence of atherogenic lipid profile was highest among group 3 *(87.5%, p=0.001)* (table 2). Moreover, being on combined typical and AAP was independently associated with LDL >130mg/dl *(β:3.22, odds ratio:25.08, p=0.0001)* together with female gender *(β:1.44, odds ratio:4.23,p value 0.012)* and smoking *(β:3.07, odds ratio:23.09, p=0.0001).* Triglycerides > 150mg/dl was independently associated with age >30 years *(β:0.922, odds ratio:2.51, p=0.02)* .HDL-C <40mg/dl in males and <50mg/dl in females was independently predicted by duration of therapy >8 weeks *(β:1.74, odds ratio:5.69, p=0.03).*

Although total cholesterol, LDL and LDL/HDL ratio were higher in each of the medicated groups compared to the neuroleptic naïve group, the difference is statistically insignificant *(p>0.05).* Also there was statistically insignificant difference between the patient groups as regards triglycerides and HDL *(p>0.05)* (table 1).

Fasting adiponectin level showed highly significant lower levels among neuroleptic naive and medicated patients compared to the controls *(p=0.0001)* with patients on AAP showing the lowest level (1.73±0.58 ng/ml) (table 1). Adiponectin did not show a significant correlation with any of the parameters of insulin resistance in the studied patient groups. It showed significant negative correlation with BMI among group 2 *(r=-0.412, p=0.008).* In group 3 there was a significant positive correlation between adiponectin and total cholesterol *(r=0.591, p=0.016)* and LDL *(r=0.681, p=0.004),* where as there was highly significant negative correlation with equivalent dose of treatment *(r=-0.841, p=0.0001).*

Because of the presence of many confounding factors for insulin resistance and dyslipidemia, logistic regression analysis was done and we found that: age >40, female gender, and treatment with resperidone or clozapine were independent predictors of insulin resistance among the studied patients (table 3); female gender, family history of DM and BMI>25 were independent predictors of moderate risk of atherosclerosis (LDL/HDL 3-6) (table 4). None was an independent predictor of severe risk of atherosclerosis (LDL/HDL >6).

We studied the metabolic effect of the most commonly used AAP mono therapy in the present study (resperidone and clozapine). Both patients on respiridone and clozapine showed significantly lower insulin sensitivity as evidenced by the higher HOMA IR *(9.57±4.94 and 10.73±5.94, respectively),* fasting insulin *(39.42±17.77 and 52.56±27.31 μIU/ml, respectively)* and lower QUICKI *(0.06273±0.009 and 0.06173±0.0123, respectively)* compared to neuroleptic naïve patients *(4.9±2.25, 23.53±10.72 and 0.0745±0.009, p=0.0001),* but there was insignificant difference as regards the lipid profile *(p>0.05).* There was no significant difference in age, gender, BMI and waist circumference between these groups. Fasting adiponectin level was lowest among patients on clozapine *(1.57± 0.58ng/ml)* followed by resperidone *(1.93± 0.53ng/ml)* then neuroleptic naïve patients *(2±0.63ng/ml, p=0.027).* Clozapine treatment together with BMI and family history of diabetes mellitus were found to be independent predictors of fasting adiponectin level *(p=0.0001, 0.01 and 0.029, respectively)* (table 5).

Table 1: characteristics of the studied population.

	Group 1 N=36	Group 2 N=40	Group 3 N=16	Group 4 N=30	Group 5 N=30
Age	32.05±10.36	36.2±11.5	31.5±11.9	11.6±34.06	34.06±11.65
Gender Male Female	28(77.8%) 8(22.2%)	30 (75%) 10(25%)	10(87.5%) 6(12.5%)	18(60%) 12(40%)	18(60%) 12(40%)
Cigarette smoking %	16 (44.4%)	19 (47.5)	5 (31.3%)	12(40%)	11(36.6%)
Equivalent drug dose	1430.5±559.37	846.30±493.16	1425±367**	----------	----------
Family history of DM	14 (38.9%)	8(20%)	2(12.5%)	10(33.3%)	10(33.3%)
Duration of treatment in wks#	10.44± 9	10.7±8.43	9.5±5.2	----------	----------
BMI Kg/ht2	25.02±5.97	25.13±3.19	25.92±4.7	24.9±4	24.87±4
Waist in cm	88.08±13.46	90.18±14.5	98.5±14.7	80.7±16.4	**81.87±15.86****
FBS mg/dl	81.77±10.86	86.8±14.22	89.38±16.3	85.33±12.52	82.47±9.47
Fasting s.insulin µIU\ ml #	22.83±13.43	41.78±23.46	40.88±21.2	23.53±10.72	**6.27±1.02****
HOMA IR %#	4.63±2.91	9.013±5.33	8.66±3.8	4.9±2.25	**1.29±0.32****
QUICKI#	0.0768±0.009	0.0645±0.01.	0.0637 ±0.009.	0.0745±0.009	**0.1270±0.021****
TC mg/dl	212.5±62.21	207.35±45.6	221.75±47.31	203±73.14	151.8±24.54**
TG mg/dl	127.11±70.08	144.4±64.9	119.13±34.09	149.93±54.32	**86.93±19.39****
HDL mg/dl	39.89±8.07	36.5±5	38.5 ±11.11	36±8	**51.13±8.26****
LDL mg/dl	147.17±55.43	142.1±49.1	159.45±44.45	121.29±55.12	**85.74±13.52****
LDL/HDL	3.73±1.3	3.98±1.56	4.33±1.48	3.51±1.55	**1.72±0.38****
Adiponectin ng/ml	2.067±0.45	1.73±0.58	2.03±0.7	2±0.63	**11.57±1.93****

* p value <0.05, **p value<0.01, #Kruskall Wallis test. BMI: body mass index. FBS: fasting blood sugar. HOMA IR: homeostatic model assessment for insulin resistance. QUICKI: quantitative insulin-sensitivity check index. TC: total cholesterol, TG: triglycerides, LDL: low density lipoprotein, HDL: high density lipoprotein.

Table 2: Prevalence of insulin resistance, atherogenic lipid profile and family history of DM in the different studied groups.

	Group 1 N=36		Group 2 N=40		Group 3 N=16		Group 4 N=30		Group 5 N=30	
	No	**percent**	**no**	**Percent**	**no**	**percent**	**no**	**percent**	**no**	**percent**
Insulin resistance	26	72.2%	38	95%	16	100%	26	86.7%	**0**	**0%****
LDL/HDL >3	26	72.2%	30	75%	14	87.5%	16	60%	**2**	**6.7%****

**p value<0.01,

Table 3: Independent predictors of insulin resistance (decreased insulin sensitivity).

					95.0% C.I	
	B coefficient	**S.E.**	**Sig.**	**Odds ratio**	**Lower**	**Upper**
Age>40 years	1.61	.622	.01	5.004	1.477	16.948
Female gender	1.018	.511	.046	2.766	1.017	7.525
TTT with Risperidone	2.523	.801	.002	12.472	2.593	59.981
TTT with Clozapine	1.807	.618	.003	6.091	1.813	20.461

SE: standard error of beta. CI: confidence interval. TTT: treatment

Table 4: Independent predictors of moderate risk of atherosclerosois (LDL/HDL 3-6).

	B coefficient	S.E.	Sig.	Odds ratio	95.0% C.I	
					Lower	Upper
Female gender	3.637	0.873	0.0001	37.979	6.868	210.032
Family history of DM	1.424	0.642	0.027	4.152	1.180	14.605
BMI>25	1.688	0.630	0.007	5.408	1.573	18.588

SE: standard error of beta. CI: confidence interval

Table 5: Independent predictors of adiponectin.

	Standardized Coefficients			95% Confidence Interval for B	
	Beta	t	Sig.	Lower Bound	Upper Bound
Treatment with Clozapine	-.307-	-3.746-	.000	-.690-	-.213-
BMI	-.223-	-2.574-	.011	-.051-	-.007-
Family history of DM	.192	2.217	.029	.027	.473

DISCUSSION

The prevalence of diabetes in Egypt is high. Egypt is among the 10 countries estimated to have the highest numbers of people with diabetes (6.7 million) in 2030[11]. Insulin-resistant diabetic subjects are two to five times more likely to die from cardiovascular disease (CVD) than those without diabetes[12]. Moreover, there is increasing prevalence of the main risk factors of CVD in Egypt[13] therefore; the health of Egyptians is vulnerable to any additional factors that could increase the development of type 2 diabetes.

In the present study both patients and control subjects were drawn from the Egyptian population and had comparable age, sex, BMI and family history of DM. However, insulin sensitivity was significantly lower among the different patient groups when compared to the controls. These results seem to confirm earlier findings that the disturbance of glucose metabolism tends to be more severe in patients with schizophrenia than in the general population and that there is higher prevalence of diabetes or abnormal glucose metabolism even in neuroleptic naïve patients[14-15].

AAP use has been associated with metabolic disturbances, such as alterations of glucose homeostasis[16]. In our study, patients on AAP either alone or combined with conventional antipsychotics were more insulin resistant than patients on conventional antipsychotics or neuroleptic naïve patients. Moreover, the duration of treatment had a positive correlation with fasting serum insulin level and a negative correlation with QUIKI among patients on AAP.

These results are comparable to other studies that reported the association of certain AAP with a higher risk for insulin resistance[7, 17]. Contrary to our results[15] who studied 200 unselected mainly Caucasian patients with schizophrenia or schizoaffective disorders reported the

absence of an effect of the class of antipsychotic medication on glucose metabolism. The absence of descriptive data concerning the duration of treatment of both groups in Cohen study might have underpowered the results, which was evident in the results of the randomized prospective study that was performed by[18] who found a significantly raised glucose level at 8 weeks with clozapine and haloperidol and further elevation among the olanzapine group after extra 6 weeks, which point to the influence of treatment duration on interpretation of study outcome.

Surprisingly the current study revealed a significant negative correlation between FBS and duration of treatment, similar results were presented where the median FBS in the schizophrenic patients was lower than the control group in spite that patient group were more insulin resistant[12].

In the current study, patients on combined conventional and AAP had the highest prevalence of insulin resistance which implicate a greater metabolic risk and also higher propensity toward metabolic syndrome, as evidenced by the highest waist circumference among those patients *(98.5±14.7cm.).*

It has been suggested that the association of antipsychotic treatment with both weight gain and diabetes in patients is confounded by the lack of exercise and alterations in diet common to psychiatrically ill patients[12]. However, in our study, patient groups and controls showed insignificant difference in BMI, which indicates that the increased insulin resistance is additional to that conferred by weight gain. Moreover, multivariate analysis revealed that treatment with risperidone or clozapine in addition to age >40 years and female gender were independent predictors of insulin resistance. This point to the presence of a significant class effect of the high risk AAP on the parameters of insulin resistance which in addition to various environmental and genetic factors interact together to pose such metabolic risks on this group of patients.

Accumulating evidence in previous and current literature indicates potential role of antipsychotic medications and in particular AAP in the development of dyslipidemia and cardiovascular diseases among schizophrenic patients, nevertheless lipid profile data among various studies conducted upon treated and neuroleptic naïve patients are limited and contradictory.

In the current study, the patients (whether medicated or naïve) had higher serum TG, TC, LDL-C and lower HDL-C compared to the controls. But there were no significant differences in between patient groups. Moreover, there was insignificant difference between patients on resperidone, clozapine and neuroleptic naïve patients.

These results are consistent with that patients are more hypertriglyceridemic than healthy controls[12], also there is increased TC in neuroleptic naïve patients[19]. Contrary to our results previous study showed that there was no significant difference between schizophrenic patients and healthy controls regarding TC, LDL-C, HDL-C, yet they found that serum TG were significantly elevated in patients on AAP[20], also found that olanzapine/clozapine treated patients had higher TG and lower HDL-C levels than unmedicated subjects, similar results were reported lately by[7, 21] who studied 28 schizophrenic patients on monotherapy with 6 different AAP for 4 weeks and found that olanzapine/clozapine constitute a high risk

group for metabolic derangement including dyslipidemia.

Not withstanding results from other trials showed different results from the above, first episode psychosis with schizophrenia do not differ from healthy controls in lipid parameters[22], and (patients with first episode psychosis, 6-month treatment with AAP is associated with the exacerbation of pre-existing and emergence of new CVD and diabetes risk factors[23].

In the current study, prevalence of atherogenic lipid profile (LDL-C\HDL-C >3) was highest among patients on combined typical and AAP (87.5%) .In addition, being on combined typical and AAP was independently associated with LDL-C>130mg/dl together with the female gender and smoking. This reflects in part what was published in earlier reports about the dyslipidemic effect of various antipsychotic drugs including conventional drugs, as significant elevation of TC, VLDL-C and LDL-C were found among patients on conventional antipsychotics (24), also there was significant elevations in LDL-C in such patients[25], thus the additive effect of combining two generation with relatively different effects on lipid profile was evident in our study, taking in consideration the special characteristics of this specific group of patients with a poorer metabolic health.

Multivariate analysis in the current study revealed that female gender, family history of diabetes and BMI >25Kg/m2 are the independent predictors of moderate atherogenic lipid profile (LDL-C/HDL-C 3-6) thus given the multiple cardiovascular risk factors seen in patients with schizophrenia, great care must be exercised in the choice of antipsychotic therapy taking into consideration these factors.

Adiponectin is a recently identified adipocyte-derived protein, with low adiponectin levels being associated with metabolic abnormalities such as obesity, insulin resistance and type 2 diabetes, leading several investigators to postulate that circulating adiponectin levels might serve as a useful marker for monitoring changes of weight and insulin resistance during AAP treatment[26].

Our study showed a highly significant lower adiponectin level among neuroleptic naïve and medicated groups compared to controls, being lowest in patients on AAP ***(1.73±0.58ng/ml),*** similar results showed significantly lower total and high molecular weight adiponectin in patients on AAP than conventional antipsychotics[27-28]. Although there was significantly lower insulin sensitivity among patients on resperidone or clozapine compared to neuroleptic naïve patients, only clozapine was independently associated with adiponectin level together with BMI and waist circumference. These results are in line with[29] who found that antipsychotic medication independently influenced adiponectin levels, with the lowest mean levels in patients on clozapine and olanzapine.

Contrary to our results, patients on AAP had significantly higher adiponectin levels[30], while other studies found no significant change in adiponectin level[31-34].

CONCLUSION

Schizophrenia and mood disorders carry a metabolic burden reflected as higher rates of morbidity and mortality than rest of population. This metabolic burden could be linked to the pathophysiology of schizophrenia that might involve genetic factors, and is aggravated by environmental

factors as sedentary life style, poorer diet and obesity.

Antipsychotic medications especially AAP pose further encumbrance on the metabolic milieu of schizophrenic patients, with adiponectin playing a role in mediating such metabolic effects, so it comes mandatory to monitor metabolic changes as early as within the first eight weeks of treatment, as changes can be determined very early in antipsychotic treatment.

Further, special care to patients receiving antipsychotic polytherapy should be directed toward consideration of cardiovascular risk when prescribing antipsychotics, as close monitoring of metabolic changes during treatment. Management of these patients has to not only encompass mental illness but general health issues and therefore treatment should be multi-disciplinary.

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