HYPERGLYCEMIA AND TREATMENT WITH ANTIPSYCHOTICS – A STUDY FROM A TERTIARY CARE CENTRE

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ABSTRACT

Objective: To assess the frequency of hyperglycemia in chronic schizophrenics and describe its correlates.

Design: Cross-sectional study.

Place and duration of the study: This study was carried out in a Department of Psychiatry Jinnah Postgraduate Medical Center, Karachi, Karachi Pakistan in the summer of 2007.

Subject and method: Fifty patients suffering from chronic schizophrenia (14 female and 36 male), between the ages of 18 and 60 years, who had been taking antipsychotic medication for the past two years or more were included. These patients were assessed on detailed history, physical examination supported with fasting blood sugar, checked by glucometer, BMI, blood pressure and mental state examination by psychiatrists

Results: A Positive association was found between hyperglycemia and chronic schizophrenia. 10% of the patients were found to be suffering from hyperglycemia. Out of these 8% had been on atypical antipsychotics on an average of 4 years. There was no relationship found between gender and altered blood glucose levels.

Conclusions: There have been countless studies on the antipsychotics induced hyperglycemia in the past. Though the sample size of our study was small, but it established the contributory relationship between atypical antipsychotics and hyperglycemia in this part of the world. More studies with a larger sample size should be conducted in the near future.

Key words: Hyperglycemia, chronic schizophrenia, antipsychotics.

INTRODUCTION

Henry Maudsley in 1879 wrote in his book "*The Pathology of Mind*", that diabetes is a disease which often manifests itself in the families where insanity prevails[1].

According to studies conducted previously, it has been seen that there is 1.5 to 2 times increased prevalence of diabetes mellitus in people suffering from severe mental illness as compared with the general population[2].

In this particular type of diabetes, there is a failure of insulin to tempt the glucose into various cells of skeletal muscle and adipose tissue, an inability of insulin to suppress extra glucose production by the liver coupled with compensatory increased insulin secretion by the pancreas to overcome the insulin resistance[3].

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In some studies, findings indicate that there is impaired glucose tolerance and insulin resistance in schizophrenic patients[4] whereas in some 18 to 19%, a family history of type 2 diabetes mellitus has been found[5].

Another risk factor is iatrogenic, that is caused by antipsychotics. The advent of antipsychotics in 1960s ushered in a new era of treatment in schizophrenia banishing the insulin shock treatments and sometimes unnecessary electroconvulsive therapy. The new breed of medicine, the conventional antipsychotics such as the phenothiazines and butyrophenones, though effective in abating the signs and symptoms of schizophrenia, caused a multiple of side effects such as extra-pyramidal effects, weight gain and altered blood levels of glucose. Thonnard-Newman in 1968[6] found that 25% of schizophrenic patients on phenothiazines were diabetic. The cases of type 2 diabetes in Schizophrenic patients started increasing further with the introduction of 2nd and 3rd generation neuroleptics in the 1990s, which, while possessing fewer extra pyramidal side effects, caused increased cases of hyperglycemia (diabetes type 2) in such patients[7].

The propensity of Typical versus Atypical antipsychotics in causing type 2 diabetes is currently the subject of a lot of trials. As to how do these medicine cause the dysregulation of glucose metabolism is yet

unknown though Silvestre & Prous[8] found that anti-psychotics have an increased affinity for muscranic M3 receptors which is highly expressed by the B-cells of the pancreas which may play an active role in the regulation of glucose metabolism. A broad range of receptors have been implicated in the neuroleptics induced hyperglycemia, but despite a lot of research the actual pathophysiology by which these drugs cause diabetes is not yet known.

Though there have been a lot of studies conducted on the relationship between anti-psychotics and altered blood glucose levels in the west, there have been few documented in our part of the world. Schizophrenic patients suffer from increased mortality because of high risk factors such as smoking, sedentary lifestyle, weight gain and poor nutrition and it has been postulated by some studies that increased weight in some patients is not due to the medications but because of their lifestyle itself[9-10]. For this purpose we decided to use only non-obese patients in our investigation to find the prevalence of type 2 diabetes in chronic schizophrenics who had been using typical or atypical anti psychotics for over two years.

SUBJECTS AND METHODS

Study Setting: The study was carried out in a tertiary care hospital located in Karachi, Pakistan. All patients were recruited from the special schizophrenia clinic being run for the past 18 years in the psychiatry department. It usually has a turn-over of 75 patients per week.

Participants: Information was obtained from patients approaching for their follow up evaluation. There were 14 female and 36 male patients totaling up to 50 inducted in the study. Any patients with a positive family history of diabetes mellitus or already suffering from diabetes were excluded automatically. So were the obese and the patients younger than 18 years or older than 60 years.

Data Collection: Cases were assessed by a semi-structured proforma supported with a detailed history, physical and mental state examination. Ethical issues such as consent and confidentiality were taken care of.

Statistical Analysis**:** The data was entered into SPSS-version 16.0. Frequency was used to calculate BMI, altered blood glucose levels, gender, type of therapy etc. Chi square test were used to compare variables. A p value of <0.005 was considered significant.

RESULTS

Fifty cases out of 76 (female & male) were inducted after consent and exclusion of family history of diabetes. They were assessed on various factors namely the duration of their illness, fasting blood sugar levels, family history for obesity/Diabetes Mellitus and the time period they had been taking treatment either with typical or atypical anti-psychotics amongst others. 68% of the patients were single, 20% were married whereas 6% were either separated or divorced. (Table 1)

21 were on typical anti-psychotic mono-therapy, 22 were on atypical anti-psychotics. 7 were on combined poly therapy of the two (table 2). The fasting status of every patient was confirmed before performing fasting blood sugar test. 5 (10%) of the patients in result were found to be suffering from hyperglycemia (above126mg/dl)[11]. Out of these, 4 (8%) had been on atypical anti-psychotics on an average of 4 years, the remaining 1 (2%) were on typical mono-therapy. (Table 2)

Nearly 72% had been psychiatrically ill for over 5 years, 12% for the past 2 to 5 years and 16% had been diagnosed just over 2 years ago. However, duration of illness was seen to have no impact on the Fasting Blood Glucose of these patients (fig 1) neither did gender have any statistical impact. However, there was a significant correlation ($p<0.001$) amongst the patients in Body Mass Index (BMI) compared with their fasting blood glucose test (FBS). (Table 1). The degree of education patients possessed compared with their altered blood glucose levels yielded no positive findings. (Table 1).

DISCUSSION

Studies conducted amongst South Asians (Pakistanis, Indian and Bangladeshis) have found a 4 times increased risk of getting type 2 diabetes as compared to their European counterparts[12]. The correlation of schizophrenia and diabetes has also been quite significant. Studies assessing the prevalence of type 2 diabetes in people with schizophrenia broadly agree that the condition may be at least two to four times more prevalent than in the general population[13]. In one particular study, the lifetime prevalence of known diabetes reported for the people with schizophrenia was 15%, with increasing age, being female and being of African American or 'other' non-White racial origin such as Asian increasing the likelihood of having diabetes[14].

Obviously for us in Pakistan these are alarming figures. By the year 2025 it is almost estimated that the number of diabetics in India, Bangladesh and Pakistan cumulatively shall grow to a staggering 80 million[15].

Apart from schizophrenia as a risk factor for hyperglycemia, antipsychotic medications have also been known to cause disturbed blood glucose levels especially atypical ones[16]. In our study some patients (n=24) had been taking second generation antipsychotics namely Risperidone and Olanzapine whereas some (n=20) had been on typical antipsychotics such as Haloperidol, Trifluperazine. The remaining (n=6) were on typical depot (fluphenazine) preparation. The patients using second generation antipsychotics with disturbed glucose metabolism had been on it for an average of 4 years. There was no significant co-relation found between hyperglycemia and duration of illness in our study.

Table 1

General characteristics of patients

Variables	Overall (n=50)		Hyperglycemia (n=5)		Normal (n=45)		P-value
	No.	%	No.	%	No.	%	
Gender							
Male	36	72	3	60	33	73	0.529
Female	14	28	2	40	12	27	
Age in years							
< 30	19	38	2	40	17	38	0.664
30-39	18	36	1	20	17	38	
40 & above	13	26	2	40	11	24	
Mean ± S.D.	32.6 ± 8.41		35.4 ± 14.4		32.3 ± 7.67		0.438
BMI							
Normal weight	35	70	1	20	34	76	0.010 *
Over weight	15	30	4	80	11	24	
Mean ± S.D.	22.7 ± 3.57		26.7 ± 2.34		22.6 ± 3.42		0.006 *
Marital status							
Single	34	68	3	60	31	69	0.840
Married	10	20	1	20	9	20	
Separated	6	12	1	20	5	11	
Education							
Illiterate	7	14	–	–	7	16	0.490
Primary to middle	13	26	2	40	11	24	
Matric	10	20	2	40	8	18	
Intermediate	10	20	1	20	9	20	
Graduate	10	20	–	–	10	22	
Occupation							
Employed	5	10	–	–	5	11	0.432
Unemployed	45	90	5	100	40	89	
Family system							
Nuclear	15	30	1	20	14	31	0.607
Joint	35	70	4	80	31	69	

*Statistically significant $p<0.01$

Most people of Pakistan live in a joint family system rather than a nuclear system. It has been seen that people are more rigid in their traditions and supernatural beliefs when living in the traditional joint family style. But the positive aspect associated with this kind of system culturally is that 'everyone' is taken care of in the extended family umbrella. A study conducted in India, which is a neighboring country of Pakistan and is similar in culture and family oriented lifestyle, it was observed that living in a nuclear family was associated with longer duration of untreated psychosis and increased sadness amongst patients[17].

The BMI- Body Mass Index is a simple index of weight for height that is commonly used worldwide to classify under weight, overweight and obesity amongst adults[18]. It's the same for both genders and though studies now show that the Asian BMI should be considered

Table 2

Patients current status

Variables	Overall (n=50)		Hyperglycemia (n=5)		Normal (n=45)		P-value
	No.	%	No.	%	No.	%	
Duration of Illness							
< 2 years	8	16	1	20	7	16	0.680
2-5 years	6	12	0	0	6	13	
>5 years	36	72	4	80	32	71	
Mean ± S.D.	9.2 ± 6.59		10.4 ± 10.21		9.0 ± 6.22		0.667
Psycho tropics							
Typical	19	38	0	0	19	42	0.179
Atypical	24	48	4	80	20	44	
Combined	7	14	1	20	6	13	

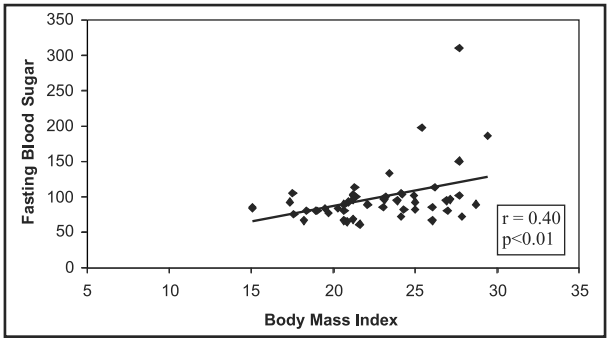

Fig. 1: Correlation amongst the patient's Body Mass Index with Fasting Blood Sugar

different from other ethnicities as they have high percentage of BF-body fat at lower BMIs as compared to their Caucasian counterparts[19], but, as yet as there has been no attempt to redefine cut off points for each population separately, so that's why we have used the universal Index.

By our study we established that patients who were hyperglycemic came in the over weight category. Hence there was a significant relationship in their increased BMI and hyperglycemia. As the weight of the patients had been steadily increasing since the start of medications, it's not difficult to pinpoint as to why and how there is a positive co-relation between the two. After all, increased BMI, that is general obesity can cause complications to arise in an stereotypical manner either from the effect of increased body mass on mobility or respiration, or from the tendency of excess body fat to cause Metabolic syndrome (dyslipidemia, insulin resistance and high blood pressure)[20].

It has also been seen that educational level usually has an inverse relationship with general obesity due to awareness of the importance of physical exercise and nutrition[21]. It was hypothesized by the authors that level of education amongst the patient might lead them to take measures such as exercising/nutritious diet to reduce their propensity towards weight gain or developing metabolic syndrome.

However there appeared no significant relationship whatsoever between the level of our patients level of education and hyperglycemia. Patients had altered blood glucose levels regardless of their educational background.

One of the limitations of our study was that we could not ascertain patients on the basis of Metabolic Syndrome. Though this study was done primarily for evaluating the frequency of hyperglycemia in schizophrenic patients, fasting lipid profiles could also have been conducted to assess the triglyceride and HDL level. Checking waist circumferences and Blood pressures could have also assured us more of the results in terms of metabolic syndrome.

Recommendations:

As people suffering from schizophrenia seem to be have a 2- 3 increased risk of developing Metabolic syndrome[22], psychiatrists should, before the start of pharmacotherapy, have lipid profiles, fasting and random blood glucose levels, BMI, blood pressure of the patient so that appropriate measures can be taken by the treating physician in case there are any abnormalities in the test results.

It is also the authors' humble opinion that more educational awareness programs should be introduced in the future for patients and their families to instruct about the importance of physical exercise and food. Walking programs and published pamphlets detailing proper nutritious diet should be given to patients and their families.

In addition to the above, instead of sitting in one corner of the house, patients should be encouraged to perform certain chores in their homes so that they can

too get some change plus feel a worthy member of the household.

Lastly, as the rate of Diabetic Mellitus has reached epidemic proportions especially in South East Asia[23], the findings of the study need to be replicated with larger samples.

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