

METABOLIC SYNDROME: RELEVANCE TO PSYCHIATRY

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ABSTRACT

The treatment of mental illnesses is receiving considerable attention in the current medical literature and has been a focus of reviews for adapting a holistic approach for recognition and management of the physical health needs of these patients. Metabolic syndrome, a major public health problem linked to cardiovascular and other morbidities, has gained a significant importance in clinical settings and patients with severe mental illnesses who are at higher risk for different components of this syndrome due to their illness and its treatment require careful and regular monitoring in this regard. This article summarises the current thinking about the concept, nature and extent of this syndrome with special reference to mental health and discusses its relevance in the current management of these disorders.

KEY WORDS: Mental disorders, Metabolic syndrome, Antipsychotic drugs, Lifestyle management.

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Metabolic syndrome is assuming a paramount importance in clinical medicine. Its relevance to cardiovascular diseases and many other illnesses is getting a lot of attention in current medical literature.¹ Metabolic syndrome has also been referred as "Syndrome X" and "Insulin Resistance Syndrome" and various definitions have been proposed for this disorder.² In general this syndrome is conceptualised as a major public health problem that identifies individuals who are at risk for developing diabetes mellitus and / or

cardiovascular diseases and can be used as a starting point for clinical interventions known to reduce such risks.³

Competing definitions: There are two competing definitions of metabolic syndrome that are generally referred in the current medical writings. The first one is known as Adult Treatment Panel-III (ATP 111) or NECP criteria (Third report of the National Cholesterol Education Programme Expert Panel on Detection, Evaluation and Treatment of high blood cholesterol in adults) and the other one comes from WHO and is commonly abbreviated as WHO criteria.^{4,5} Both definitions include criteria relating to the risk factors of abdominal obesity, hypertriglyceridaemia, low HDL-cholesterol and hypertension but WHO definition also mandates the presence of abnormal glucose regulation and microalbuminuria as additional factors. Other definitions also exist, including American Association of Clinical Endocrinologists (AACE) and from the European Group for the study of Insulin Resistance (EGIR).⁶ Studies using all these definitions may show some variations in their results but it is generally agreed that metabolic syndrome describes a cluster of cardiovascular risk factors and

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metabolic abnormalities that include abdominal obesity, hypertriglyceridaemia, low HDL-cholesterol, hypertension and abnormal fasting glucose.⁷

Essential features: Looking at the essential features of metabolic syndrome (abdominal obesity, hypertriglyceridaemia, low HDL-cholesterol and hypertension), current epidemiological data vary in their prevalence in different studies but the rates approximately range from 20-30% in majority of these studies. These figures increase as age advances and similarly different rates are reported for different gender, race and ethnicity.⁸⁻¹⁰ The National Health & Nutrition Examination Survey III, which was conducted among 8814 US adults aged at least 20 years, demonstrated that the percentage of individuals with at least one metabolic abnormality was 71%, at least two was 44% and at least three (meeting criteria for metabolic syndrome) was 24%. Nearly, 10% of individuals had at least four metabolic abnormalities and 3-5% had all components of the metabolic syndrome.¹¹ Ethnicity is also emerging as an important risk factor in the development of metabolic syndrome and a recent study in UK found that South Asians, living in the UK have a higher prevalence of diabetes, coronary heart disease and cardiovascular deaths with a three to fourfold increase as compared to the local white population.¹²

While recent reports are showing an increase of this syndrome among general population, a growing concern is being expressed about this problem among mentally ill as well.¹³ It is an agreed fact that chronic mentally ill are more vulnerable for physical health problems and they show significant increase in relation to their physical health as compared to the general population.^{14,15} If we look at the risk factors contributing to the high prevalence of medical health problems in mentally ill, the presence of Metabolic Syndrome emerges as an important risk factor for Cardiovascular and Diabetic morbidity. It is generally estimated that Metabolic Syndrome is especially common in patients with Severe Mental Illnesses (SMI) with high prevalence in the range of 30-60% for schizophrenic and bipolar disorders.¹⁶⁻¹⁹ The

high prevalence of obesity, sedentary lifestyle, smoking and poor diet contributes further to physical morbidity among this group of patients.²⁰ Among the natural causes of death in severely mentally ill, cardiovascular & respiratory diseases are again at the top. Schizophrenics, in particular, die at least 10 years earlier than age matched contemporaries & have an increased relative risk of premature death by two to four fold. A number of studies looking at this association confirm a greater risk of developing metabolic syndrome in the mentally ill as compared to the general population and may explain the increased risk of death in this group of patients due to cardiovascular diseases. Newman & Bland's study from Canada has shown that 20% of the 301 deaths among 3623 schizophrenic patients were attributed to cardiovascular diseases, resulting in Standardized Mortality Ratio (SMR) of 1.4.²¹ Similarly, among 307 patients with schizophrenia from a UK study, cardiovascular diseases resulted in 18% of the 79 deaths with a SMR of 1.9.²²

The link between various mental illnesses and different components of metabolic syndrome are also getting clearer. Consistent reports suggest that people with schizophrenia are at an increased risk for the development of diabetes mellitus particularly type 2 diabetes mellitus, with a prevalence rate of between 15% and 20%.^{23,24} These observations clearly echo what Henry Maudsley said in year 1879 that diabetes is a disease which often shows itself in families in which insanity prevails and was also endorsed by Raphael in 1921.^{25,26} It is true that most mentally ill with diabetes have traditional diabetes risk factors like family history, physical inactivity and dietary variations but abnormalities in glucose and insulin resistance also seem common in many patients. The recent literature is again consistent about the prevalence rate of diabetics ie. around 15% in population with schizophrenia, which represents a two to threefold increase in risk compared to the general population.^{23,24,27} Based on these findings, the Canadian Diabetic Association in 2003 gave schizophrenia the status of an independent risk factor for Diabetes.²⁸

The clinical manifestations of increased lipid profiles are also among the main causes of morbidity and mortality for cardiovascular diseases and increase in serum cholesterol is considered as a major risk factor for such diseases.²⁹ The main lipids present in serum are cholesterol & triglycerides and their measurement is therefore essential in individuals who are vulnerable for cardiovascular diseases or type 2 diabetes.^{30,31} Elevated levels of lipids may be attributed to a combination of life style, genetic & many other factors but evidence is accumulating that lipid values above the optimal maximum are observed in many patients who suffer from severe mental illnesses. In terms of lipids profiles in mentally ill, although there is a paucity of data, but there are reports available that shows an increased prevalence of elevated lipid levels or at least the same extent as in the most vulnerable general population. The recent Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study that involved a large sample of schizophrenic patients showed that 64% of subjects met criteria for hyperlipidemia.³² Similarly a Finish study reported that individuals treated with antipsychotic medications were three times more likely to have high cholesterol or high triglyceride than those who were not taking these drugs.³³

Side effects of antipsychotic drugs: Antipsychotic drugs control the symptoms of psychiatric illnesses very effectively but there is a growing concern about some of their side effects that contribute to the excess physical morbidity among patients taking these drugs.^{34,35} This is true for both atypical and typical antipsychotics and looking at different side effect profiles of these drugs, metabolic syndrome again emerges as an important adverse reaction that requires urgent attention of the clinicians.³⁶ Current reports may vary about the differences among second generation antipsychotics (atypicals) drugs for contributing to the different components of Metabolic Syndrome but there is a consensus that this syndrome is emerging as a major side effect of these drugs. Of all the components of metabolic syndrome, statistically significant difference have been

found in prevalence rates for weight gain, obesity, elevated BMI, waist circumference & triglycerides and HDL-cholesterol levels among the patients taking these drugs as compared to the general population.³⁷

Diabetes and severe mental illness: Although the association between diabetes and severe mental illnesses are manifolds, a number of publications have mentioned the potential relationship between antipsychotic drugs and hyperglycemia.³⁸⁻⁴² The findings that first episode and drug naive patients may show insulin resistance complicates the underlying mechanisms in this regard.⁴³ Worsening of glucose control may not be explained exclusively on the individual drugs itself but the contribution of these drugs for other components of metabolic syndrome including cardiovascular risks and dyslipidaemia certainly contribute to such predisposition.⁴⁴

Weight gain is an established side effect of most of the antipsychotic drugs (including typical and atypical antipsychotics). This association is well documented for the first generation typical antipsychotics (as far back as 1960) and more recently same association has been described for the newer or second generation atypical antipsychotic drugs.⁴⁵⁻⁴⁷ Many underlying mechanisms operate in weight gain after intake of these drugs. Genetic variation may also play a role⁴⁸ and though the underlying mechanism remains uncertain, most of these drugs increase weight primarily by increasing caloric intake leading to an increase in adiposity. Excessive weight gain has many adverse clinical consequences including predisposition to a number of physical illnesses like cardiovascular disorders, diabetes, stroke, osteoarthritis and sleep apnoea in addition to low self esteem, decreased quality of life and reduced adherence to treatment. The weight changes has been associated with almost all antipsychotic drugs & this has been consistently observed in clinical experiences both in naturalistic studies as well as in short term & long term Randomized Control Trials (RCTs).⁴⁵⁻⁴⁷ Although current clinical trials and evidence point towards an increase in weight after use of all the typical and atypical antipsychotics but

among the atypicals mean weight gain is greatest with Olanzapine and Clozapine and least with Aripiprazole and Ziprasidone.⁴⁹⁻⁵¹ This has important clinical implications in that it exposes these patients to the risk associated with weight gain such as obesity, hypertension, coronary heart disease and many other physical problems. It is important to know that mentally ill are already at risk with higher standardised mortality rate and this particular side effect of the prescribed medication certainly pose more disadvantages. It is still unclear whether antipsychotics affect glucose metabolism directly or increase the weight by insulin resistance or work through social disadvantages or some another mechanism.⁵⁰ Given the growing epidemic of obesity and its consequences, the weight changes in the mentally ill taking antipsychotic medication however remains increasingly relevant.

Antipsychotic medication and adverse lipid levels: Similarly the links between antipsychotic medication and adverse lipid levels is also worth noting. During the last few decades, reports did appear in the medical literature showing an increase in cholesterol and triglycerides in patients taking typical antipsychotics.⁵² A number of reports have also shown the comparative effects of atypical antipsychotics on lipid levels and current reports⁵³⁻⁵⁵ showing links between atypical antipsychotic medication & impaired glucose tolerance and changes in lipids profiles strengthen these views. But one should not forget that poor diet, lack of exercise and increased body weight that are common in mentally ill, are all major predisposing factors for these changes. Similarly majority of these studies are short term and regular monitoring of lipids is not taking place routinely at many centres. But despite these methodological shortcomings in these studies, the concern continues to be of high magnitude.⁵⁶

SUMMARY

In summary, the current trends in psychiatry and mental health are proposing a comprehensive and holistic approach to the

understanding of mental illnesses & their treatment. There is a growing evidence that severe mental illnesses are associated with significant physical co-morbidities⁵⁷⁻⁵⁹ that lead to increased risk of premature mortality in many psychiatric patients.⁶⁰⁻⁶³ The challenges in advancing mental health are therefore linked to the physical well being of these individuals and better understanding and more awareness about physical needs of these patients are advocated in the current literature.^{64,65} Unfortunately physical illnesses are generally overlooked in many patients. Lack of routine physical examinations in psychiatric settings is well known⁶⁶ but limited awareness among the clinicians about causative & contributing factors leading to adversities in physical health among these patients are also equally important. The need of the time is that mental illnesses are to be integrated into a holistic and comprehensive care system that should also address physical aspects of these illnesses with special reference to their treatment and prevention.⁶⁷

Metabolic syndrome, a cluster of factors including obesity, hypertriglyceridaemia, low HDL-cholesterol, hypertension and abnormal glucose levels, is highly prevalent in mentally ill and adds to further complications and adverse outcomes in these illnesses. This syndrome is considered as an important public health construct that is designed to identify individuals at risk for CVD and / or Diabetes. It is an important condition that has gained worldwide recognition for clinical interventions aimed at reducing these risks as the consequences of this syndrome often include reduced quality of life as well as reduced life expectancy. Its incidence & prevalence are increasing over time in general population but patients with mental illnesses are more prone to developing metabolic disorder than others due to the causes in the illness as well as the side effects of antipsychotic drugs. It is true that antipsychotic medication will continue as an essential treatment strategy for the well being of mentally ill but there is a need to look at the side effects of these drugs and their potential & detrimental effects on physical health as well.⁶⁸

There is also a need for doing more research about health promotion, quality of life, life style guidance and dietary advice for this group of patients. During the last few decades enough evidence has emerged for predisposition of the severely mentally ill for unhealthy life style that leads to physical inactivity, smoking, drug & alcohol use, weight gain, obesity, cardiovascular diseases and many other health hazards.⁶⁹ This of course sets an agenda for future action and requires ongoing reviews in pharmacological & non pharmacological interventions for mental illnesses.

A number of guidelines have been proposed looking at effective pharmacological treatment of different mental illnesses, making choices for appropriate drugs and advice about physical healthcare and life style managements for the mentally ill.^{70,71} Keeping in view the importance of Metabolic Syndrome and related physical health problems, it is expected that clinicians will focus more attention to its diagnosis, treatment and prevention and will also give due consideration to the current drug treatment guidelines in this area. The need to provide some form of management in improving the life style for these patients is also universally accepted & the current evidence does provide clear guidelines and directions for more awareness for programmes needed to promote and support physical well being of the patients with severe mental illnesses.^{72,73} This is certainly a way forward for the mentally ill who are at higher risk for these problems or many reasons and require a holistic approach for the treatment of their illnesses.

It is hoped that the awareness of different aspects of mental health care and integration of physical healthcare into everyday practice will ensure better physical and mental well being for these patients and would help them to move forward in getting a better quality of life with their physical needs met.

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