

Co-morbidities in Schizophrenia: A Brief Review

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Abstract

Schizophrenia is a severe mental illness, which causes significant morbidity and disability. Patients suffering from schizophrenia have a relatively shorter life span in comparison to their healthy counterparts. It follows chronic, waxing-waning course and needs long term treatment. Co-morbidities are common in patients with schizophrenia, may it be co-morbidities involving physical or mental health. Presence of co-morbidities compromises quality of life and increases the disability as well as burden of care. Every patient suffering from schizophrenia should be evaluated and treated for their co-morbidities adequately to have a better quality of life.

Keywords: Schizophrenia; Co-Morbidities; Quality of Life.

Introduction

Schizophrenia is a severe mental disorder with point prevalence upto 1%. It has a waxing-waning course and is highly disabling in nature. Wide arrays of symptoms manifest among patients with schizophrenia such as delusions, perceptual abnormalities, disorganized behaviour, apathy and social withdrawal, emotional dysregulation, cognitive deficits as well as changes in personality. This may have a significant negative impact on health and socio-occupational functioning of the patients. Impairment in certain aspects of cognition may lead to avolition

and diminished self-concern in the patients. Till date, there exist no definite cure for schizophrenia and long term (usually life-long) pharmacotherapy is advised. Chronic use of medications along with illness specific factors and psychological stress add to the physical morbidity in patients. Patients with schizophrenia are often reluctant to elaborate about their health problems and the physical co-morbidities might go unnoticed and undertreated.

Moreover, co-morbidities adversely affect the illness course and vice-versa. Presence of co-morbidities narrow down the options of psychotropic medications that can be used and enhance the likelihood of developing side-effects. Additionally, they may lead to non-adherence to medications and illness relapse.

Co-Morbidities in Schizophrenia

Co-morbidities are common in schizophrenia. The disability, morbidity and mortality associated with schizophrenia may get exacerbated by associated co-morbidities.

Broadly the co-morbidities associated with schizophrenia can be classified into – psychiatric co-morbidities and medical co-morbidities. Co-morbidities have significant impact on various aspects of schizophrenia. Figure 1 highlights the impact of co-morbidities in schizophrenia.

Psychiatric Co-Morbidities in Schizophrenia

Depression and anxiety were often reported in patients suffering from schizophrenia [1]. Presence of depressive and anxiety symptoms in schizophrenia may increase the risk of suicide and relapse of psychotic symptoms [1]. In a study on patients with schizophrenia, it was found that anxiety and

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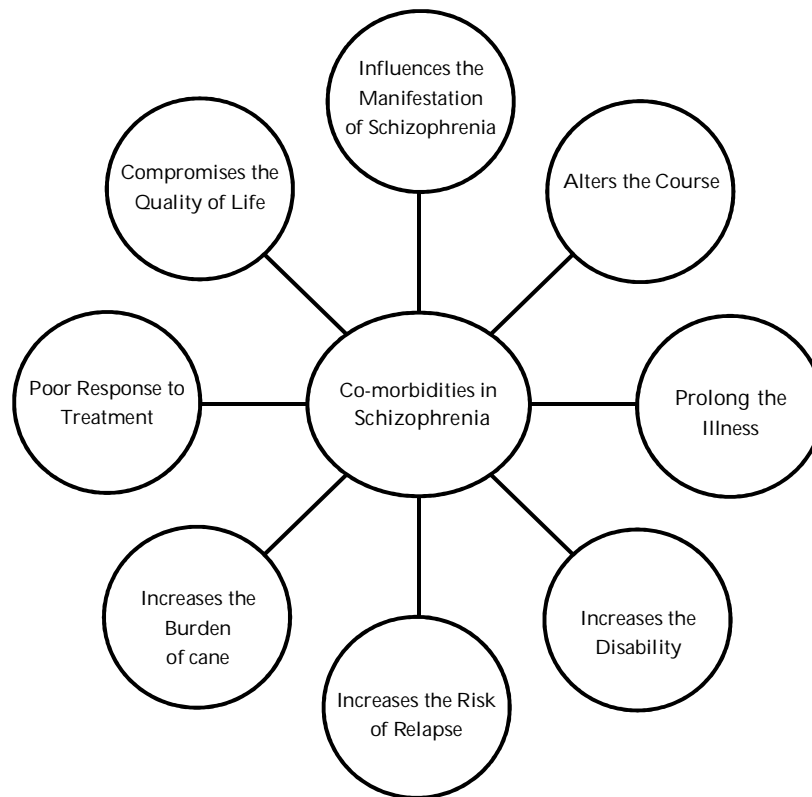


Fig. 1: Impact of co-morbidities on schizophrenia

depressive symptoms to be more intense during first episode of psychosis, in female patients and in the presence of positive symptoms like – delusions and hallucinations [1].

Anxiety disorders are common in patients suffering from schizophrenia and treating them in conventional way alleviate the symptoms of anxiety [2, 3]. Obsessive compulsive disorder (OCD) is also commonly associated with schizophrenia. Patients of schizophrenia with co-morbid OCD have some unique characteristic pattern; hence may together be called as “schizo-obsessive” disorder [4]. The prevalence of obsessive compulsive symptoms and OCD in patients with schizophrenia range from 10 - 52% and 7.8 - 26%, respectively [4]. Suicide risk in patients with schizophrenia is 10 to 20 times higher than general population [5]. Presence of certain risk factors increases the vulnerability for suicide in patients with schizophrenia. These risk factors are – male gender, unmarried, socially isolated, co-morbid substance use, co-morbid depression and high level of functioning before the onset of illness [6, 7]. Detailed evaluation and identification of risk factors of suicide in schizophrenia, helps in its prevention.

Co-morbid substance use disorder (SUD) is considerably high in patients with schizophrenia. Studies have reported SUD in nearly half of schizophrenic patients, which is much higher than

the prevalence in general population. Nicotine, cannabis and alcohol are the substances, most commonly used by the patients [8]. In their study, Goff et al., had included the participants of Clinical Trials of Antipsychotic Treatment Effectiveness (CATIE) Schizophrenia Trial and they found that prevalence of smoking is approximately two times higher in patients with schizophrenia in comparison to healthy adults [9]. Multiple theories have been proposed to explain the higher use of substances in patients with schizophrenia. They have tried to explain it in terms of neurobiological predisposition, socio-economical adversities, psychological stressors and use of substance for self medication. Most of the substances alter various neurotransmission processes in the brain, involving – dopaminergic, glutaminergic, cholinergic and GABAergic systems [8]. These neurochemical mediators also regulate the pathogenesis of schizophrenia, hence co-morbid substance use largely influences the illness manifestation as well as progression. Substance use may lead to decreased treatment effectiveness, illness relapse and treatment non-adherence [10]. Nicotine use, a common co-morbidity in schizophrenia increases the metabolism of psychotropic medications in liver and decrease their therapeutic efficacy [11]. Co-morbid SUD, thus adds considerably to the overall health care and financial burden.

Medical co-morbidities in schizophrenia

Patients with schizophrenia have increased burden of chronic medical co-morbidities in comparison to general healthy population [12]. The association of medical co-morbidities in schizophrenia can be due to –

1. A chance association.
2. The direct effect of schizophrenia itself.
3. Effect of psychotropic medications.

The second generation antipsychotics have the propensity to cause metabolic derangements in patients with schizophrenia [13]. Presence of certain risk factors like – first episode of psychosis, drug-naïve schizophrenia, use of antipsychotics like clozapine & olanzapine and schizophrenia in pediatric population (children & adolescents) increases the risk of antipsychotic induced metabolic syndrome [13]. Several new antipsychotic molecules were studied for their metabolic safety profile, and preliminary data suggests that short-term (<12 weeks) metabolic safety of asenapine and iloperidone is good [13]. Newer antipsychotic drug lurasidone is also found to be safe, by having lowest weight gain potential [13]. In a 10 year naturalistic study on patients with schizophrenia receiving clozapine, it was found that clozapine increases the risk of diabetes, hypertension, dyslipidemia and obesity [14]. Risk of metabolic syndrome also increases with increasing duration of schizophrenia [15]. Metabolic syndrome in patients with schizophrenia is a predictor of cardiovascular morbidity and mortality [16]. Hence, it should not be ignored during clinical assessment. Patients receiving antipsychotic medications at high risk for metabolic syndrome should undergo serial monitoring of their metabolic parameters at regular intervals. Various non-pharmacological strategies like – life style modification and dietary modification are effective in controlling metabolic disturbances. Switching to a different antipsychotic drug with low risk of metabolic side effects may also be effective. When the above strategies fail to bring changes, adding oral hypoglycemic agent metformin may be beneficial [17].

Diabetes has a close association with schizophrenia and the explanation of the association is not only limited to side effects of antipsychotic medications, but also to the unhealthy life style, poor general care and may be due to some genetic factors [18-20]. Approximately, 15- 21% patients with schizophrenia have diabetes mellitus as found in various studies [19]. Similarly, the risk of developing diabetic ketoacidosis is also higher in patients with schizophrenia as compared to healthy population

[21]. Targeted interventions for diabetes in schizophrenia, like – life style modification, starting oral hypoglycemic agents like metformin gives promising results [20]. At the same time there is a need to increase awareness among general care physicians about this co-morbid association and requirement of antipsychotic drug to keep the symptoms of schizophrenia controlled, for an effective management [20].

Obesity is a common co-morbid association in patients with severe mental illnesses, including schizophrenia, which may be due to the side effect of psychotropic medications used or may be related to life style or genetic factors [21]. The risk of weight gain is maximum with antipsychotic medications like – clozapine and olanzapine, whereas risperidone and quetiapine poses moderate risk of weight gain [21]. The risk of weight gain and obesity is minimal with Aripiprazole, Ziprasidone, amisulpride and asenapine [21].

Patient with schizophrenia are at higher risk of cardiovascular diseases compared to their healthy counterparts [22]. Kelly et al., in their study had revealed that patients who were started antipsychotic clozapine or risperidone at age younger than 55 years have equal incidences of cardiovascular mortality; however at or beyond 55 years of age, patients receiving clozapine have significantly higher cardiovascular mortality than those receiving risperidone [22]. Due to increased cardiovascular morbidity and mortality, the life expectancy of patients suffering from schizophrenia has reduced by nearly 20%, which may range from 10 to 25 years [5, 23, 24]. Other than cardiovascular causes, cancer is an important cause of premature mortality in patients suffering from schizophrenia [25]. Among the different causes of mortality in schizophrenia, cardiovascular causes, cancer and diabetes attribute to 35%, 17% and 5% respectively [26]. Laursen et al., had explained about four major causes of morbidity and mortality in patients with schizophrenia [24], which can be summarized as –

1. Suicide
2. Adverse effects of antipsychotic medications
3. Life-style related risk factors
4. Medical co-morbidities associated with schizophrenia

Increased cardiovascular mortality in patients with schizophrenia may be attributed to risk factors like – excessive smoking, hypertension, gross derangement of lipid and carbohydrate metabolism, poor dietary habit, unhealthy life styles, peripheral resistance to insulin and diabetes [5, 23]. Evidences also suggest

about the overlapping hereditary factors & pathophysiology between cardiovascular disorders and schizophrenia, to explain this co-morbid association [23]. Arrhythmia and QT prolongation can be another important cause of cardiovascular mortality in patients with schizophrenia [21]. Various conventional as well as newer antipsychotic drugs cause QT prolongation [21].

Patients with schizophrenia also pose higher risk for cerebrovascular disorders [21, 27, 28]. The risk of cerebrovascular accidents in patients with schizophrenia is explainable by the metabolic syndrome, obesity, smoking and life style related factors [21]. A recent study by Hoirisch-Clapauch *et al.*, had revealed that patients with schizophrenia have deficiency of free-protein S, which is a important regulator of coagulation pathway [29].

In a population based controlled study, it was found that in comparison to general healthy population, patients suffering with schizophrenia are at increased risk for iron deficiency anemia, fluid & electrolyte imbalance, hypothyroidism, neurological disorders, chronic obstructive pulmonary diseases, tuberculosis, pneumonia, liver disease including hepatitis C infection [12, 21]. Patients with schizophrenia may indulge in unprotected sexual relationships; increased substance use in this group of patients also increases the high risk sexual behavior [21, 30]. This might be responsible for higher prevalence of HIV infection and Hepatitis in patients with schizophrenia [21, 30].

Sexual dysfunction is also commonly seen in patients with schizophrenia, which can be due to the ongoing illness, side effect of antipsychotic drugs or associated co-morbidities [21]. Sexual dysfunction is common with typical antipsychotics, risperidone, olanzapine and least with aripiprazole as found in a study [31]. Sexually transmitted diseases are also commonly seen due to high risk sexual behavior in patients with schizophrenia [21].

Poor self care and personal hygiene in patients with schizophrenia may lead to dermatological infections, poor oral health, pediculosis and chronic ulcers.

A potential cause of co-morbidity and mortality & morbidity due to co-morbidities in patients with schizophrenia is due to their poor accessibility to medical care [5]. Non adherence to prescribed treatment regimen is also a potential attributing factor [5]. Patients with schizophrenia usually have unhealthy and sedentary life style, which attribute to increased cardiovascular mortality [24, 32]. Patients suffering from schizophrenia with co-morbid medical or psychiatric illnesses should be evaluated routinely for life style related factors, physical parameters as well as for the side effects of medications used [21].

Conclusion

Many risk factors that attribute to the co-morbidities in patients with schizophrenia are modifiable. The focus should be targeting the modifiable risk factors to minimize the development of co-morbidities in patients with schizophrenia. Co-morbidities with schizophrenia, may it be medical or mental health related, increase the financial burden as well as compromise the quality of life, hence need to be given adequate attention. Patients suffering from schizophrenia, often face multiple barriers to access, avail and adhere to the treatment for their illness. Hence special attention and through evaluation is required to meet their health needs.

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