# An Overview on Schizophrenia Diagnosis and Management Approach

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**ABSTRACT**

*Introduction: One of the important psychiatric conditions is schizophrenia, since patients with it often suffer from acute psychosis. Therefore, they could harm themselves or inadvertently other family members or co-workers. Objective: Our aim was to discuss the approach to schizophrenia in the psychiatric clinic, and how it is diagnosed and managed. Methods: PubMed database was used for articles selection, papers from where were obtained and reviewed. Review: The development of schizophrenia is not well understood, but links to family history and data from twin studies have proven useful in understanding some of the pathophysiological mechanisms of disease. Schizophrenia is a combination of positive and negative symptoms, with most patients presenting with an acute psychotic episode. Conclusion: Schizophrenia is best managed in a multidisciplinary approach, where a combination of medication prescription, psychological therapy and cognitive behavioral therapy is used.*

**Keywords:** *Schizophrenia, Clinical features, Diagnosis, Management*

## 1. INTRODUCTION

Schizophrenia is one of the most notable psychiatric diseases with psychosis. Psychosis is the symptom most references consider as the hallmark for schizophrenia. This can be presented with the patient experiencing delusions and hallucinations (mainly auditory). Although schizophrenia is a relatively low prevalent disorder, the prevalence of schizophrenia increased dramatically during the recent decades. In 2016, the global estimate was 0.28% of the general population, which signified a major increase in people affected with the condition from 1990. (Charlson *et al.*, 2018) On the contrary, a review study that included the data of 33 countries, suggested that schizophrenia incidence is varying according to geographic location. Early age onset is more common in males than females, as opposed to late onset presenting predominantly in females. In addition, the typical age is different with onset usually between 18–25 years old in males and 25–35 years old in females. (Messias *et al.*, 2007) The

effects of schizophrenia on patients is of substantial burden, with high mortality rates, low rates of marriage, independency, and employment compared to others. The diagnosis of schizophrenia is clinical and must be differentiated from other psychiatric (or medical) disorders. Treatment usually involves a medical approach with psychosocial and psychological interventions. In this paper, we will review the relevant publications discussing the approach to this disease along with its diagnosis, and management.

## 2. METHODOLOGY

PubMed database was used for articles selection, and the following keys used in the mesh: (("Schizophrenia "[Mesh]) AND ("Diagnosis"[Mesh] OR "Management"[Mesh])). In regards to the inclusion criteria, the articles were selected based on inclusion of one of the following topics: schizophrenia' evaluation, management, and diagnosis. Exclusion criteria were all other articles which did not have one of these topics as their primary endpoint.

### 3. REVIEW:

**Pathophysiology:**

Structural, neurotransmission, and immunity abnormalities all been proved to be contributing factors in the pathophysiology of schizophrenia. Some of these abnormalities have been visualized due to the breakthroughs in neuroimaging techniques in the recent decades. For instance, the size of the ventricles is considered larger, leading to a decreased brain volume especially in medial temporal regions, and these findings are accompanied by hippocampal changes. (Tamminga *et al.*, 2010) This is also found in children with childhood-onset schizophrenia. Studies have shown a significant reduction in hippocampal volume when these children are compared with their unaffected siblings. (Mattai *et al.*, 2011) Moreover, these regional changes usually occur bilaterally in the amygdala and parahippocampus as well. (Wright *et al.*, 2000) Interestingly, these former areas are similarly affected in patients with sexually deviant behavior, especially when frontal cortex is also involved. (Kirk-Provencher *et al.*, 2020) Furthermore, there has been an interest in the variety of connections in the brain in opposition to only localizing a single affected part in the brain. Studies using magnetic resonance imaging (MRI) show that structural abnormalities in the limbic system and neocortex along with the interconnecting white matter tracts are present in these patients. (Heller *et al.*, 2020) Examining white matter with diffusion tensor imaging in a meta-analysis found that there is a reduction of two networks of white matter tracts in schizophrenia. (Ellison-Wright and Bullmore, 2009) Imaging of the brain in another study showed decrease in brain volumes and specifically in right and left prefrontal and temporal regions and volumes in seventeen out of a hundred forty-six people who were considered to be having high genetic risk for schizophrenia. The more changes the prefrontal lobes had, the more chances of severe psychotic symptoms to occur. (McIntosh *et al.*, 2011) Glutamatergic dysfunction have been associated in the pathogenesis of some clinical features, specifically cognitive dysfunction. (Kantrowitz and Javitt, 2010; Barch and Ceaser, 2012) A theory suggests that in schizophrenia, glutamatergic dysfunction is related to a deterioration in hippocampal parvalbumin positive interneurons and in the cerebral cortex, which are considered sensitive to any modification in the NMDA glutamate receptors. Moreover, immune system dysfunction was noted in the pathophysiology of schizophrenia (Lewis, 2012).

**Risk Factors**

Schizophrenia is considered a multifactorial disease. Risk factors of this condition are predominantly categorized as genetic, and socio-environmental factors. (Arteaga-Henríquez *et al.*, 2019) In the population, they are pregnant women who are at an increased risk of schizophrenia due to immune dysfunction, which is exacerbated in pregnancy. Moreover, pregnancy puts the mother at an increased risk of neural pathology through infections, malnourishment and perinatal complications. (Brown, 2011) Opportunistic organisms linked to schizophrenia would affect pregnant mothers, these include herpes simplex viruses and toxoplasma gondii both leading to increased risk of schizophrenia. (Khandaker *et al.*, 2013) Moreover, the fetus may suffer from intrauterine growth retardation. (Brown, 2011) Common comorbid conditions in schizophrenics include insulin resistance and metabolic disturbances. Which are linked to immunity abnormalities and inflammation. (Fan *et al.*, 2007) In Denmark, there is an increased incidence of schizophrenia in second generation migrants. In comparison, Danes had more incidence of bipolar disorder, affective conditions and schizophrenia spectrum conditions. (Cantor-Graae and Pedersen, 2013) This disease development predisposition may be related to ethnicity, socioeconomic factors, and geographical location. (Davies *et al.*, 2003; Paksarian *et al.*, 2015) Socioeconomic status and environmental risks including urban living, family history and latent genetic risk are central in the development of psychosis in children. (Newbury *et al.*, 2020) Furthermore, Studies have shown that adolescents who use cannabis, particularly compounds of high THC levels are associated with an increased risk of schizophrenia. This risk factor could be on the rise, especially with legalization of marijuana in many countries. (Radhakrishnan *et al.*, 2014) Other studies have also shown a high risk association, such as severe infections, head injury, autoimmune diseases, family history, and epilepsy with this disorder. (Benros *et al.*, 2014; Clancy *et al.*, 2014)

**Clinical Manifestation**

Core manifestations of schizophrenia are categorized into positive symptoms, negative symptoms, cognitive symptoms, and mood symptoms. Positive symptoms are hallucinations and delusions collectively called psychotic symptoms in which the person has lost contact with reality. Negative symptoms are when patient experiences inertia, decreased spontaneous speech, social isolation, and loss of interest. Cognitive symptoms include neurocognitive dysfunction where patients experience memory and attention deficits along with deficits in executive functions like organizing or abstract thinking. Mood symptoms are when patients experience mood swings but mostly depressive states.

**Diagnosis**

Diagnosing schizophrenia is merely clinical and is dependent on the clinical manifestations of the patient. According to the (DSM-5) Diagnostic and Statistical Manual of Mental Disorders, the criteria for diagnosing schizophrenia is that the patient must report at two of the following: delusions, hallucinations, disorganized speech, catatonic behavior or negative symptoms. And must at least have one of either hallucinations, delusions, or disorganized speech. The signs and symptoms must last at least six months and at least one month of active symptoms. Changes to the diagnostic criteria of schizophrenia occurred in both the DSM-5 and in the International Classification of Diseases 11th edition (ICD-11). (Schultze-Lutter *et al.*, 2020) This diagnostic definition currently includes a general requirement of two key clinical features with at least one of them to be a positive symptom. (Schultze-Lutter *et al.*, 2020)

**Management**

Approaching the management of schizophrenia is largely dependent on which medications are able to control the positive symptoms and prevent relapsing episodes, while also having manageable adverse effects (Table 1). Choice of medication also depends on effectiveness, cost, and tolerability of side effects. The atypical antipsychotics are preferred over

their predecessors, typical antipsychotics, for many reasons including their ability to control symptoms while also having milder side effects.

**Table 1:** Adverse Effects of Typical Schizophrenic Drugs

| Drug | Generation | Common Adverse Effect |
|------|-----------|----------------------|
| Clozapine | Atypical Antipsychotics | Increased Weight, Somnolence, Agranulocytosis, Seizures, Hyperlipidemia, Hyperglycemia |
| Risperidone | Atypical Antipsychotics | Hyperprolactinemia, Extrapyramidal Symptoms, Orthostatic Hypotension, Amenorrhea, Erectile Dysfunction |
| Olanzapine | Atypical Antipsychotics | Increased Weight, Somnolence, Hyperlipidemia, Hyperglycemia |
| Ziprasidone | Atypical Antipsychotics | Qtc Interval Prolongation |
| Haloperidol | Typical Antipsychotics | Extrapyramidal Symptoms, Somnolence, Increased Weight Gain, Hyperglycemia, Erectile Dysfunction |
| Chlorpromazine | Typical Antipsychotics | Extrapyramidal Symptoms, Somnolence, Increased Weight Gain, Hyperglycemia, Orthostatic Hypotension |

The main mechanism of action in antipsychotic drugs for schizophrenic is blocking the dopaminergic pathway via blocking the DRD2. Generally, drugs have been divided into typical and atypical subgroups, with difference in potency and side effect profile. Some antipsychotic exert their action on other receptors like in clozapine where it exerts its action on serotonin receptors 2 (5HT-2R). (Meltzer, 1989) Moreover, Clozapine is considered as the most efficient medication for schizophrenia, however, this drug is used as a last resort when other antipsychotics with lesser side effects do not perform well. (Yada *et al.*, 2020) This is due to its dangerous side effects including agranulocytosis, and neutropenia which happen in 1–3% of cases, and thus patients starting this drug will require an ongoing blood monitoring. (Dragoi *et al.*, 2020)

Controlling the positive symptoms including, hallucinations (auditory), and delusions is achievable with atypical antipsychotics to a very efficient rate. Thus, these drugs are the mainstay in the management in both the acute and the long term treatment of these cases. Nevertheless, controlling cognitive dysfunction, and negative symptoms is poor by these group of drugs, unfortunately, these have been associated with long term functional impairment more than positive symptoms. Recently, Cariprazine, a partial dopamine receptor agonist has been reported as effective against negative symptoms of schizophrenia. (Fagiolini *et al.*, 2020)

Regarding long term management, maintenance is effective and prevents relapses of psychotic symptoms. Nevertheless, side effects are more common as well in these patients, these include, movement disorders, weight gain, and sedation. A lot of patients suffering of these side effects will stop taking the medications lowering the compliance. Individual response is

variable between patients and is very hard to accurately predict them. Fortunately, the more recent atypical psychotic has lesser movement disorder side effects profile, but a higher metabolic based ones. Thus, the choice of the antipsychotic needs to be decided by the clinician based on balancing the risks and costs. However, a multidisciplinary approach to these patients with medications, psychosocial treatment is important and this includes training the patients on social and behavioral skills, and cognitive behavioral therapy. The objective is to relieve the patients of schizophrenia symptoms or at least have them retain near-normal daily functioning. This would allow less hospitalization for acute psychotic episodes, as nearly half of patients who presented with psychosis relapse within the first year. (Strålin *et al.*, 2020) Additionally, patients may return to work or schooling and lead a near-normal life if properly managed. (Strålin *et al.* 2019)

## 4.    CONCLUSION

As previously mentioned, the approach to schizophrenia is a combination of medications, psychological treatment and cognitive behavioral management, hence necessitating a multidisciplinary team led by the psychiatrist. Moreover, patients with schizophrenia may be suffering from other medical comorbidities, and these may be overlooked in an acute episode but require attention and follow-up with the help of the general medicine physicians.

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