

## Schizophrenia: Drug Target And Overview

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### ABSTRACT -

The long-term state of mental ambiguity is schizophrenia. It is one of the most deadly and scary of all psychic diseases. The relationship between action, thinking and feeling can be stopped. Over all cultures, it impacts 1% of the population. It affects both men and females in similar numbers, although in women typically the assault causes severe disruptions and a major use of health resources later in life than in men. It appears that people with schizophrenia have lost touch with reality. According to the National Institute for Mental Health, this disease affects roughly 0.25 percent to 0.64 percent of persons in the USA (NIMH). It may have a profound effect on the lives and lives of a person. The symptoms occur mostly in the late teenager to the early 30s. In certain situations, a person will demonstrate strange children's behaviors, but only as individuals become older will this become important.

Schizophrenia is a lifelong disorder. Therapy can assist with symptom management. Clozapine, a 1961 dibenzodiazepine created for the treatment of refractory schizophrenia, is an atypical multireceptor antipsychotic. In treatment resistant schizophrenia, it has remained the medicine of choice. The schizophrenia is of several kinds: paranoid, undifferentiated, disrupted, residual, and catatonic. The reasons of all this disorder are still not fully known to doctors. Researchers have suggestions that certain neuronal chemicals are responsible for it. The article presents a short overview and discusses the current options for treatment for Schizophrenia.

**Keywords** – Clozapine, Mental illness, Hallucination, Delusions.

### I. INTRODUCTION –

Schizophrenia is a word which is derived from the Greek 'schizo' (splitting) and 'phren' (mind) with the term first coined by Eugen Bleuler in 1908. It is a functional psychotic disorder characterized by the presence of delusional beliefs,

hallucinations, and disturbances in thought, perception, and behavior. The diagnosis of schizophrenia is clinical, made exclusively after obtaining a full psychiatric history and excluding other causes of psychosis. Risk factors include birthing complications, the season of birth, severe maternal malnutrition, maternal influenza in pregnancy, family history, childhood trauma, social isolation, cannabis use, minority ethnicity, and urbanization.<sup>[1,2]</sup>

Schizophrenia is a chronic psychiatric disorder with a heterogeneous genetic and neurobiological background that influences early brain development and is expressed as a combination of psychotic symptoms. Schizophrenia affects both men and women with equal frequency. It is not as common as other mental diseases it can be very disabling as approximately 7-8 individuals out of 1000 will have this disorder. Schizophrenia is a word used to describe a mental disorder which has a spectrum of symptoms including sense of a self-decrease in violation, psychomotor slowing and displays of antisocial behavior.<sup>[3]</sup> The early onset of the disease, along with its chronic course, make it a disabling disorder for many patients and their families.<sup>[4]</sup> Disability often results from both negative symptoms (characterized by loss or deficits) and cognitive symptoms, such as impairments in attention, working memory, or executive function.<sup>[5]</sup>

In addition, relapse may occur because of positive symptoms, such as suspiciousness, delusions, and hallucinations.<sup>[4,5]</sup> The inherent heterogeneity of schizophrenia has resulted in a lack of consensus regarding the disorder's diagnostic criteria, etiology, and pathophysiology.<sup>[4,6]</sup> The diagnosis correlates with a 20% reduction in life expectancy, with up to 40% of deaths attributed to suicide.<sup>[7]</sup>

### Heredity and Genetics of Schizophrenia –

As can be seen from the below graph, Schizophrenia definitely has a very significant

genetic component. Those persons who have a third degree relative with schizophrenia are twice as likely to develop schizophrenia as those in the general population. Those persons who have second degree relative have a several-fold higher incidence of schizophrenia than the general

population and firstdegree relatives have of schizophrenia an order of magnitude higher than general population. Below image (fig.1) describe average risks for developing schizophrenia for different group of people.

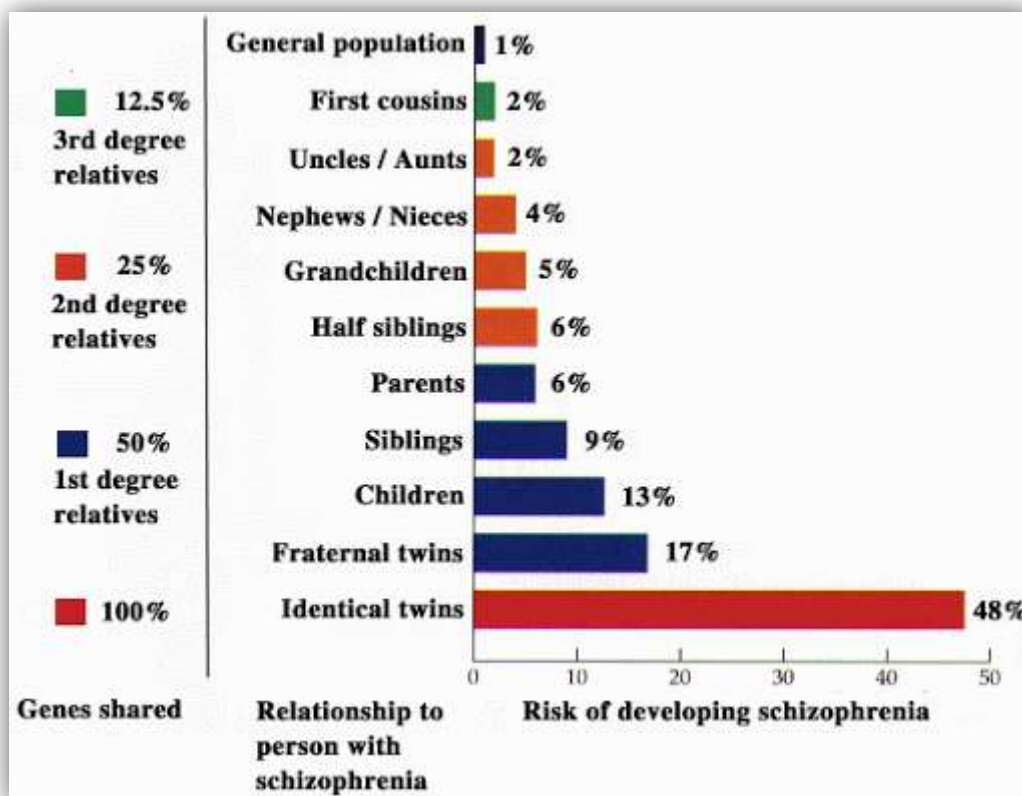


Fig.1- Schizophrenia Genetics and Heredity

**History -**

The first term schizophrenia as a mental illness was coined way back in 1887 by Dr. Emile Kraepelin. He had chosen the term "dementia praecox" to describe the symptoms now known as schizophrenia. Later, Kraepelin believed that dementia praecox was primarily a disease of the brain, but he was mistaken in describing that schizophrenia was a form of dementia. Dementia praecox means "early dementia". He differentiated 'early dementia', from other dementias that occur later in life for example Alzheimer's disease (senility). It was later cleared that schizophrenia and dementia (mental deterioration) are distinct disorders.<sup>[8]</sup>

The word schizophrenia was first officially termed by the Swiss psychiatrist and eugenicist Eugen Bleuler in 1908. He presented the

schizophrenia as a disorder on 24 April 1908 in a lecture given at a psychiatric conference in Berlin and he published it in same year, and he tried to describe the separation of function between personality, thinking, memory, and perception. Bleuler later elaborated his new disease concept into a monograph in 1911, The monograph was later translated into English in 1950.<sup>[9]</sup>

**Pathophysiology -**

Theory on the pathogenesis of schizophrenia has been based on abnormalities in neurotransmission. The majority of these hypotheses focus on neurotransmitters, including dopamine, serotonin, and glutamate, either excess or inadequate. As part of the neurochemical disorder of schizophrenia, the other ideas include aspartate, glycine, and gamma-aminobutyric acid

(GABA). Dopamine receptor sites (particularly, D2) have abnormal activity have been connected with several of the schizophrenia symptoms. There have been four dopamine pathways involve. The nigrostriatal route begins in the substantial nigra and finishes in the nucleus of caudate. The extrapyramidal system, resulting to motor symptoms, is hypothesized to have low levels of dopamine. In the context of extra dopamine, mesolimbic can play a major role in the positive symptoms of schizophrenia, which rang over from the ventral tegmental area (VTA) to the limbo region. The mesocortical route from the VTA to the cortex stretches. In schizophrenia, adverse symptoms and cognitive difficulties are considered caused by low levels of mesocortical dopamine. The TB project from the Hypothalamus to the Hypothalamus. Tuberoinfundibular trajectory diminished or blocked TBD leads to high prolactin levels and so galactorrhea, amenorrhea, and decreased libido. As a consequence of discovered lysergic acid diethylamide (LSD) improved the effects of serotonin on the brain, the notion for serotonin development for schizophrenia was found.

Further research led to the discovery of pharmacological molecules that, in contrast to prior drugs that impacted just dopamine receptors, have inhibited both dopamine and serotonin receptors. The newest chemicals have been shown efficient to alleviate both positive and negative schizophrenia symptoms. Glutamate, the main excitatory neurotransmitter in the brain, is also a possibility explaining symptoms of schizophrenia. This notion emerged because of the fact that two non-competitive antagonists of NMDA/glutamate phenylcyclidine and ketamine induces schizophrenic symptoms. This indicated in turn that NMDA receptors were inactive for normal mesocortical dopamine neuron control and indicated probable explanations of the negative, emotional and cognitive symptoms in people suffering from schizophrenia

In people with schizophrenia, the brain tissue itself seems to undergo noticeable physical alterations. For instance, persons at high risk of a schizophrenia episode had smaller medial temporal lobe, in addition to increasing the size of the three lateral and ventricles.<sup>[10]</sup>

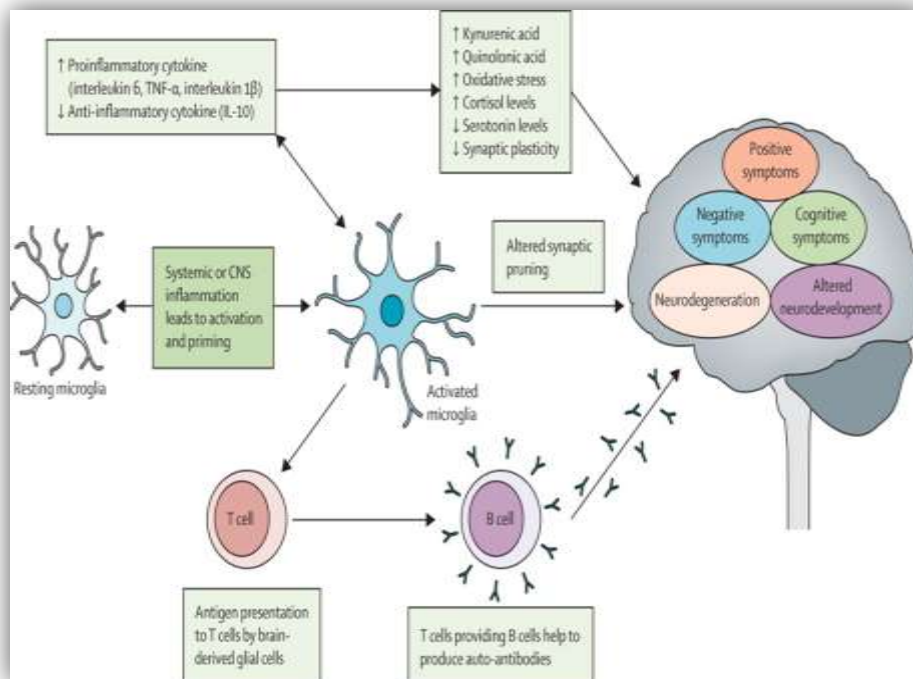


Fig.2 – Pathophysiology Of Schizophrenia

**Etiology -**

The precise causes of schizophrenia are obscure. Investigate recommends a combination of physical, hereditary, mental, and natural components can make an individual more likely to

create the condition. Some individuals may be inclined to schizophrenia, and an upsetting or passionate life occasion might trigger an insane scene. In any case, it's not known why a few

individuals create side effects whereas others do not.

❖ Increased risk

▪ Genetics:

Schizophrenia tends to run in families, but no single quality is thought to be responsible. It's more likely that diverse combinations of qualities make individuals more helpless to the condition. Nevertheless, having these qualities does not essentially create schizophrenia. Evidence that the clutter is incompletely acquired comes from considers of twins. Indistinguishable twins share the same genes. In identical twins, on the off chance that a twin creates schizophrenia, the other twin includes a 1 in 2 chance of creating it, as well. Usually, genuine indeed in the event that they're raised separately.

In non-identical twins, who have distinctive hereditary make-ups, when a twin creates schizophrenia, the other as it were includes a 1 in 8 chance of developing the condition. While this is higher than within the common populace, where the chance is around 1 in 100, it recommends qualities are not the only calculate affecting the advancement of schizophrenia.

▪ Brain development:

Studies of individuals with schizophrenia have appeared there are inconspicuous contrasts within the structure of their brains. These changes are not seen in everybody with schizophrenia and can happen in individuals who don't have a mental ailment. But they propose schizophrenia may incompletely be a disorder of the brain.

▪ Neurotransmitters:

Neurotransmitters are chemicals that carry messages between brain cells. There's an association between neurotransmitters and schizophrenia since drugs that modify the levels of neurotransmitters within the brain are known to soothe a few of the indications of schizophrenia.

Investigate suggests schizophrenia may be caused by alter within the level of 2 neurotransmitters: dopamine and serotonin. Some considers indicate a lopsidedness between the 2 may be the premise of the issue. Others have found a alter within the body's affectability to the neurotransmitters is portion of the cause of schizophrenia.

▪ Pregnancy and birth complications: -

Research has appeared individuals who create schizophrenia are more likely to have experienced complications some time recently and amid their birth, such as:

- A low birthweight

- Premature labor
- A need of oxygen (asphyxia) amid birth.

It may be that these things have an unobtrusive impact on brain development.

➤ Triggers:

Triggers are things that can cause schizophrenia to create in individuals who are at risk. These include:

• Stress:

The fundamental mental triggers of schizophrenia are unpleasant life occasions, such as:

- Bereavement
- Losing your work or home
- Divorce
- The conclusion of a relationship
- Physical, sexual, or emotional abuse.

These sorts of encounters, in spite of the fact that unpleasant, don't cause schizophrenia. In any case, they can trigger its advancement in somebody as of now defenseless to it.

• Drug abuse:

Drugs don't straightforwardly cause schizophrenia, but ponders have appeared medicate abuse increments the hazard of creating schizophrenia or a comparable illness. Certain drugs, particularly cannabis, cocaine, LSD, or amphetamines, may trigger side effects of schizophrenia in individuals who are susceptible. Using amphetamines or cocaine can lead to psychosis, and can causes backslide in individuals recuperating from a prior episode. Research has appeared that young people and youthful grown-ups who utilize cannabis routinely are more likely to create schizophrenia in afterward adulthood.<sup>[11]</sup>

### Epidemiology -

In India, where about 1.1 billion people reside, the prevalence of schizophrenia is about 3/1000 individuals (Gururaj, Girish, & Isaac, 2005). It is more common in men, and in terms of age of onset, men tend to be younger by an average of about five years than women when they develop schizophrenia.<sup>[39]</sup>

### Sign and symptoms -

Schizophrenia is a serious mental illness that affects how a person thinks, feels, and behaves. Schizophrenia is typically diagnosed in the late teen years to early thirties and tend to emerge earlier in males (late adolescence early twenties) than females (early twenties-early thirties). A diagnosis of schizophrenia often follows the 1st episode of psychosis, when individuals first display symptoms of schizophrenia. schizophrenia occurs in

younger children, but it is rare occur before late adolescence.

The symptoms of schizophrenia fall into following Three categories-

1. Psychotic symptoms
2. Negative symptoms
3. Cognitive symptoms.

#### 1. PSYCHOTIC SYMPTOMS-

They are including altered perceptions (e.g., changes in visions, hearing, smell, touch, and taste), abnormal thinking, and odd behavior. People with psychotic symptoms May loss a shared sense of reality and experience themselves and world in a distorted way. Specifically individual typically experience:

Hallucinations, such as hearing voices or seeing things that aren't there

Delusions, which are firmly held beliefs not supported by objective facts (e.g., paranoia - irrational fears that others are "out to get you" or believing that the television, radio, or internet are broadcasting special messages that require some response)

Thought disorder, which includes unusual thinking or disorganized speech.

#### 2. NEGATIVE SYMPTOMS-

Negative symptoms include -

- Loss of motivation, disinterest, or lack of enjoyment in daily activities, social withdrawal, difficulty showing emotions, and difficulty functioning normally. Specifically, individuals typically experience:
- Reduced motivation and difficulty planning, beginning, and sustaining activities
- Diminished feelings of pleasure in everyday life. "Flat affect" or reduced expression of emotions via facial expression or voice tone. Reduced speaking.

#### 3. COGNITIVE SYMPTOMS-

Cognitive symptoms include -

- Problems in attention, concentration, and memory. For some individuals, the cognitive symptoms of schizophrenia are subtle, but for others, they are more prominent and interfere with activities like following conversations, learning new things, or remembering appointments. Specifically, individuals typically experience:
- Difficulty processing information to make decisions
- Problems using information immediately after learning it

- Trouble focusing or paying attention.<sup>[12]</sup>

#### Diagnosis for Schizophrenia: -

There is no demonstrative test to survey for schizophrenia.<sup>[29]</sup> A specialist will diagnose it by watching person's behavior. They will inquire almost their history. Authentic & collateral information are basic for diagnosis.<sup>[30]</sup>

Blood Test:-The doctor can use a variety of diagnostic tests – for example MRI or CT scans or blood tests – to exclude physical illness from the cause of your symptoms. There are no laboratory tests to diagnose schizophrenia in specific.<sup>[31]</sup>

Schizophrenia is analyzed by two ways i.e., DSM-5 (Diagnostic & Statistical Manual on Mental Disorders 5<sup>th</sup> edition) & ICD-11 (International Classification of Diseases 11<sup>th</sup> Revision)

DSM-5 (Diagnostic & Statistical Manual on Mental Disorders 5<sup>th</sup> edition):-

A patient-specific sign & symptoms evaluation, as described in a DSM-5, will be used in order to diagnose schizophrenia.<sup>[32]</sup> It states that, symptomatic criteria an individual must have at slightest two side effects of the taking after for month

- Delusion
- Hallucination
- Disorganized speech, horribly disorganized or catatonic behavior
- Negative side effects such as lack of speech, enthusiastic levelness or need of motivation.<sup>[33]</sup>

Hallucination and delusion are most related with schizophrenia. There must moreover be continuous sign of schizophrenia for at slightest six month, counting the one-month period of active stage indications famous above.<sup>[33]</sup>

ICD-11 (International Classification of Diseases 11<sup>th</sup> Revision).

ICD-11 incorporates the choice of giving a detail of the level of seriousness for six side effect spaces for schizophrenia.<sup>[34]</sup> These taking after indications can be evaluated as not display, mellow, direct, or serious.<sup>[35]</sup> The nine ICD-10 subtypes will be excluded as these were not steady and of flawed prognostic validity.<sup>[36]</sup>

- Positive – continuous delusion, hallucinations, encounters of lack of involvement and control, disorganized behavior, and thinking
- Negative – covers a lessening or confinement in influence, speech, motivations and social interactions
- Depressive/Manic – refers to mood symptoms that do not match all of the criteria for a

schizoaffective disorder diagnosis. Rather than mood disorders, these dimensions indicate mood symptoms (e.g., symptoms related to disruption of appetite and sleep)

- Psychomotor indications – include a wide run of engine unsettling influences counting expanded action within the shape of purposeless behaviors such as wriggling, stereotypy, wringing of hands and failure to sit; generalized abating of discourse and/or developments; and catatonia symptoms
- Cognitive impedance – incorporates shortages in preparing speed, attention/concentration, introduction, judgment, and working memory. This would be best surveyed through locally approved neuropsychological testing.<sup>[37]</sup>

According to over criteria an individual has at slightest 2 to 3 nonstop indications of them for one month.

It is necessary to analyse that the symptoms analyzed as schizophrenia, since all psychosis isn't schizophrenia. Individuals with a few other major mental sicknesses, counting major discouragement and bipolar clutter, can show indications comparable to those of schizophrenia. In these people, in any case, the disposition indications of misery or lunacy are more noticeable. A few classes of substances counting hallucinogens, amphetamines, and stimulants can cause inebriation disorders that mirror schizophrenia, but the length of indications ought to be restricted by the pharmacology of the medicate.<sup>[38]</sup>

#### Severity of disease and complication -

Schizophrenia it is not uncommon for people with schizophrenia to have substance use disorders. Almost half of people with schizophrenia are addicted to alcohol and illegal drugs in their lifetime. Generally, drug addiction is related to a poor recovery. It can also increase the risk of other mental illnesses, as well as the risk of suicide, injury, and homelessness.<sup>[13]</sup> Substance abuse is also associated with an increased risk of violence in patients with schizophrenia. This does not mean that people with schizophrenia have a tendency to violence. There is considerable uncertainty regarding schizophrenia itself and the increased risk of violence.<sup>[14]</sup> From a medical point of view, schizophrenia is associated with an increased risk of metabolic syndrome. Diseases in this group, including obesity, hypertension, and insulin resistance, increase the risk of type 2 diabetes or cardiovascular disease.<sup>[15]</sup>

The proportion of people with schizophrenia and other mental disorders among the homeless is too high. The life expectancy of patients with schizophrenia is 20% shorter than the average life expectancy of the general population, mainly due to physical illness.<sup>[16]</sup>

#### Treatment And Therapy –

Schizophrenia is a serious mental illness that affects your thinking, emotions, relationships, and decision making. And because there's no cure, getting the proper treatment early is the best way to improve chances of managing the illness.

Schizophrenia treatment will center on managing your symptoms. You may need to stay on medication for a long time, possibly even for life. Psychotherapy, a kind of talk therapy, will likely also be a big part of the plan to help you understand and manage your symptoms. The right treatments, along with practical and emotional support from your loved ones, will go a long ways to help you navigate your life.

#### Types of Psychotherapy -

1. Individual psychotherapy- During sessions, a therapist or psychiatrist can teach the person how to deal with their thoughts and behaviors. They'll learn more about their illness and its effects, as well as how to tell the difference between what's real and what's not. It also can help them manage everyday life.

2. Cognitive behavior therapy (CBT)- This can help the person change their thinking and behavior. A therapist will show them ways to deal with voices and hallucinations. With a combination of CBT sessions and medication, they can eventually tell what triggers their psychotic episodes (times when hallucinations or delusions flare up) and how to reduce or stop them.

3. Cognitive enhancement therapy (CET) - This type of therapy is also called cognitive remediation. It teaches people how to better recognize social cues, or triggers, and improve their attention, memory, and ability to organize their thoughts. It combines computer-based brain training and group sessions.

#### Types of Psychosocial Therapy-

If a person with schizophrenia sees improvement during psychotherapy sessions, it's likely they'll need more help learning how to become part of a community. That's where psychosocial therapy comes in.

1. Social skills training- This type of instruction focuses on improving communication and social interactions.

2. Rehabilitation- Schizophrenia usually develops during the years we are building our careers. So, rehabilitation may include job counseling, problem-solving support, and education in money management.

3. Family education- Your knowledge of psychosis and schizophrenia can help a friend or family member who has it. Research shows that people with schizophrenia who have a strong support system do better than those without the encouragement of friends and family.

4. Self-help groups- You should encourage your loved one to participate in community care and outreach programs to continue working on their social skills. The National Alliance on Mental Illness (NAMI) is an outreach organization that offers a free peer-to-peer program, for instance. It includes 10 sessions for adults with mental illness who want to learn more about their condition from people who have experienced it themselves or been through it with a loved one.

5. Coordinated specialty care (CSC)- This is for people experiencing an episode of psychosis for the first time. It's a team approach that combines medication and psychological therapies. It includes social and employment services and tries to include the family whenever possible. The aim is to change the direction and prognosis for the disease by catching it in its earliest stages. Research shows that people with schizophrenia who get early and intensive treatment have the best long-term results.

6. Assertive community treatment (ACT)- This offers highly personalized services to help people with schizophrenia meet life's daily challenges, like taking medications. ACT professionals also help them handle problems proactively and work to prevent crises.

7. Social recovery therapy- This treatment puts the focus on helping the person set and achieve goals and building a sense of optimism and positive beliefs about themselves and others.

#### Electroconvulsive Therapy (ECT)

ECT is a procedure in which, electrodes are attached to the person's scalp. While they're under general anesthesia, in this treatment doctors send a small electric shock to the brain. ECT therapy mainly involves 2-3 treatments per week for several weeks. Each shock treatment causes a controlled seizure. It improves the mood and thinking as they give series of treatment over time

leads. Scientists don't fully understand exactly how ECT Therapy and the controlled seizures it causes help, research also says that ECT-induced seizures may affect the release of neurotransmitters in the brain. It is most helpful when medications no longer work or if severe depression or catatonia makes treating the illness difficult.

#### Medications-

The psychiatric treatment for schizophrenia is antipsychotic medication which can reduce the symptoms in about 7-14 days.

##### ❖ First-Generation Antipsychotic Drugs-

You can get to know that these drugs called typical or conventional. These medications block a brain chemical called dopamine and are more likely than second-generation antipsychotics to cause significant movement disorders like severe muscle stiffness (called dystonia) or another side effect that may develop over long-term exposure called tardive dyskinesia. Drugs in this group include:

- Chlorpromazine (Thorazine)
- Fluphenazine (Prolixin)
- Haloperidol (Haldol)
- Loxapine (Loxitane)
- Perphenazine (Trilafon)
- Pimozide (Orap)
- Thioridazine (Mellaril)
- Thiothixene (Navane)
- Trifluoperazine (Stelazine)

Ways for taking medication - Most antipsychotics are pills administered by mouth. Several drugs come in tablets that dissolve easily in your mouth. Some people have trouble taking pills every day, so they can get shots for several second-generation antipsychotics. These long-acting drugs require injections every couple of weeks to every 3 months. They include drugs like iaripiprazole, haloperidol, olanzapine, paliperidone, and risperidone.

##### ❖ Newer Antipsychotic Drugs-

These are also called second-generation or atypical antipsychotics. They are newer than the first-generation drugs. They generally cause such as repetitive or involuntary movements like eye blinking, then older antipsychotics which are fewer side effects. Medications include:

1. Aripiprazole (Abilify)
2. Asenapine (Saphris)
3. Brexpiprazole (Result)
4. Cariprazine (Vraylar)

5. Clozapine (Clozaril)
6. Iloperidone (Fanapt)
7. Lumateperone tosylate (Caplyta)
8. Lurasidone (Latuda)
9. Olanzapine (Zyprexa)
10. Paliperidone (Invega)
11. Pimavanserin (Nuplazid)
12. Quetiapine (Seroquel)
13. Risperidone (Risperdal)
14. Ziprasidone (Geodon)

Second-generation antipsychotics work about equally as the older drugs. Exceptional case is clozapine, which is more effective against schizophrenia that doesn't respond to other treatments.

Side effects- Different atypical antipsychotics maybe show some different side effects. You have to pick a drug which your doctor suggests which will work best for you with the minimum number of adverse effects.

Some common issues may include:

- Weight gain
- Higher blood sugar and cholesterol levels
- Low blood pressure
- Drowsiness
- Type 2 diabetes
- Constipation
- Blurry vision
- Dry mouth<sup>[40]</sup>

❖ Complementary & Alternative Medicine -  
▪ Animal Assisted Therapy -

As with other conditions, animal assisted therapy (AAT) which help ease and manage some of the symptoms of schizophrenia. Anhedonia, joy, or pleasure are not experienced by in this, and which is a common symptom. Total six research has found that, in clinical trials using animal assisted therapy as part of treatment, patients rated higher levels of pleasurable feelings than the animal assisted treatment group.

▪ Dietary Supplements -

Some selected nutritional supplements have a positive impact on symptoms experienced in some patients with schizophrenia. Although there is insufficient information to recommend them to everyone as a treatment, some of the vitamins and nutritional supplements that have been researched in schizophrenia include things like:

- B Vitamins
- Omega-3 fatty acids
- Amino acids
- Vitamin D
- Antioxidants

Important note: - Although the use of these supplements has shown promise in research, before taking them it is best to speak with your doctor, to make sure you are not at risk for things like medication interactions or other things that could slow or stop your progress.

- CBD Oil -Cannabidiol is an ingredient in the marijuana plant that has also shown good results in managing certain symptoms of schizophrenia. Some people are worried that they will experience a "high" using CBD oil as you would smoking marijuana, but that's not true. The ingredient that would make you feel "high" and have that psychoactive component is called tetrahydrocannabinol or THC. THC is removed from CBD oil so you may experience relief from symptoms without worries about being in an altered state.
- INVEGA (paliperidone): This is available in three different formulation an extended-release tablet and long-acting injectables (INVEGA SUSTENNA and INVEGA TRINZA)
- Risperdal (risperidone)
- Abilify (aripiprazole)
- Seroquel (quetiapine)
- Zyprexa (olanzapine)
- Caplyta (lumateperone)<sup>[17]</sup>

### Generic and Trade Names of Drugs for Treatment of Schizophrenia -

#### 1. Cariprazine -

Cariprazine is an atypical antipsychotic drug which is prescribed for the treatment of schizophrenia (a serious mental illness that interferes with the person's behavior and emotions).

Cariprazine is a medication that works in the brain to treat schizophrenia. Cariprazine is also known as a Second-Generation antipsychotic (SGA) or atypical Antipsychotic. Cariprazine reverses the balance of dopamine and serotonin to improve thinking, mood, and behavior. It can also be helpful when prescribed "off-label" for other mental health conditions. "Off-label" means that it has not been approved by the Food and Drug Administration for this condition. In recommending an "off-label" treatment your mental health provider should justify his or her thinking.<sup>[18]</sup>

#### 2. Amisulpride

Amisulpride is an atypical antipsychotic agent, prescribed for schizophrenia.

Trade Names:



Zonapride | Zonapride (100 mg) | Zonapride (200 mg) | Amisure (50mg) | Stozen (50 mg) | Amgrace | Sizopride (50 mg) | Psyride (50 mg) | Ampicon (50 mg) | Solaze (50 mg)

Amisulpride 400 to 1200 mg/day is the daily consumption that showed efficacy in reducing overall symptomatology and positive symptoms similar to that of conventional antipsychotics and newer atypical antipsychotics in patients with acute exacerbations of schizophrenia. More than this, its effective alleviation of negative and affective symptoms, have lower association with extrapyramidal symptoms and loss of cognitive function than conventional antipsychotics and its long-term efficacy justifies consideration of the use of higher dosages of amisulpride in this group of patients.<sup>[19]</sup>

### 3. Asenapine

Asenapine is an atypical antipsychotic agent, prescribed for acute mania and schizophrenia with disorder of bipolar.

Trade Names:

Asenapt (5mg)

Mechanism of action of asenapine is not known, but, like other anti-psychotics, it is considered that asenapine affects the way the brain works by interfering with communication among the brain's nerves. Nerves communicate with each other by making and releasing chemicals called neurotransmitters. Neurotransmitters travel to other nearby nerves for attachment to receptors on the nerves. The attachment of the neurotransmitters either stimulates or inhibits the function of the nearby nerves. Asenapine blocks most of the receptors on nerves including dopamine type 2, serotonin type 2, and alpha 2 adrenergic receptor.<sup>[20]</sup>

### 4. Brexpiprazole

Brexpiprazole belongs to a group of drugs called atypical antipsychotics used for the treatment of schizophrenia.

It is a new antipsychotic drug approved by the U.S. Food and Drug Administration in July 2015 for the treatment of schizophrenia, which consists of novel serotonin-dopamine receptor modulator with partial agonist activity at serotonin 1A (5-HT<sub>1A</sub>) and D<sub>2/3</sub> receptor. It showed significant improvement of psychotic symptoms for patients with schizophrenia in clinical trials. Many of the clinical trials demonstrated the antipsychotic effect of brexpiprazole using Positive and Negative Syndrome Scale (PANSS) in acute schizophrenia

patients, and found that higher doses (2-4 mg daily) of brexpiprazole have better outcomes.<sup>[21]</sup>

### 5. Clozapine

Clozapine is an antipsychotic, prescribed for schizophrenia.

Trade Names:

Clomach (100 mg) | Ekloz (100 mg) | Syclop (100 mg) | Zopizone (100 mg) | Skizoril (100 mg) | Sizopine (100 mg) | Zopin (100 mg) | Syzopin | Lozin (100 mg) | Leponex (100 mg)

Clozapine is an antipsychotic medication which is only used to treat severe schizophrenia symptoms in people who have not responded to other medications. It also reduces the risk of suicidal behavior in people with schizophrenia or similar disorders. Clozapine is available under the following different brand names: Clozaril, FazaClo ODT, and Versacloz.

Dosages of Clozapine:

Dosage Forms and Strengths –

1. Tablet – (25 mg/50 mg/100 mg/200 mg)
2. Tablet, orally disintegrating (FazaClo ODT) – (12.5 mg/25 mg/100 mg/150 mg/200 mg)
3. Oral suspension (Versacloz) -(50 mg/mL).<sup>[22]</sup>

### Cost of treatment of schizophrenia –

According to the reports of National Mental Health Survey (NMHS) the average monthly estimate of care and treatment for various diseases has total cost of Rs. 2,250 for alcohol use disorder, Rs.1,000 for schizophrenia and other mental illnesses and Rs. 1,500 is depression. The total minimum cost based on median out-of-pocket costs for treating the three diseases (schizophrenia, depression, and alcohol use disorder) is only 698 Crores per month according to NMHS.<sup>[23]</sup>

### Inpatient Treatment cost –

About 0.6% of people with mental illness may need to be hospitalized at least once a year.<sup>[24]</sup> This means that at least 780,000 PMI are hospitalized each year. The average length of stay per admission is approximately 21 days.<sup>[25]</sup> The estimated cost of treatment per hospital admission is According to Ayushman Bharat's plan, Rs 1500 per day.<sup>[26]</sup> So, the total cost will become Rs. Each admission is 31,500 per person per year. Estimated costs include length of stay, doctor's office costs, nursing costs, documentation costs, food, investigations, psychosocial evaluations, and medications. Estimated annual cost of inpatient treatment for 7.8 lakh PMI × Rs. 31,500 = Rs. 2,457 crores.

This will be the lowest estimate because the cost of treatment will vary from disease to disease, and the method of estimation only involves the minimum amount of treatment for mental illness. According to NMHS data, this will be the amount the government uses to treat mental illness, based on its prevalence.

#### Outpatient treatment cost -

Government treatment costs can also be estimated as the total number of mental illnesses based on NMHS data multiplied by the minimum cost of medical consultation. If we assume that the patient is receiving outpatient care at the nearest government-run medical center, the treatment cost may be 100 Rs. per patient per month.<sup>[27]</sup> This is the minimum amount the government must invest in mental health care (100 rs per patient per month). The calculation is based on discussion and consensus among researchers. However, if SMEs obtain mental health care services in the private health sector, the cost will increase exponentially (at least 10 to 15 times).

The government's minimum cost for outpatient treatment of mental illness is as follows: Estimated monthly outpatient treatment cost is the total number of patients with mental illness × Rs.100/month, or 13 Crores × Rs.100 = Rs. 1,300 Crores per month. The calculation method used is similar to the calculation method used by Math and Srinivasa Raju in 2010.<sup>[28]</sup> The estimated annual outpatient treatment cost is 1,300 crore Rs. × 12 months = Rs.15,600 Crores/year<sup>[27,28]</sup>

## II. CONCLUSION –

We concluded from this study that Schizophrenia is a complex disorder that requires prompt treatment at the first signs of a psychotic episode. we need to actively intreatment, & adapt a better life for yourself. The schizophrenia should be more optimistic & not live despair even though life challenges in many way. The society play a vital role in accepting the patients & give them their deserved chance in this material world Clinicians must consider the potential for nonadherence and treatment related adverse effects when developing a comprehensive treatment plan. Although patients can increase adaptive functioning through available pharmacological and nonpharmacological treatment options, it is hoped that future research will address gaps in treatment and potentially a cure for schizophrenia.

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