ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14959364

The Impact of Environmental Factors on Schizophrenia Risk

[1]A. Lahari; [2]K. Gnanankitha; [3]V. Poojitha; [4]Paila. Bhanuji Rao; [5]Nimmala. Phani Satyavathi

Doctor of Pharmacy
Sri Venkateswara College of Pharmacy, Etcherla, Srikakulam, Andhra University, Vishakapatnam

Publication Date: 2025/03/03

Abstract: This journal explores the role of environmental influences in increasing the risk of developing schizophrenia, a complex mental health condition. While genetics play a significant role, research suggests that environmental elements such as prenatal infections, early life trauma, growing up in urban areas, and substance abuse significantly elevate the chances of schizophrenia, particularly in individuals with a genetic vulnerability. The interaction between these environmental triggers and genetic factors is complex, and gaining a deeper understanding of this relationship is essential for creating better prevention and treatment strategies. This review emphasizes the importance of considering both genetic and environmental factors for more effective management and prevention of the disorder.

Keywords: *Environmental Factors, Risk Factors, Mechanisms and Pathways, Public Health and Prevention.*

How to Cite: A. Lahari; K. Gnanankitha; V. Poojitha; Paila. Bhanuji Rao; Nimmala. Phani Satyavathi (2025) The Impact of Environmental Factors on Schizophrenia Risk. *International Journal of Innovative Science and Research Technology*, 10(2), 1145-1153. https://doi.org/10.5281/zenodo.14959364

I. INTRODUCTION

Schizophrenia is a debilitating brain disorder that often leads to lifelong disability and emotional suffering for those affected (1). The disorder's clinical symptoms typically manifest in the late teens to early twenties, with males generally experiencing onset about five years earlier than females. Although schizophrenia impacts around 1% of the global populatio,(2) the exact causes of the illness remain unclear. Numerous studies have attempted to pinpoint genetic and environmental factors that, either separately or together, may contribute to its development.

However, this body of research is complex and often contradictory, with initial findings sometimes failing to be replicated in later studies.(3)These inconsistencies could reflect the intricate nature of schizophrenia, where subtle brain abnormalities lead to a disorder that begins in early adulthood and progresses with minimal degeneration throughout life.

Schizophrenia, like many other diseases, might result from a variety of different pathological pathways. Efforts to create a unified understanding of its origins have suggested biological mechanisms tied to developmental processes occurring before the appearance of clinical symptoms.(4) While there is still no consensus on the precise causal factors or the timing of their impact, the neurodevelopmental model of schizophrenia remains a compelling theory.(5)

II. SIGNS AND SYMPTOMS

➢ *Categorizing Schizophrenic Symptoms:*

Since (6) originally used the name "schizophrenia," it has been generally accepted that the condition probably has multiple different forms, leading to the development of numerous subgroups. I suggest that schizophrenia can be divided into at least two categories in order to better comprehend the symptoms. A helpful framework is offered by Crow's two-syndrome model (Crow, 1980a), which combines several earlier distinctions,(7)including acute versus chronic and high versus poor premorbid performance. Crow has also attempted to connect these clusters of symptoms to underlying physiological changes and long-term consequences.(8-12)

According to Crow's method, there are two main types of schizophrenia symptoms: positive and (13-15)negative. The occurrence of atypical experiences, which are uncommon in healthy people, is what defines positive symptoms.(16-20)

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14959364

➢ *Explaining Schizophrenic Symptoms:*

Many explanations of schizophrenic symptoms propose that the cognitive dysfunction lies within the perceptual system.(21)For example, theories like the 'defective filter' theory suggest that hallucinations result from misperceptions and misinterpretations of stimuli, while delusions arise from focusing on irrelevant stimuli and struggling to differentiate between what is significant and what is not. Thought disorder is linked to the perception of word meanings and associations that are unrelated to the current context.(22-24) Negative symptoms of schizophrenia, however, are not easily explained by perceptual dysfunction alone. Instead, they can be viewed as coping mechanisms developed in response primary perceptual difficulties, such as social withdrawal and limited speech, which serve to reduce the overwhelming stimuli causing distress to the patient.

➢ *Control of Action and the Symptoms of Schizophrenia:*

A deficit in response selection or action control could help explain the symptoms of schizophrenia. For this explanation to be meaningful, we must define key terms like "action" and "control" with precision, but this precision should be shaped by the lived experience of those with schizophrenia. Two particular aspects stand out.(25) One is the sensation of passivity or delusions of control, where the patient believes that their actions are not directed by themselves, but by an external force. In extreme cases, this belief can extend to the idea that foreign thoughts are being implanted in their mind. (26-27)

Additionally, research by (28) suggests that some individuals with schizophrenia experience auditory hallucinations where the voice they hear is actually their own, but they perceive it as coming from an external source. In these situations, the individual may speak but feel as if the voice is not their own. These experiences may arise from a disconnection between the will to act and the execution of the action itself. In severe cases, the patient might not even be conscious of performing the action at all.

III. EPEDIMOLOGY

Research on schizophrenia suggests that the disorder is often unequally distributed across society, with higher prevalence rates observed in lower socio-economic groups. Recent meta-analyses have reinforced the belief that men have a higher lifetime risk of developing schizophrenia compared to women, with the risk for men being 1.4 times higher (29)

In a review by(30) three systematic reviews on schizophrenia's incidence, prevalence, and mortality were analyzed. They found that, contrary to previous views, schizophrenia's incidence showed significant variation between regions. The median incidence was 15.2 cases per 100,000 people, with estimates varying widely (7.7–43.0 per 100,000). The male-to-female ratio for incidence was 1.4:1. Prevalence estimates also varied considerably, with the median lifetime risk of schizophrenia being 7.2 per 1,000 people. People with schizophrenia had a two- to threefold higher mortality rate compared to the general population, with a median standardized mortality ratio of 2.6 for all causes of death, and this gap in mortality has widened over recent decades.

Migrants were found to have a higher incidence and prevalence of schizophrenia compared to native-born individuals. Factors such as urban living, economic status, and latitude were also linked to the frequency of the disorder.(31-33) concluded that the epidemiology of schizophrenia displays notable variability, offering potential directions for future research.

Prevalence Lifetime Prevalence The lifetime prevalence of schizophrenia typically ranges from 0.14% to 0.46%. A recent literature review by (34) on data from Central and Eastern Europe found that lifetime prevalence ranged from 0.4% to 1.4%. In Finland, based on DSM-IV criteria, the lifetime prevalence was 0.87% for schizophrenia and 0.32% for schizoaffective disorder.(35) These estimates should be seen as approximate, as demographic differences such as age-specific mortality and migration can affect the data.

Prevalence in the Czech Republic In the Czech Republic, the prevalence of schizophrenia in 2013, based on the number of treated patients, was highest in Prague (0.608%) and lowest in the Central Bohemian Region (0.307%). The national average prevalence for the year was 0.462%, placing the country among those with higher prevalence rates.(36) However, since about 1% of the global population is affected by schizophrenia, equating to roughly 100,000 individuals in the Czech population, the actual number of cases is closer to 50,000 due to factors like migration and age-specific mortality.

IV. RISK FACTORS

While the precise origins of schizophrenia are not fully understood, both genetic and epidemiological studies have identified a range of genetic and environmental risk factors.(37)

Numerous investigations have concentrated on the impact of environmental elements on the development of schizophrenia. Several risk factors have been recognized that can indicate the likelihood of experiencing psychosis, applicable to both individuals with a family history of the disorder and those without.

In a study conducted by researchers (38- 40), they examined environmental risks associated with schizophrenia, considering factors such as complications during childbirth, being born in the winter or spring, delays in motor and speech development, behavioral anomalies, trauma from stressful life events, and substance usage.

They assessed a sample of 100 patients (45 females and 55 males) and discovered that complications at birth and cannabis consumption were associated with an earlier onset of schizophrenia in individuals without a family history of

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14959364

the condition. However, no environmental risk factors were found to predict an earlier onset in cases of familial schizophrenia.

➢ *Seasonal Effects , Birth Place and Place of Birth:*

Schizophrenia: (41). The flu epidemic and other acute respiratory tract illnesses are particularly common during the winter months. Pregnant women who contract viruses run the risk of developing schizophrenia because they can alter the brain. Although there are no established causes for this phenomenon, there are some signs that imply a higher number of people with schizophrenia are born in the winter. A combination of pathogenic agents, temperature, weather, food, pollution, and light intensity is the most likely cause.

The importance of sunlight is enormous since it gives the body more than 90% of the vitamin D it needs. Vitamin deficits during pregnancy may cause fetal growth factor deficiency, which has Among acute respiratory ailments, influenza and other flu-like conditions are the most common. while the wintertime. Pregnant women who contract viruses run the risk of developing schizophrenia because they can alter the brain. Although there are no established causes for this phenomenon, there are some signs that imply a higher number of people with schizophrenia are born in the winter.(42-44). A combination of pathogenic agents, temperature, weather, food, pollution, and light intensity is the most likely cause.

The importance of sunlight is enormous since it gives the body more than 90% of the vitamin D it needs. Pregnant women who are vitamin deficient may suffer fetal growth factor insufficiency, which can hinder brain development. Neo natals with both high and low vitamin D levels are linked to

Higher The likelihood of developing schizophrenia is almost doubled for those who are born in urban regions. As mentioned by, the risk of As the population increases, the prevalence of schizophrenia also increases. Stress, excessive noise, pollution, crime, the availability of illegal drugs, family separation, and other unpleasant aspects of urban living are thought to contribute to the development of schizophrenia.

➢ *Pregnancy And Birth Complications:*

Research examining the link between schizophrenia and birth complications has lent support to both developmental and non-genetic models of the disorder (45) . One of the most common complications identified is fetal hypoxia, which may raise the likelihood of developing schizophrenia. Other birth-related factors, such as preeclampsia, malformations, and the use of vacuum extraction, can also increase the risk of the condition.

Children born to mothers with schizophrenia are especially susceptible to perinatal damage,(46) placing them at high risk. These children often experience lower birth weights, which are linked to developmental challenges in their first year. Additionally, evidence indicates that stress during pregnancy may play a role in triggering schizophrenia in those with a genetic predisposition.

➢ *Infection:*

Although the evidence for an infectious cause is typically indirect and frequently lacks specificity, it is nonetheless a significant factor to take into account. Infections with bacteria, protozoa, and viruses can cause both acute and subacute alterations. (47)

Influenza virus infection during pregnancy is known to increase the incidence of neurodevelopmental problems, such as schizophrenia, in the offspring (48) . The sixth month of fetal development is the time of greatest risk (49), and there is a link between maternal infection and viral serological evidence (50). Being exposed to influenza Kynurenic acid levels have been demonstrated to momentarily rise in response to a virus during development, which may interfere with normal brain growth and cause cognitive deficits later in life. This process could shed light on how virally driven modifications in tryptophan metabolism during development lead to symptoms similar to schizophrenia. signs. (51)

Congenital central nervous system anomalies have also been connected to measles infection. Adult psychosis and schizophrenia may be more likely to develop in those exposed to measles during pregnancy (52) . The genetic composition at schizophrenia-associated human leukocyte antigen loci may alter the impact of inflammatory processes and infections in determining the possibility of developing schizophrenia.(53)

➢ *Substance And Drug Abuse:*

Substance addiction is a common complication for individuals with psychotic disorders, involving substances such as cocaine, methamphetamine, LSD, phencyclidine, opiates, alcohol, tobacco, and cannabis. Drug use can trigger psychosis in individuals at risk or those with a history of psychotic episodes. In some cases, distinguishing between the onset of drug use and the early signs of psychosis can be challenging. However, substance abuse often precedes the classic symptoms of schizophrenia.

Research indicates (54) , that the most commonly abused substances among individuals with schizophrenia are alcohol, tobacco, and cannabis. The link between cannabis use in adolescence and an increased risk of schizophrenia remains debated. Some studies suggest that cannabis use may contribute to the development of schizophrenia in those already predisposed to it. (55)

Individuals with schizophrenia also have a higher tendency to smoke tobacco. Nicotine has been found to alleviate some symptoms of the disorder, such as enhancing memory, attention, and information processing—areas often impaired in people with schizophrenia. Additionally, nicotine can reduce the effectiveness of certain antipsychotic medications by lowering their blood levels, necessitating careful monitoring and potential adjustments in medication dosages.

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14959364

Statistics show that up to 50% of individuals with schizophrenia also abuse alcohol, which is another substance commonly misused. If substance and alcohol abuse (56) are not addressed, the likelihood of relapse increases significantly.

V. PREVENTIVE MEASURES

Only a few intervention studies have been carried out thus far, indicating that research on psychosis prevention is still in its infancy. (57-60) Four randomized controlled trials (RCTs) have looked at pharmacological interventions or a combination of psychological and pharmacological treatments, whereas seven RCTs have assessed the impact of psychological interventions on treatment-resistant (TR) psychosis. Furthermore, seven published meta-analyses support the preventive effects of pharmacological treatments like olanzapine, risperidone, and omega-3 fatty acids over a 12-month period, as well as psychological interventions like Cognitive Behavioral Therapy (CBT), integrated psychological approaches, and family-focused interventions.

(61-65) and colleagues, for instance, showed a 54% decrease in 12-month TRs with a pooled risk ratio (RR) of 0.46 (95% CI: 0.33 to 0.64).required to treat nine (NNT). In contrast, the NNT for acetylsalicylic acid-assisted stroke prevention in atrial fibrillation ranges from 24 to 87. Schmidt et al. also discovered an NNT of 10 (95% CI: 8 to 17) and a 12-month RR of 0.44 (95% CI: 0.31 to 0.61). According to these results, pharmaceutical and psychological therapies, either separately or in combination, are just as successful in lowering TRs at 6- and 12-month follow-ups.

As a result, contemporary treatments range from low-dose antipsychotics to gentle, well-tolerated therapies like psychotherapy. A risk stratification technique may one day make it possible to choose the best intervention for each person according to their risk level.(66-70) More research is required, though, with brequired to treat nine (NNT). In contrast, the NNT for acetylsalicylic acid-assisted stroke prevention in atrial fibrillation ranges from 24 to 87. Schmidt et al. also discovered an NNT of 10 (95% CI: 8 to 17) and a 12-month RR of 0.44 (95% CI: 0.31 to 0.61). According to these results, pharmaceutical and psychological therapies, either separately or in combination, are just as successful in lowering TRs at 6- and 12-month follow-ups.

As a result, contemporary treatments range from low-dose antipsychotics to gentle, well-tolerated therapies like psychotherapy.(70-75) A risk stratification technique may one day make it possible to choose the best intervention for each person according to their risk level. More research is required, though, with bigger sample sizes and longer follow-up times. Thankfully, three extensive trials are almost finished, including two that seek to duplicate the positive outcomes of treatment with omega-3 fatty acids.(76-86)

In contrast to later phases of the illness, the first omega-3 experiment demonstrated that therapies could be beneficial in avoiding the onset of psychosis in persons at risk.(87-90) Furthermore, even among patients in the same risk category, a single intervention is unlikely to be universally beneficial due to the complex, multivariate character of psychosis.(91-98) The low level of long-term adherence to psychological and pharmacological prevention techniques may be a reflection of the difficulties in implementing preventive measures.(99-111) The necessity for a more varied, modular "toolbox" is highlighted by the possibility that many at-risk persons' long-term needs or subjective preferences may not be adequately met by current therapies interposition.(112-115)

VI. CONCLUSION

A complex mental illness that impairs a number of cognitive abilities is schizophrenia. Some people could need long-term treatment in a mental health facility, while others might recover completely and never exhibit symptoms again (116). Disturbed thinking, a distorted sense of reality, and, in certain situations, poor motor coordination—especially in its catatonic form—are the hallmarks of this severe illness. The symptoms of schizophrenia usually appear in late adolescence or early adulthood, and they frequently affect a large amount of the person's life.(117)

REFRENCES

[1]. Lewis DA, Lieberman JA. 2000. Catching upon schizophrenia: natural history and neurobiology. Neuron 28:325–34
[2]. Lewis DA, Pierri JN, Volk DW, Melchitzky DS,Woo T-U. 1999. Altered GABA neurotransmission and prefrontal cortical dysfunction in schizophrenia. Biol. Psychiatry 46:616–26
[3]. Lillien L. 1995. Changes in retinal cell fate induced by overexpression of EGF receptor.Nature 377:158–62
[4]. Lipska BK, Weinberger DR. 2000. To model a psychiatric disorder in animals: schizophrenia as a reality test. Neuropsychopharmacology 23:223–39
[5]. Malmberg A, Lewis G, David A, Allebeck P.1998. Premorbid adjustment and personality in people with schizophrenia. Br. J. Psychiatry 172:308–13 INTRODUCTION
[6]. Bowen, F. P., Kamienny, R. E., Burns, M. M. & Yahr, M. D. (1975).Parkinsonism: effects of levodopa treatment on concept formation Neurology 25, 701-704.
[7]. Brindley, G. & Merton, P A. (1960). The absence of position sense in the human eye. Journal of Physiology London, 153, 127-130.

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14959364

[8]. Brown, R., Colter, N., Corsellis, J. A. N., Crow, T. J., Frith, C. D.,Jagoe, R., Johnstone, E. C. & Marsh, L. (1986). Post-mortem evidence for structural brain changes in schizophrenia. Archives of General Psychiatry (in the press).
[9]. Callaway, E. & Naghdi, S. (1981). An information processing model of schizophrenia. Archives of General Psychiatry 39, 339-347.
[10].Carpenter, M. D. (1976). Sensitivity to syntactic structure: good versus poor premorbid schizophrenics. Journal of Abnormal Psychology 85, 41-50.
[11].Cohen, B. D. (1978). Referent communication disturbances in schizophrenia. Language and Cognition in Schizophrenia, (ed.S. Schwartz), pp. 1-34. Erlbaum: Hillsdale, NJ.
[12].Connell, P. H. (1958). Amphetamine Psychosis. Institute of Psychiatry Maudsley Monographs No. 5. Chapman and Hall: London.
[13].Cromwell, R. J. (1968). Stimulus redundancy and schizophrenia Journal of Nervous and Mental Disease 146, 360-375.
[14].Crow, T. J. (1980a). Molecular pathology of schizophrenia. More than one dimension of Pathology? British Medical Journal 280 66-68.
[15].Crow, T. J. (19806). Drug treatment of schizophrenia and itsrelationship to disturbances of dopaminergic transmission. In TheBiochemistry of Psychiatric Disturbances (ed. G. Curzon), pp.73-88. Wiley: Chichester.
[16].Dennett, D. C. (1969). Content and Consciousness. Routledge andRegan Paul: London.Denny-Brown D. (1968). Clinical symptomatology of diseases of thebasal ganglia. In Handbook of Clinical Neurology. Volume 6, (ed.P. J. Vinken and G. W. Bruyn), p. 136. North Holland:Amsterdam.
[17].Dickinson, A. (1980). Contemporary Animal Learning Theory.Cambridge University Press: Cambridge.Done, D. J. & Frith, C. D. (1984a. The effect of context during word perception in schizophrenic patients. Brain and Language 23318-336.
[18].D. J. & Frith, C. D. (1984*). Automatic and strategic controlof eye movements in schizophrenia. In Theoretical and AppliedAspects of Eye Movement Research, (ed. A. G. Gale andF. Johnson), pp. 481-487.
[19].Elsevier: Amsterdam.Feighner, J. P., Robins, E. Guze, S. B., Woodruff, R, WinokurG. & Munoz, R. (1972)Diagnostic criteria for us in psychiatric research. Archives of General Psychiatry 26, 57-63.
[20].Feinberg, I. (1978). Efference copy and corollary discharge: implications for thinking and its disorders. Schizophrenia Bulletin4, 636-640.
[21].Flowers, K. (1978). Lack of prediction in the motor behaviour of Parkinsonism. Brain 101, 35-52.
[22].Flowers, K. A. (1982). Frontal lobe signs as a component ofParkinsonism. Behaviour and Brain Research 5, 100-101.
[23].Frith, C. D. (1979). Consciousness, information processing and schizophrenia. British Journal of Psychiatry 134, 225-235.
[24].Frith, C. D. & Done, D. J. (1983). Stereotyped responding by schizophrenic patients in a two-choice guessing task. Psychological Medicine 13, 779-786.
[25].Frith, C. D. & Done, D. J. (1987). Routes to action in reaction time tasks. Psychological Research (in the press).
[26].Gerver, D. (1967). Linguistic rules and the perception and recall of speech by schizophrenic patients. Journal of Social and Clinical Psychology 6, 204-211.
[27].Goldberg, G. (1985). Supplementary motor area structure and function: review and hypotheses. Behavioral and Brain Sciences 8, 567-616.
[28].Goldberg, G., Mayer, N. H. & Toglia, J. U. (1981). Medial frontal cortical infarction and the alien hand sign. Archives of Neurology 38, 683-686.
[29].Green, P. & Preston, M. (1981). Reinforcement of vocal correlates of auditory hallucinations by auditory feedback. British Journal of Psychiatry 139, 204-208.
[30].Aleman A, Kahn RS, Selten JP (2003). Sex differences in the risk of schizophrenia: evidence from meta-analysis. Arch Gen Psychiatry. 60: 565–571.
[31].Andreou D, Söderman E, Axelsson T, Sedvall GC, Terenius L, Agartz I, et al. (2014). Polymorphisms in genes implicated in dopamine, serotonin and noradrenalin metabolism suggest association with cerebrospinal fluid monoamine metabolite concentrations in psychosis. Behav Brain Funct. 10: 26.
[32].Arroll MA, Wilder L, Neil J (2014). Nutritional interventions for the adjunctive treatment of schizophrenia: a brief review. Nutr J. 13: 91.
[33].Avramopoulos D, Pearce BD, McGrath J, Wolyniec P, Wang R, Eckart N, et al. (2015). Infection and inflammation in schizophrenia and bipolar disorder: a genome wide study for interactions with genetic variation. PLoS One. 10: e0116696.

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14959364

[34].Boydell J (2001). Risk factors for schizophrenia. Expert Rev Neurother. 1: 183–191.
[35].Butterworth RF (1998). Excitatory neurons and schizophrenia. Lancet. 352: 1643.
[36].Cannon M, Jones PB, Murray RM (2002). Obstetric complications and schizophrenia and meta-analytic review. Am J Psychiatry.159: 1080–1092.
[37].Clarke MC, Harley M, Cannon M (2006a).EPEDIMOLOGY
[38].Schwartz PJ (2011). Season of birth in schizophrenia: a maternal-fetal chronobiological hypothesis. Med Hypotheses. 76: 785–793.
[39].Semple DM, McIntosh AM, Lawrie SM (2005). Cannabis as a risk factor for psychosis: systematic review. J Psychopharmacol. 19: 187–194.
[40].Sørensen HJ, Mortensen EL, Reinisch JM, Mednick SA (2005). Breastfeeding and risk of schizophrenia in the Copenhagen Perinatal Cohort. Acta Psychiatr Scand. 112: 26–29.
[41].Šerý O, Přikryl R, Častulík L, Šťastný F (2010). A118G polymorphism of OPRM1 gene is associated with schizophrenia. J Mol Neurosci. 41: 219–222.
[42].Šerý O, Šťastný F, Zvolský P, Hlinomazová Z, Balcar VJ (2011). Association between Val66Met polymorphism of Brain-Derived Neurotrophic Factor (BDNF) gene and a deficiency of colour vision in alcohol-dependent male patients. Neurosci Lett. 499: 154–157.
[43].Šerý O, Povová J, Balcar VJ (2014). Perspectives in genetic prediction of Alzheimer's disease. Neuro Endocrinol Lett. 35: 359–366.
[44].Šerý O, Sultana N, Kashem MA, Pow DV, Balcar VJ (2015a). GLAST But Not Least-Distribution, Function, Genetics and Epigenetics of L-Glutamate Transport in Brain-Focus on GLAST/EAAT1. Neurochem Res. DOI 10.1007/s11064-015-1605-2
[45].Šerý O, Lochman J, Povová J, Janout V, Plesník J, Balcar VJ (2015b). Association between 5q23.2-located polymorphism of CTXN3 gene (Cortexin 3) and schizophrenia in European-Caucasian males; implications for the aetiology of schizophrenia. Behav Brain Funct. 11: 10.
[46].Szkultecka-Dębek M, Walczak J, Augustyńska J, Miernik K, Stelmachowski J, Pieniążek I, et al. (2015). Epidemiology and Treatment Guidelines of Negative Symptoms in Schizo-phrenia in Central and Eastern Europe: A Literature Review. Clin Pract Epidemiol Ment Health. 11: 158–16552 Szöke A, Charpeaud T, Galliot AM, Vilain J, Richard JR, Leboyer M, et al. (2014). Rural-urban variation in incidence of psychosis in France: a prospective epidemiologic study in two contrasted catchment areas. BMC Psychiatry. 14: 78
[47].Takei N, Murray RM, Sham P, O'Callaghan E (1995). Schizophrenia risk for women from in utero exposure to influenza. Am J Psychiatry. 152: 150–151.54 Tandom R, Keshavan MS, Nasrallah HA (2008). Schizophrenia, "Just the facts" what we know in 2008. 2. Epidemiology and etiology. Schizophr Res. 102: 1–18.
[48].Thoma P, Daum I (2013). Comorbid substance use disorder in schizophrenia: a selective overview of neurobiological and cognitive underpinnings. Psychiatry Clin Neurosci. 67: 367–383.
[49].ÚZIS ČR (2014).RISK FACTORS
[50].Addington J, Epstein I, Liu L et al (2011) A randomized controlled trial of cognitive behavioral therapy for individuals at clinical high risk of psychosis. Schizophr Res 125:54–61
[51].Amminger GP, Schafer MR, Papageorgiou K et al (2010) Long chain omega-3 fatty acids for indicated prevention of psychoticdisorders: a randomized, placebo-controlled trial. Arch Gen Psychiatry 67:146–154
[52].Antonini L, Mollica C, Auriti A et al (2014) A prognostic index for risk stratification for acute heart failure and death in subjects with ischemic cardiomyopathy and cardiac defibrillator. Heart Vessels. doi:10.1007/s00380-014-0494-7
[53].Barch DM, Bustillo J, Gaebel W et al (2013) Logic and justification for dimensional assessment of symptoms and relatedclinical phenomena in psychosis: relevance to DSM-5. Schizophr Res 150:15–20
[54].Bechdolf A, Muller H, Stutzer H et al (2011) Rationale and baseline characteristics of prevent: a second-generation intervention trial in subjects at-risk (prodromal) of developing firstepisode psychosis evaluating cognitive behavior therapy, aripiprazole, and placebo for the prevention of psychosis. Schizophr Bull 37(Suppl 2):S111–S121
[55].Bechdolf A, Wagner M, Ruhrmann S et al (2012) Preventing progression to first-episode psychosis in early initial prodromal states. Br J Psychiatry 200:22–29
[56].Bell RQ (1992) Multiple-risk cohorts and segmenting risk assolutions to the problem of false positives in risk for the major psychoses. Psychiatry 55:370–381
[57].Bodatsch M, Ruhrmann S, Mu¨ller R, Klosterko¨tter J, Brockhaus-Dumke A (2010) Mismatch negativity is reduced inschizophrenia patients with deficit syndrome. Schizophr Res117:360–361

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14959364

[58].Bodatsch M, Ruhrmann S, Wagner M et al (2011) Prediction of psychosis by mismatch negativity. Biol Psychiatry 69:959–966
[59].Fusar-Poli P, Borgwardt S, Bechdolf A et al (2013) The psychosis high-risk state: a comprehensive state-of-the-art review.JAMA Psychiatry 70:107–120
[60].Hutton P, Taylor PJ (2014) Cognitive behavioural therapy forpsychosis prevention: a systematic review and meta-analysis.Psychol Med 44:449–468
[61].Lee TY, Shin YS, Shin NY et al (2014) Neurocognitive function as a possible marker for remission from clinical high risk for psychosis. Schizophr Res 153:48–53
[62].Lip GY, Edwards SJ (2006) Stroke prevention with aspirin,warfarin and ximelagatran in patients with non-valvular atrial fibrillation: a systematic review and meta-analysis. Thromb Res118:321–333
[63].Marshall M, Lockwood A (2004) Early intervention for psychosis. Cochrane Database Syst Rev 4:CD004718
[64].McGlashan T, Walsh B, Woods SW (2010) The psychosis-risk syndrome. Handbook for diagnosis and follow-up. Oxford University Press, New York
[65].McGlashan TH, Zipursky RB, Perkins D et al (2006) Randomized, double-blind trial of olanzapine versus placebo in patients prodromally symptomatic for psychosis. Am J Psychiatry 163:790–799
[66].McGorry PD, Nelson B, Phillips LJ et al (2013) Randomizedcontrolled trial of interventions for young people at ultra-high risk of psychosis: twelve-month outcome. Journal clin psychiatry 74:349–356
[67].McGorry PD, Yung AR, Phillips LJ (2003) The ‘‘close-in’’ or ultra high-risk model: a safe and effective strategy for research and clinical intervention in prepsychotic mental disorder.Schizophr Bull 29:771–790
[68].McGorry PD, Yung AR, Phillips LJ et al (2002) Randomizedcontrolled trial of interventions designed to reduce the risk of progression to first-episode psychosis in a clinical sample with subthreshold symptoms. Arch Gen Psychiatry 59:921–928
[69].Michel C, Ruhrmann S, Schimmelmann BG, Klosterko¨tter J,Schultze-Lutter F (2014) A stratified model for psychosis prediction in clinical practice. Schizophr Bull. doi:10.1016/j.schres.2014.01.025
[70].Michel C, Schimmelmann BG, Kupferschmid S, Siegwart M,Schultze-Lutter F (2014) Reliability of telephone assessments of at-risk criteria of psychosis: a comparison to face-to-face interviews. Schizophr Res 153:251–253
[71].Miklowitz DJ, O’Brien MP, Schlosser DA et al (2014) Family focused treatment for adolescents and young adults at high risk for psychosis: results of a randomized trial. J Am Acad Child Adolesc Psychiatry 53:848–858
[72].Morrison AP, French P, Stewart SL et al (2012) Early detection and intervention evaluation for people at risk of psychosis: multisite randomised controlled trial. BMJ 344:e2233
[73].Morrison AP, French P, Walford L et al (2004) Cognitive therapy for the prevention of psychosis in people at ultra-high risk: randomised controlled trial. Br J Psychiatry 185:291–297
[74].Mo¨ssner R, Schuhmacher A, Wagner M et al (2010) Daoa/g72 predicts the progression of prodromal syndromes to first episode psychosis. Eur Arch Psychiatry Clin Neurosci 260:209–215
[75].Mrazek PJ, Haggerty HJ (1994) Reducing risks for mental disorders: frontiers for preventive research. Academy Press, Washington
[76].Nelson B, Yuen HP, Wood SJ et al (2013) Long-term follow-up of a group at ultra high risk (‘‘prodromal’’) for psychosis: the pace 400 study. JAMA Psychiatry 70:793–802
[77].Nieman DH, Ruhrmann S, Dragt S et al (2013) Psychosis prediction: stratification of risk estimation with information-processing and premorbid functioning variables. Schizophr Bull.doi:10.1093/schbul/sbt145
[78].Nieman DH, Velthorst E, Becker HE et al (2013) The strauss and carpenter prognostic scale in subjects clinically at high risk of psychosis. Acta Psychiatr Scand 127:53–61
[79].Nuechterlein KH, Dawson ME, Gitlin M et al (1992) Developmental processes in schizophrenic disorders: longitudinal studies of vulnerability and stress. Schizophr Bull 18:387–42561. Olvet DM, Carrion RE, Auther AM, Cornblatt BA (2013) Self awareness of functional impairment in individuals at clinical high-risk for psychosis. Early Interv Psychiatry. doi:10.1111/eip.12086
[80].Perez VB, Woods SW, Roach BJ et al (2014) Automatic auditory processing deficits in schizophrenia and clinical high-risk patients: forecasting psychosis risk with mismatch negativity. Biol Psychiatr 75:459–469

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14959364

[81].Perkins DO, Jeffries CD, Addington J et al (2014) Towards a psychosis risk blood diagnostic for persons experiencing high risk symptoms: preliminary results from the napls project. Schizophr Bull. doi:10.1093/schbul/sbu099

[82].Piskulic D, Addington J, Cadenhead KS et al (2012) Negative symptoms in individuals at clinical high risk of psychosis. Psychiatry Res 196:220–224

[83].Preti A, Cella M (2010) Randomized-controlled trials in people at ultra high risk of psychosis: a review of treatment effectiveness. Schizophr Res 123:30–36

[84].Pukrop R, Ruhrmann S (2012) Neurocognitive indicators ofhigh-risk states for psychosis. In: Borgwardt S, McGuire P, Fusar Poli P (eds) Vulnerability to psychosis: from neuroscience to psychopathology. Psychology Press, Hove, pp 73–94

[85].Riecher-Ro¨ssler A, Aston J, Ventura J et al (2008) the basel screening instrument for psychosis (BSIP): development,structure, reliability and validity. Fortschr Neurol Psychiatr76:207–216

[86].Riecher-Ro¨ssler A, Pflueger MO, Aston J et al (2009) Efficacy of using cognitive status in predicting psychosis: a 7-year follow-up. Biol Psychiatry 66:1023–1030

[87].Ro¨ssler W, Salize HJ, van Os J, Riecher-Ro¨ssler A (2005) Size of burden of schizophrenia and psychotic disorders. Eur Neuropsychopharmacol 15:399–409

[88].Ruhrmann S, Klosterko¨tter J, Bodatsch M et al (2012) Pharmacological prevention and treatment in clinical at-risk statesfor psychosis. Curr Pharm Des 18:550–557

[89].Ruhrmann S, Klosterko¨tter J, Bodatsch M et al (2012) Chances and risks of predicting psychosis. Eur Arch Psychiatry ClinNeurosci 262(Suppl 2):S85–S90

[90].Ruhrmann S, Schultze-Lutter F, Klosterk¨tter J (2003) Early detection and intervention in the initial prodromal phase ofschizophrenia. Pharmacopsychiatry 36(Suppl 3):S162–S167

[91].Ruhrmann S, Schultze-Lutter F, Klosterko¨tter J (2010) Probably at-risk, but certainly ill—advocating the introduction of a psychosis spectrum disorder in DSM-V. Schizophr Res 120:23–37

[92].Ruhrmann S, Schultze-Lutter F, Klosterko¨tter J (2010) Sub threshold states of psychosis—a challenge to diagnosis and treatment. Clin Neuropsychiatry 7:72–87

[93].Ruhrmann S, Schultze-Lutter F, Salokangas RK et al (2010) Prediction of psychosis in adolescents and young adults at high risk: results from the prospective European prediction of psychosis study. Arch Gen Psychiatry 67:241–251

[94].Salokangas RK, Heinimaa M, From T et al (2014) Short-term functional outcome and premorbid adjustment in clinical high risk patients. Results of the epos project. Eur Psychiatry 29:371–380

[95].Salokangas RK, Nieman DH, Heinimaa M et al (2013) Psychosocial outcome in patients at clinical high risk of psychosis: a prospective follow-up. Soc Psychiatry Psychiatr Epidemiol48:303–311

[96].Salokangas RKR, Ruhrmann S, von Reventlow HG et al (2012) Axis i diagnoses and transition to psychosis in clinical high-risk patients epos project: prospective follow-up of 245 clinical high risk outpatients in four countries. Schizophr Res 138:192–197

[97].Schaffner N, Schimmelmann BG, Niedersteberg A, Schultze Lutter F (2012) pathways-to-care for first-episode psychotic patients–an overview of international studies. Fortschr Neurol Psychiatr 80:72–78

[98].Schimmelmann BG, Walger P, Schultze-Lutter F (2013) The significance of at-risk symptoms for psychosis in children and adolescents. Can J psychiatry Revue canadienne de psychiatrie 58:32–40

[99].Schmidt SJ, Grunert VM, Schimmelmann BG, Schultze-Lutter F,Michel C (2014) Differences in coping, self-efficacy, and external control beliefs between patients at-risk for psychosis and patients with first-episode psychosis. Psychiatry Res 219:95–102

[100]. Schmidt SJ, Schultze-Lutter F, Schimmelmann BG et al (2015) EPA guidance on the early intervention in clinical high-risk states of psychoses. European Psychiatry (in press)

[101]. Schultze-Lutter F (2009) Subjective symptoms of schizophrenia in research and the clinic: the basic symptom concept. Schizophr Bull 35:5–8

[102]. Schultze-Lutter F, Addington J, Ruhrmann S, Klosterko¨tter J (2007) Schizophrenia proneness instrument - adult version (spia). Giovanni Fioriti, Rome

[103]. Schultze-Lutter F, Klosterko¨tter J, Picker H, Steinmeyer E, Ruhrmann S (2007) Predicting first-episode psychosis by basicsymptom criteria. Clin Neuropsychiatry 4:11–22

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14959364

[104]. Schultze-Lutter F, Klosterko¨tter J, Ruhrmann S (2014) Improving the clinical prediction of psychosis by combining ultra-high risk criteria and cognitive basic symptoms. Schizophr Res 154:100–106
[105]. Schultze-Lutter F, Michel C, Schmidt SJ et al (2015) EPA guidance on the early detection of clinical high risk states of psychoses. European Psychiatry (in press)
[106]. Schultze-Lutter F, Ruhrmann S, Berning J, Maier W,Klosterko¨tter J (2010) Basic symptoms and ultrahigh risk criteria: symptom development in the initial prodromal state.Schizophr Bull 36:182–191
[107]. Schultze-Lutter F, Schimmelmann BG, Ruhrmann S, Michel C (2013) 'A rose is a rose is a rose', but at-risk criteria differ. Psychopathology 46:75–87
[108]. Smieskova R, Fusar-Poli P, Allen P et al (2010) Neuroimaging predictors of transition to psychosis-a systematic review and meta-analysis. Neurosci Biobehav Rev 34:1207–1222
[109]. Stafford MR, Jackson H, Mayo-Wilson E, Morrison AP, KendallT (2013) Early interventions to prevent psychosis: systematic review and meta-analysis. BMJ 346:f185
[110]. Tarbox SI, Addington J, Cadenhead KS et al (2013) Premorbid functional development and conversion to psychosis in clinical high-risk youths. Dev Psychopathol 25:1171–1186
[111]. Valmaggia LR, Stahl D, Yung AR et al (2013) Negative psychotic symptoms and impaired role functioning predict transition outcomes in the at-risk mental state: a latent class cluster analysis study. Psychol Med 43:2311–2325
[112]. van der Gaag M, Nieman DH, Rietdijk J et al (2012) Cognitive behavioral therapy for subjects at ultrahigh risk for developing psychosis: a randomized controlled clinical trial. Schizophr Bull 38:1180–1188
[113]. van der Gaag M, Smit F, Bechdolf A et al (2013) Preventing a controlled prevention trails of 12 month and longer term follow- ups schizophr res 149: 56-62.
[114]. Hosak L (2013). New findings in the genetics of schizophrenia World J Psychiatry. 3: 57–61.
[115]. Hosáková J, Jarosova D (2015). Quality of life and needs of hospitalized schizophrenic patients in the Czech Republic. Neuro Endocrinol Lett. 36: 288–293.