

Research Article

Summer Birth and Clinical Characteristics in Schizophrenia: A Cross-Sectional Study

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Introduction: Schizophrenia is a complex syndrome with numerous risk factors, one of which is the season or month of birth. Therefore, the principal objective of this study was to test the relationship between summer birth and clinical features in schizophrenia.

Methodology: Study design: We conducted a cross-sectional analytic study with retrospective data collection. Sample: Were included in this study all the patients having met the DSM-IV criteria for schizophrenia during their first psychotic episode requiring hospital admission spanning from January,1, 2013 to December,31,2022. in the psychiatry department of Fattouma Bourguiba teaching Hospital Monastir, and who kept the same diagnosis of schizophrenia according to their medical files and the follow-ups. Variables and instruments: The recruitment was conducted through the patients' medical files using a questionnaire including socio-demographic, clinical, and therapeutic characteristics, as well as the month of birth and season of birth for each patient. Data analysis: Data entry and analyses were carried out using the software package IBM SPSS Statistics 25.0. To look for an association between the qualitative variables, we used the chi-square test, and if needed, Fisher's exact test.

Results: Our study included 333 patients with a mean age of 31.6 years. Several clinical features were associated with season of birth. Regarding types of schizophrenia, the paranoid type was significantly associated with the summer season of birth($p=0.005$). We also found a significant association between delusional themes like influence theme being significantly associated with the summer birth ($p=0.02$). As for the mechanisms of delusion only intrapsychic hallucinations had an association with summer birth ($p=0.039$).

Conclusions: The season of birth is one of the most consistently identified risk factors in the epidemiology of schizophrenia, although the underlying causes remain unclear. This underscores the importance of additional research in this field to enhance our understanding of schizophrenia and explore potential preventive measures.

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Introduction

Schizophrenia is a complex syndrome with heterogenous combination of negative, positive, and cognitive symptoms^[1]. This three-syndrome model is the resolution of numerous models dating two hundred years starting with Pinel^[2].

Schizophrenia's complexity depends on several factors^[3]. For example, the genetic component, in the one hand has long been established with an estimate heritability percentage of 80%, thanks to twin heritability studies and the genome-wide association study (GWAS) of schizophrenia^[4]. On the other, environmental risk factors act as stressors which can be biological or psychosocial^[5]. These stressors can be found within a continuum going from antenatal and perinatal periods, early and late childhood, adolescence, and early adulthood. They include maternal stress, advanced paternal age, viral infections, malnutrition, obstetric complications, childhood adversity, parental death, bullying, and adolescent cannabis use especially the early debut use the extent and frequency of use and the high potency tetrahydrocannabinol (THC) cannabis and others^[6].

While studies have identified no specific risk factor, genetic or environmental, directly causing schizophrenia, the hypothesis has turned to the association of all these factors from genetic to environmental highlighting the importance of gene-environment interaction^[6].

One particular environmental factor has attracted much interest: month of birth and more specifically season of birth as a risk factor in schizophrenia. Since times immemorial, the season of birth has been correlated with the onset of certain diseases like stated here by Hippocrates:

“Whoever wishes to pursue properly the science of medicine must proceed thus. First, he ought to consider what effects each season of the year can produce; for the seasons are not all alike

but differ widely both in themselves and at their changes." Hippocrates, "On Airs, Water and Places"^[7]

This seemingly simple question has been the focus of numerous investigations conducted since the late 1920s starting with Tramer in 1929^[8]. After that, a number of studies several investigations explored this topic, initially in the northern hemisphere and subsequently in the southern hemisphere and equatorial regions. These studies consistently found a 5-8% increase in the incidence of schizophrenia among individuals born in the winter and spring months, with some reports indicating increases as high as 11-15%^[9].

Across various studies, the consistent presence of a seasonality effect has been confirmed globally and throughout different periods. However, there is a notable scarcity of studies from North Africa addressing this specific topic. Consequently, this study, which describes the seasonality pattern, stands as one of the rare contributions to explore this subject in Monastir, Tunisia.

Thus, the objective of this study is to test the relationship between summer birth and clinical features in schizophrenia.

Design and Methods

I. Study design

1. Type of the survey

We conducted a cross-sectional analytic study with retrospective data collection on patients who were hospitalized for the first time in the department of psychiatry of Fattouma Bourguiba teaching Hospital in Monastir for a time period of 10 years going from the 1st of January 2013 to the 31st of 2022 and who were diagnosed with schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria.

We applied DSM-IV criteria as a classification tool because it uses clinical types of schizophrenia needed for the analysis. (appendix 1+2+3)

2. Place and period of the survey

The data was collected from inpatients medical files using a questionnaire over a period of four month going from march to June 2023 from the psychiatry department archives' in Fattouma Bourguiba Teaching Hospital Monastir. We contacted some patients with missing data from their medical files through telephone.

Psychiatric department in Fattouma Bourguiba Hospital is one of the reference centers in Tunisia for intrahospital care of patients suffering from schizophrenia.

3. Survey population

The recruitment was conducted through the patients' medical files using a pre-established form including socio-demographic, clinical, and therapeutic characteristics, as well as the month of birth and season of birth for each patient. The pre-established form was made after thorough examination of the available bibliography concerning the subject of seasonality of birth in schizophrenia (Appendix4).

Meteorological definition was used to define seasons: Summer is defined as the period from June 1st to August 31st; Spring from March 1st to May 31st; Autumn from September 1st to November 30th and Winter from December 1st to February 28th (or 29th in leap years).

The source population was made up of patients who were hospitalized for the first time in the department of psychiatry of Fattouma Bourguiba teaching Hospital in Monastir for a time period of 10 years going from the 1st of January 2013 to the 31st of 2022 and who were diagnosed with schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria.

- a. **Inclusion criteria:** Were included in this study all the patients having met the DSM-IV criteria for schizophrenia requiring hospital admission during the time lapse from 2013 to 2022 in the psychiatry department of Fattouma Bourguiba teaching Hospital Monastir, and who kept the same diagnosis of schizophrenia according to their medical files and the follow-ups.
- b. **Exclusion criteria:** Were excluded from this study all the patients having not met the DSM-IV criteria for schizophrenia either in the first episode or ulterior episodes having required hospital admission or after reviewing their symptoms during their follow-ups.

c. **Non-inclusion criteria:** We did not include the study patients with lost hospital records, patients with empty hospital records and patients who had missing data in their files (concerning their dates of birth) and which we were unable to obtain via telephone contact.

II. Data analyses

Data entry and analyses were carried out using the software package IBM SPSS Statistics 25.0.

The statistical analyses included a descriptive study and univariate comparisons.

We have described the quantitative variables by means and standard deviations if the variable is normally distributed and by medians and interquartile ranges if the distribution is asymmetric. Normality was assessed by the Kolmogorov-Smirnov test. Categorical variables were summarized by frequencies and percentages. We examined the socio-demographic, clinical, therapeutic, prognostic characteristics and the month and season of birth by quarters and half-years.

To look for an association between the qualitative variables, we used the chi-squared test, and if needed, Fisher's exact test. We looked for associations between the season of birth and the clinical characteristics of schizophrenia.

The strength of the associations was measured by Odds Ratios and their confidence intervals at 95%.

The significance level for all statistical tests has been set at 5% ($p \leq 0,05$).

III. Bibliographic research

The bibliographic research was based on databases like PubMed, Science Direct and Google Scholar without limitation of time concerning the articles date of publication.

The key words used: Schizophrenia, pathophysiology, season of birth, symptoms, signs, Treatment-Resistant Schizophrenia.

IV. Ethical considerations

This study was based on a retrospective collection of data from medical records. These data were collected on pre-established form. There was no direct intervention with patients. All personal information was anonymized. No ethical objections were raised.

In addition, verbal consent was obtained from patients contacted by telephone to complete missing data.

Results

I. Descriptive analyses

1. Socio-demographic characteristics:

Socio-demographic characteristics	Frequency (n)	Percentage (%)
Age (years)		
≤ 18	11	3.3
19-44	285	85.6
≥ 45	37	11.1
Gender		
Male	295	88.6
Female	38	11.4
No consanguinity	262	78.7
Consanguinity	71	21.3
2 nd degree	54	16.2
3 rd degree	5	1.5
Distant	12	3.6
Educational level		
Illiterate	9	2.7
Primary	95	28.5
Secondary	180	54.1
University	49	14.7
Marital status		
Single	271	81.1
Married	47	14.1

Socio-demographic characteristics	Frequency (n)	Percentage (%)
Divorced	13	3.9
Widowed	2	0.6
Number of children		
None	290	86.5
1-3 children	37	11.1
More than 3 children	6	1.8
Origin		
Urban	298	89.5
Rural	35	10.5
Profession		
Student	11	3.3
Unemployed	260	78.1
Daily worker	47	14.1
Seasonal worker	3	0.9
Long-term leave	2	0.6
Invalidity	3	0.9
Retirement	7	2.1
Socio-economic level		
Low	136	40.8
Average	175	52.6
High	22	6.6

Table I. Summary table of the socio-demographic characteristics of the patients (n=333)

This sample included initially 396 inpatients who were hospitalized for the first time for

schizophrenia in the department of psychiatry in Monastir, Tunisia, from whom 333 met with the inclusion criteria (Figure 1).

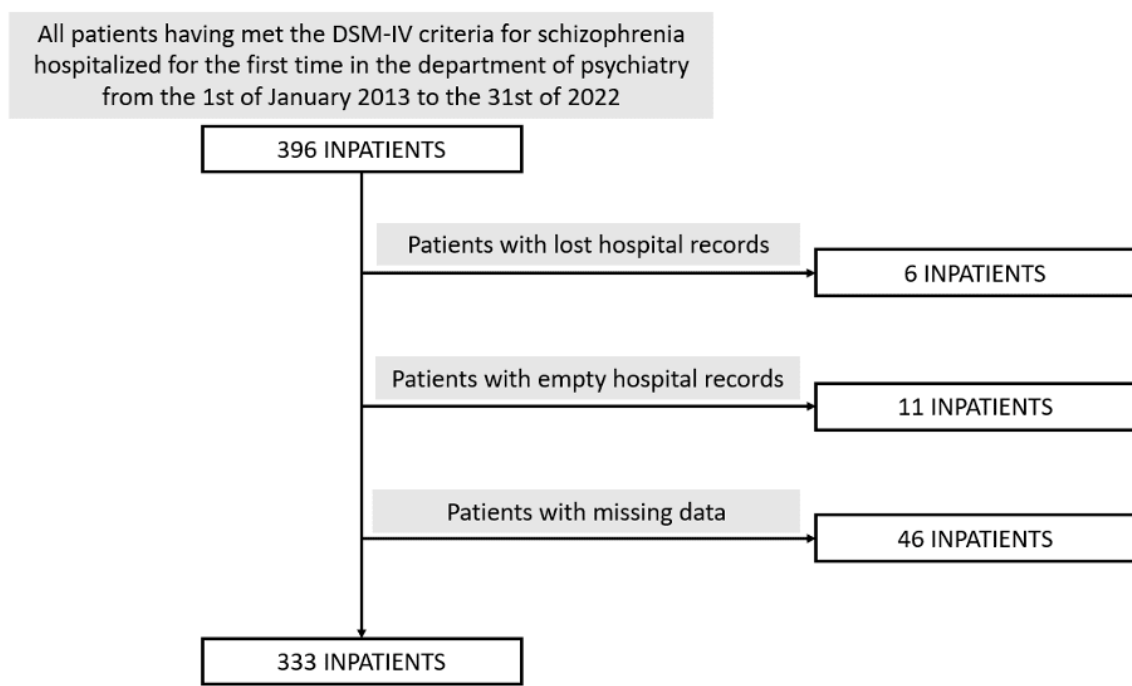


Figure 1. Flow-chart of patient inclusion

The median age was of 29 years (interquartile range: 24–37). Gender was male in 88.6%. We found that (89.5%) of the population were of urban origin, (52.6%) had secondary educational levels. Non-consanguineous marriages were found in (70.9%), (80.5%) were single, and (86.5%) had no children. In the population (77.8%) had no jobs, and (3.3%) were still students, while (91.9%) had a low to medium socio-economic level according to interprofessional guaranteed minimum wage (SMIG).

2. Season of birth

The spring and summer seasons had the highest number of births with respectively 93 (27.9%) and 94 (28.2%), as can be seen from Figure 2.

3. Clinical characteristics

The results from Table II show that (16.5%) of the population had an early onset schizophrenia. The paranoid type represented (25.5%) of the population. Disorganized speech, behavior and affect was

found in respectively (29.9%), (32.8%) and (37.3%). Delusions were found in (86.2%) of the population, and (60.7%) had more than one delusional theme. The persecution theme was found in (75.4%). The principal mechanisms found were auditory hallucinations in (54.1%) of the patients, interpretation (47.4%) and intrapsychic hallucinations in (26.1%).

	Frequency (n)	Percentage (%)
Age of onset		
≤18 years	55	16.5
>18 years	278	83.5
Type of schizophrenia		
Paranoid	85	25.5
Disorganized	64	19.2
Catatonic	18	5.4
Undifferentiated	166	49.8
Residual	0	0
Disorganization of		
Affect	310	37.3
Behavior	248	32.8
Speech	272	29.9
Delusions		
Yes	287	86.2
No	46	13.8
Delusional themes		
Persecution	251	75.4
Reference	99	29.7
Grandiosity	65	19.5
Religion	64	19.2
Somatic	35	10.5
Negation	3	0.9
Filiation	54	16.2
Influence	65	19.5

	Frequency (n)	Percentage (%)
Number of themes/patients		
Monothematic	85	25.5
Polythematic	202	60.7
Mechanisms of delusion		
Interpretative	158	47.4
Intuitive	138	41.4
Imaginative	18	5.4
Visual hallucinations	89	26.7
Auditory hallucinations	180	54.1
Olfactory hallucinations	7	2.1
Tactile hallucinations	39	11.7
Intrapsychic hallucinations	87	26.1

Table II. The clinical characteristics of the population

II. Analytical study: Association between characteristics of schizophrenia and summer birth

1. Univariate study

1.1. Type of schizophrenia

We found that summer birth was significantly associated with paranoid type of schizophrenia ($p=0.005$).

Furthermore, we didn't find an association with the other types.

These results are summarized in Table III.

SEASON	TYPE OF SCHIZOPHRENIA	n (%)		p
		(+)	(-)	
Summer	Paranoid	34 (36.1)	60 (63.9)	0.005
	Undifferentiated	38 (40.4)	56 (59.6)	NS*
	Disorganized	14 (14.9)	80 (85.1)	NS*
	Catatonic	8 (8.4)	86 (91.6)	NS*

Table III. Relation between types of schizophrenia and summer birth

*NS: non-significant

1.2. Delusional themes

We found that the influence theme is significantly associated with summer birth ($p=0.02$). (Table IV)

SEASON	DELUSIONAL THEMES	n (%)		p
		(+)	(-)	
Summer	Persecution	75 (79.8)	19 (20.2)	NS*
	Reference	30 (31.9)	64 (68.1)	NS*
	Grandiosity	20 (21.3)	74 (78.7)	NS*
	Religion	17 (18.1)	77 (81.9)	NS*
	Somatic	14 (14.9)	80 (85.1)	NS*
	Negation	0 (0)	94 (100)	NS*
	Filiation	13 (13.8)	81 (86.2)	NS*
	Influence	26 (27.7)	68 (72.3)	0.020

Table IV. Relation between themes of schizophrenia and summer birth

*NS: non-significant

1.3. Mechanisms of delusion in schizophrenia

We analyzed the mechanisms of delusion according to summer birth and we found a significant association between the summer and intrapsychic hallucinations ($p=0.039$) (Table V).

SEASON	DELUSIONAL MECHANISMS	n (%)		p
		(+)	(-)	
	Intuitive	45 (47.9)	49 (52.1)	NS*
	Interpretative	43 (45.7)	51 (54.3)	NS*
	Imaginative	3 (3.2)	91 (96.8)	NS*
Summer	Visual hallucinations	24 (25.5)	70 (74.5)	NS*
	Auditory hallucinations	47 (50)	47 (50)	NS*
	Olfactory hallucinations	0 (0)	94 (100)	NS*
	Tactile hallucinations	11 (11.7)	83 (88.3)	NS*
	Intrapsychic Hallucinations	32 (34)	63 (66)	0.039

Table V. Relation between mechanisms of delusion summer birth in schizophrenia

*NS: non-significant

2. Multivariable study

We found that summer birth was a predictive factor for the paranoid type ($p=0.021$; $OR=1.88$) and for the influence theme of schizophrenia ($p=0.029$; $OR=1.92$)

Discussion

I. Results' Interpretation

1. Birth Seasonality as a Risk Factor in Schizophrenia

From the difference in the seasonality pattern in different regions of the world, authors have put forward multiple hypotheses as to the causes mediating and moderating it. Although this aspect of the question has been the center of the recent studies, these factors remain elusive. Authors hypothesized that latitude could have a moderating effect on season of birth of schizophrenia patients^{[10][11]}.

While northern hemisphere countries have four distinctive seasons with varying temperatures, southern hemisphere countries and equatorial regions share little variation in temperatures as the weather is mild all year long. Indeed, the meta-analysis of mild temperate southern hemisphere countries showed a mild but non-significant increase in schizophrenia births^{[12][13]}. Authors have made a point to link the seasonality pattern with rainfall and found a significant increase in schizophrenia births 3^[8] and 4 months after the rainy season in Puerto Rico and northeastern Brazil^[13]. These results demonstrate a period risk between May and July, which goes in accordance with the significant increase of schizophrenia birth in the dry winter season found in a study of the southeastern part of Brazil^[14].

Giving the lack of drastic changes in temperatures that could explain the seasonality pattern in southern hemisphere countries and equatorial regions, authors thought of infectious diseases^{[8][15]}. And thus, a number of studies have looked into maternal infections and the prenatal exposure to viral agents such as influenza, *Toxoplasma gondii*, HSV-2 and enteroviruses as mediating factors for the seasonality effect^{[16][17]}. While all the studies agree on the modulating role of maternal infections on schizophrenia onset, none can determine with absolute certitude their mediating effect on season of birth. Some meta-analyses found a significant association between HSV-2 and schizophrenia, but did not link influenza^[12] or toxoplasmosis^[18] to schizophrenia. However, studies based on serological diagnosis of infectious diseases established a significant association between the prenatal exposure to toxoplasmosis as a risk factor in schizophrenia onset, while the infection by HSV-2 was thought to be a confounding factor^[19]. A study of a Spanish population analyzed data from three influenza pandemics and found a significant association to schizophrenia^[20]. Authors have also suspected

enteroviruses as a risk factor in schizophrenia^[18] and studies have confirmed the association between them. Indeed, a recent review of literature demonstrated a significant negative correlation between the excess of winter schizophrenia births and the summer peak of enterovirus cases^[12]. In the same line, a Finish study found a significant association between polio infection and catatonic schizophrenia and showed a 90% decrease of cases of catatonic schizophrenia after the eradication of polio^[19]. Although maternal infections have been extensively researched, only a few authors have looked into its mediating effect on season of birth and either found no correlation between them^[20], or found a partial association to one infectious agent in particular^[12].

Alongside temperature, latitude and maternal infections, authors have thought of vitamin D deficiency. This hypothesis was born from the hours of exposure to bright sunlight that are highly diminished during the winter/spring seasons particularly in high latitude countries^[11]. Indeed, the production of vitamin D depends on sun exposure and the action of UVB light on the skin by transforming derivatives of cholesterol into vitamin D^[21]. Experimental studies on rodents have provided strong evidence to prenatal vitamin D deficiency and brain abnormalities like enlarged lateral ventricles, altered dopamine circuits and expression of genes and proteins but also altered behavior^[22] that subsequently could lead to schizophrenia.

Alongside these mediating factors, authors have looked into meteorological factors as modulators of the seasonality pattern, as well^[9]. In such a way, the duration of sunshine exposure during the perinatal period is hypothesized to have a direct link to schizophrenia^[23]. This was demonstrated by research conducted on a large population and assessed a significant association between decreased perinatal sunshine exposure and schizophrenia and also an earlier onset of this mental disorder^[24].

All these results accentuate the polymorphism of schizophrenia and warrants more studies about the numerous risk factors and their interaction.

2. Seasonality and its clinical implications in schizophrenia

It has been demonstrated consistently that the season of birth of schizophrenia patients is a risk factor in the onset of the disease^[24]. In order to understand more this heterogeneous disorder, authors have examined the association between season of birth and the clinical and therapeutic characteristics of schizophrenia.

Many authors tried to link the clinical features of schizophrenia and seasonality; however, the trail of evidence is not strong. The studies have reviewed the subtypes of schizophrenia, the age at onset and the hospital stay.

Most of the studies divided schizophrenia into paranoid and non-paranoid types. Even by using the same subtyping, the results were still mixed. Indeed, some studies have not linked schizophrenia types with season of birth^[9]. However, when stratified by gender, the authors of an Italian study found an association between winter-born patients and paranoid schizophrenia in men, and the contrary was true for women who showed an excess of paranoid schizophrenia in non-winter months^[25]. In contrast, others reported that the paranoid subtype was more associated with winter^[26]. In our study, and partly contrary to the literature, we reported an association between the paranoid type and the summer ($p=0.005$).

Another common division in schizophrenia is into predominantly positive or negative symptoms. However, only a few studies mostly with small samples have examined this aspect and found contradicting results. While some reported no difference in birth seasonality^[27], others found an increase of negative symptoms or a decrease of positive symptoms^[28] in winter born schizophrenia patients. In between these findings, authors of an Italian study, while not demonstrating a link between season of birth and symptomatology, tried to stratify their finding by gender. With this three-way interaction, an association was found. Indeed, negative symptomatology was predominant in female patients born during the winter and early spring months and in male patients born in non-winter months^[27]. Partly in accordance with these results, a study of a southern hemisphere population, showed that avolition/apathy had a strong association with winter but also autumn. Within the negative symptoms' categorization, some authors have studied deficit and non-deficit schizophrenia. In a northern hemisphere review of literature of studies conducted in the United States, England, and Scotland, the authors reported a robust association between deficit schizophrenia and summer when the deficit group was compared with the non-deficit group^[13] and the general population, in contrast with a weaker link found between the negative symptoms' group and summer^[29].

Studies have also studied seasonality and duration of hospitalization, while some found no association between the two^[25]. Others found that patients with winter month births were more likely to have short hospital stays^[24].

II. Significance for Public Health

Season of birth, as reported in this work, can be a predictive factor and a prognostic factor for the onset and evolution of schizophrenia. Climate change may modify this finding. It is necessary to take into account the season of birth in treatment strategies by integrating the consideration of season of birth into the evaluation of clinical and therapeutic characteristics. This information could serve as practical tool for making informed treatment choices tailored to individual needs.

III. Key points of the study

The interest of this study are as follows: firstly, the seasonality effect has long been acknowledged by the world as a risk factor in schizophrenia, but has rarely been studied in North African countries, making this study one of the few to discuss this phenomenon in this area. Secondly, this study will enhance the epidemiological data about season of birth in schizophrenia in the region. Thirdly, this study can open doors for future research on the subject in the region.

IV. Limitations

The limitations of this work lie, first of all, on the type of the study which does not allow the evaluation of seasonality as a risk factor in schizophrenia. The second limitation resides in the fact that this study does not look for the covariates that interact with season of birth, genetic or environmental. The third limitation is related to the number of participants, the single centered location we used for the recruitment of the population and the use of admitted schizophrenic patients only, requiring a certain amount of caution while interpreting these results.

Conclusions

Since hundreds of years, schizophrenia has intrigued researchers by its complexity. Schizophrenia is a heterogenous disorder with multiple facades combining positive, negative, and cognitive symptoms. This complexity has led researchers to look for the cause behind it only to stumble upon multiple risk factors starting by genetic risk factors, but also the environmental risk factors and moreover the interaction between them. Indeed, schizophrenia is a multifactorial disorder, and while studies have identified numerous risk factors from genetic to environmental risk factor, no author could identify a specific explanation for the onset of schizophrenia. Today, season of birth, is considered one of the most reliable findings in the epidemiology of schizophrenia throughout the northern and southern

hemisphere, along with the equatorial regions. However substantial the studies on this topic are across the world, Northern Africa remains to deliver the schizophrenia literature with a contribution on seasonality of birth.

Appendix 1: Diagnostic criteria for schizophrenia – DSM-IV

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- A. *Characteristic symptoms*: Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):
1. Delusions
 2. Hallucinations
 3. Disorganized speech (eg, frequent derailment or incoherence)
 4. Grossly disorganized or catatonic behavior
 5. Negative symptoms, ie, affective flattening, alogia, or avolition.
- B. *Social/occupational dysfunction*: For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).
- C. *Duration*: Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (ie, active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form (eg, odd beliefs, unusual perceptual experiences).
- D. *Schizoaffective and mood disorder exclusion*: Schizoaffective Disorder and Mood Disorder With Psychotic Features have been ruled out because either 1) no Major Depressive, Manic, or Mixed Episodes have occurred concurrently with the active-phase symptoms; or 2) if mood episodes have occurred during active-phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.
- E. *Substance/general medical condition exclusion*: The disturbance is not due to the direct physiological effects of a substance (eg, a drug of abuse, a medication) or a general medical condition.
- F. *relationship to a pervasive developmental disorder*: If there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of Schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated).
- Classification of longitudinal course* (can be applied only after at least 1 year has elapsed since the initial onset of active-phase symptoms).
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Appendix 2: Types of schizophrenia – DSM-IV

<p>Paranoid Type (295.30): A type of Schizophrenia in which the following criteria are met:</p> <p>A. Preoccupation with one or more delusions or frequent auditory hallucinations.</p> <p>B. None of the following is prominent: disorganized speech, disorganized or catatonic behavior, or flat or inappropriate affect.</p>	<p>Catatonic Type (295.20): A type of Schizophrenia in which the clinical picture is dominated by at least two of the following:</p> <ol style="list-style-type: none"> 1. motoric immobility as evidenced by catalepsy (including waxy flexibility) or stupor 2. excessive motor activity (that is apparently purposeless and not influenced by external stimuli) 3. extreme negativism (an apparently motiveless resistance to all instructions or maintenance of a rigid posture against attempts to be moved) or mutism 4. peculiarities of voluntary movement as evidenced by posturing (voluntary assumption of inappropriate or bizarre postures), stereotyped movements, prominent mannerisms, or prominent grimacing 5. echolalia or echopraxia
<p>Disorganized Type (295.10): A type of Schizophrenia in which the following criteria are met:</p> <p>A. All of the following are prominent:</p> <ol style="list-style-type: none"> 1. disorganized speech 2. disorganized behavior 3. flat or inappropriate affect <p>B. The criteria are not met for Catatonic Type.</p>	
<p>Residual Type (295.60): A type of Schizophrenia in which the following criteria are met:</p> <p>A. Absence of prominent delusions, hallucinations, disorganized speech, and grossly disorganized or catatonic behavior.</p> <p>B. There is continuing evidence of the disturbance, as indicated by the presence of negative symptoms or two or more symptoms listed in Criterion A for Schizophrenia, present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).</p>	<p>Undifferentiated Type (295.90): A type of Schizophrenia in which symptoms that meet Criterion A are present, but the criteria are not met for the Paranoid, Disorganized, or Catatonic Type.</p>

Appendix 3: Defining variables

Schizophrenia: is a chronic brain disorder which is characterized by:

- **Psychosis** refers to a set of symptoms characterized by a loss of touch with reality due to a disruption in the way that the brain processes information. When someone experiences a psychotic episode, the person's thoughts and perceptions are disturbed, and the individual may have difficulty understanding what is real and what is not.
- **Delusions** are fixed false beliefs held despite clear or reasonable evidence that they are not true. Persecutory (or paranoid) delusions, when a person believes they are being harmed or harassed by another person or group, are the most common.
- **Hallucinations** are the experience of hearing, seeing, smelling, tasting, or feeling things that are not there. They are vivid and clear with an impression similar to normal perceptions. Auditory

hallucinations, “hearing voices,” are the most common in schizophrenia and related disorders.

- **Disorganized thinking and speech** refer to thoughts and speech that are jumbled and/or do not make sense. For example, the person may switch from one topic to another or respond with an unrelated topic in conversation. The symptoms are severe enough to cause substantial problems with normal communication.
- **Disorganized or abnormal motor behavior** are movements that can range from childlike silliness to unpredictable agitation or can manifest as repeated movements without purpose. When the behavior is severe, it can cause problems in the performance of activities of daily life. It includes catatonia, when a person appears as if in a daze with little movement or response to the surrounding environment.
- **Negative symptoms** refer to what is abnormally lacking or absent in the person with a psychotic disorder. Examples include impaired emotional expression, decreased speech output, reduced desire to have social contact or to engage in daily activities, and decreased experience of pleasure (81).

Appendix 4: Pre-established form

Sociodemographic Characteristics

- Date of birth:
- Age:
- Gender:
 - female
 - male
- Origine:
 - rural
 - urban
- Consanguinity:
 - no
 - yes
 - if yes, what's the degree of consanguinity?
- Educational level:

- illiterate
- primary
- secondary
- university
- Marital status:
 - single
 - married
 - divorced
 - widowed
- Nombre of children:
- Profession:
- Still a student:
 - yes
 - no
- Regularity at work:
 - active unemployed
 - retired
 - disability long-term leave
 - seasonal employment
- Economic status:
 - low
 - medium
 - high
- Psychoactive substance use:
 - no
 - yes;
 - if yes, which one?
 - cannabis amphetamine
 - cocaine trihexyphénidyle

Anamnestic Characteristics

- Familial history:
 - no
 - yes;
 - if yes, which one: SCZ; TB; TSA; TDM?
- Personal history of organic illness:
 - no
 - yes;
 - if yes, which one?
- Personal history of previous convictions:
 - no
 - yes
- Personal history of attempted suicide:
 - no
 - yes;
 - if yes, precise de number of attempted suicides, the mean:

Clinical Characteristics

- Age at onset:
- Type of SCZ:
 - paranoid
 - disorganized
 - catatonic
 - undifferentiated
- Catatonia:
 - no
 - yes
- Disorganization:
- Affects:
 - no
 - yes

- Thoughts:
 - no
 - yes
- Behavior:
 - no
 - yes
- Verbalized delirious thoughts:
 - no
 - yes
 - if yes,

What were the themes:

	Persecution	Reference	Grandeur	Religion	Influence	Somatic	Negation	Filiation
yes								
no								

What were the mechanisms:

	Interpretative	Intuitive	Imaginative	Hallucinations				Mental automatism
				auditory	visual	tactile	olfactory	
yes								
no								

References

1. ^ΔWorld Health Organization. Schizophrenia. 2022 [cited 2023 Oct 11]. Available from: <https://www.who.int/news-room/fact-sheets/detail/schizophrenia> [Internet]. 2022 [cited 2023 Oct 11].

2. [△]Almeida TA, Márcio A. Considerações nosológicas sobre a demência precoce de Pinel a Kraepelin. *Rev Latinoam Psicopa.* 2024; 27: e231293.
3. [△]Volkan K. Schizophrenia: Epidemiology, causes, neurobiology, pathophysiology, and treatment. *J. health med. sci.* 2020;3(4).
4. [△]Schmitt A, Falkai P, Papiol S. Neurodevelopmental disturbances in schizophrenia: evidence from genetic and environmental factors. *J Neural Transm.* 2023 Mar;130(3):195–205.
5. [△]Indah Iswanti D, Nursalam N, Fitryasari R, Kusuma Dewi R. Development of an integrative empowerment model to care for patients with schizophrenia disorder. *Int. J. Public Health Res.* 2023;12(3). doi:10.1177/22799036231197191
6. ^{a, b}Stilo SA, Murray RM. Non-genetic factors in schizophrenia. *Curr Psychiatry Rep.* 2019 Sep 14;21(10):100.
7. [△]Saleh A, King M, Hamilton J, Pigott T, Elkhatib R, Shah A, Selek S. Birth seasonality of schizophrenia and bipolar disorder? A review of inpatient records. *J Affect Disord.* 2021; 287: 15–18.
8. ^{a, b, c}Frederico RF, Gustavo CDP, Ricardo JVC, Erika RRB, Vanessa BMGS. Spini. Impact of season of birth on psychiatric disorder susceptibility and drug abuse incidence in a population from the Köppen Tropical Savanna region of Brazil. *Neuropsychobiology.* 28 February 2020; 79 (2): 131–140. doi:10.1159/000503069
9. ^{a, b, c}Natassia R, Alexander P, Marica L, Paul L, Kenneth SK, Sarah EB. Impact of early-life factors on risk for schizophrenia and bipolar disorder. *Schizophr Bull.* May 2023; 49 (3): 768–777. doi:10.1093/schbul/sbac205
10. [△]Alvarez-Mon MA, Guillen-Aguinaga S, Pereira-Sanchez V, Onambele L, Al-Rahamneh MJ, Brugos-Larumbe A, Guillen-Grima F, Ortuño F. Being born in winter-spring and at around the time of an influenza pandemic are risk factors for the development of schizophrenia: the apna study in Navarre, Spain. *J Clin Med.* 2021; 10(13):2859. doi:10.3390/jcm10132859
11. ^{a, b}Van der Leeuw C, De Witte LD, Stellinga A. Vitamin D concentration and psychotic disorder: associations with disease status, clinical variables and urbanicity. *Psychol Med.* 2020;50(10): 1680–1686. doi:10.1017/S0033291719001739
12. ^{a, b, c, d}Saatci D, Johnson T, Smee M, Van Nieuwenhuizen A, Handunnetthi L. The role of latitude and infections in the month-of-birth effect linked to schizophrenia. *Brain Behav Immun - Health.* 2022 Oct; 24:100486.

13. ^{a, b, c}Hinterbuchinger B, König D, Gmeiner A, Listabarth S, Fellingner M, Thenius C, Baumgartner JS, Vyssoki S, Waldhoer T, Vyssoki B, Pruckner N. Seasonality in schizophrenia—An analysis of a nationwide registry with 110,735 hospital admissions. *Eur Psychiatry*. 2020 May 11;63(1): 55. doi:10.1192/j.eurpsy.2020.47.
14. ^ΔFrederico RF, Gustavo CP, Ricardo JVC, Erika RRB, Vanessa BMGS. Impact of Season of Birth on Psychiatric Disorder Susceptibility and Drug Abuse Incidence in a Population from the Köppen Tropical Savanna Region of Brazil. *Neuropsychobiology*. 28 February 2020; 79 (2): 131–140.
15. ^ΔPettitt R, Gara T. The impact of climate change on our patients' health and the family physician's role. *Osteopath. Fam. Physician*, 14(4), 35–40.
16. ^ΔKhiari G, Cheour M, Ben Nasr S, Bouzid R, Tabbane K, Douki S. Seasons of birth of schizophrenic patients: Retrospective study of a hospitalized population in Tunisia. *L'Encephale*. 1994;20(5):473–7.
17. ^ΔTanskanen A, Taipale H, Cannon M, Cotter D, Tiihonen J. Incidence of schizophrenia and influence of prenatal and infant exposure to viral infectious diseases. *Acta Psychiatr Scand*. 2021 Jun;143(6):487–94.
18. ^{a, b}Cheslack-Postava K, Brown AS. Prenatal infection and schizophrenia: A decade of further progress. *Schizophr Res*. 2022 Sep; 247:7–15.
19. ^{a, b}Alvarez-Mon MA, Guillen-Aguinaga S, Pereira-Sanchez V, Onambele L, Al-Rahamneh MJ, Brugos-Larumbe A, et al. Being Born in Winter–Spring and at Around the Time of an Influenza Pandemic Are Risk Factors for the Development of Schizophrenia: The Apna Study in Navarre, Spain. *J Clin Med*. 2021 Jun 28;10(13):2859.
20. ^{a, b}Albiñana C, Boelt SG, Cohen AS, Zhu Z, Musliner KL, Vilhjálmsdóttir BJ, et al. Developmental exposure to vitamin D deficiency and subsequent risk of schizophrenia. *Schizophr Res*. 2022 Sep;247:26–32.
21. ^ΔJ.L. Zhu, W.W. Luo, X. Cheng. Vitamin D deficiency and Schizophrenia in adults: a systematic review and meta-analysis of observational studies *Psychiatry Res*. 2020; 288
22. ^ΔHsu CW, Tseng PT, Tu YK, Lin PY, Hung CF, Liang CS, Hsieh YY, Yang YH, Wang LJ, Kao HY. Month of birth and mental disorders: A population-based study and validation using global meta-analysis. *Acta Psychiatr Scand*. 2021; 144: 153–167. doi:10.1111/acps.13313
23. ^ΔAbrahamyan Empson L, Baumann PS, Söderström O, Codeluppi Z, Söderström D, Conus P. Urbanicity: The need for new avenues to explore the link between urban living and psychosis. *Early Interv Psychiatry*. 2020; 14: 398–409. doi:10.1111/eip.12861
24. ^{a, b, c}Saatci D, Van Nieuwenhuizen A, Handunnetthi L. Maternal infection in gestation increases the risk of non-affective psychosis in offspring: a meta-analysis. *J Psychiatr Res*. 2021 Jul; 139:125–31.

25. ^{a, b}Fraccalini T, Ricci V, TaroZZo B, Cardinale L, Primerano G, Kowsaralsadat M, Volpicelli G. Effects of seasonality in emergency admissions for mental disorders: two years of clinical experience. *Int J Psychiat Clin*. 2024; 28(1), 45–52. doi:10.1080/13651501.2024.2331481
26. ^ΔWang RR, Hao Y, Guo H, Wang MQ, Han L, Zheng RY, He J, Wang ZR. Lunar cycle and psychiatric hospital admissions for schizophrenia: new findings from Henan province, China. *Chronobiol Int*. 2020 Mar;37(3):438–449. doi:10.1080/07420528.2019.1625054.
27. ^{a, b}Gutman, BA, van Erp TG, Alpert K, Ching CR, Isaev D, Ragotheraman A, et al. A meta-analysis of deep brain structural shape and asymmetry abnormalities in 2,833 individuals with schizophrenia compared with 3,929 healthy volunteers via the ENIGMA consortium. *Hum. Brain Mapp*. 2022; 43, 352–372. doi:10.1002/hbm.25625
28. ^ΔBaselmans BML, Yengo L, Van Rheenen W, Wray NR. Risk in relatives, heritability, SNP-based heritability, and genetic correlations in psychiatric disorders: A review. *Biol Psychiatry*. 2021; 89:11–19.
29. ^ΔViejo-Romero M, Whalley HC, Shen X, Stolicyn A, Smith DJ, Howard DM. An epidemiological study of season of birth, mental health, and neuroimaging in the UK Biobank. *PLoS One*. 2024 May 22;19(5). doi:10.1371/journal.pone.0300449

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