Correlation between schizophrenia and seasonality of birth in a tropical region

Esquizofrenia e correlação da sazonalidade com período de nascimento numa região tropical

Abstract

Objective: To investigate the statistical relationship between season of birth and schizophrenia in 461 patients hospitalized in three psychiatric facilities in the towns of Araras, Itapira, and Espírito Santo do Pinhal, interior of São Paulo State, southeastern Brazil. **Methods:** Date and place of birth of the patients were collected and used to determine the season of birth. Results were analyzed by the chi-square test. Data regarding temperature and rainfall between 1952 and 1986, corresponding to the years of birth of the patients studied, were also obtained. **Results:** The results showed a higher prevalence of births in the winter months ($p = 0.0044$), a period characterized in this region by a decline in temperature and rainfall. **Conclusion:** These findings indicate a possible influence of seasonality on the pathogenesis of schizophrenia and suggest that the winter in this region, together with other factors, may contribute to the late development of the disease.

Kewwords*:* Brazil. Schizophrenia. Seasonality. Season of birth. Subtropical region.

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Resumo

Objetivo: Investigar estatisticamente a relação da sazonalidade com o período de nascimento, em 461 pacientes que apresentam esquizofrenia internados em três instituições de psiquiatria nas cidades de Araras, Itapira e Espírito Santo do Pinhal, localizadas no interior do Estado de São Paulo, região sudeste do Brasil. **Método:** Os dados coletados constam de datas e locais de nascimento dos referidos indivíduos, através dos quais se obteve os períodos estacionais dos nascimentos. Esses dados foram analisados através do teste Qui-quadrado. Também foram obtidos os dados de temperatura e precipitação pluvial nos anos de 1952 a 1986, correspondente aos anos de nascimento dos pacientes estudados. **Resultados:** Estes mostraram uma maior prevalência de nascimentos nos meses de inverno (p = 0,0044) caracterizado nessa região por queda na temperatura e na precipitação pluviométrica. **Conclusão:** Os achados indicam uma possível influência da sazonalidade na patogênese de esquizofrenia e sugerem que o período de inverno nesta região poderia, juntamente com outros fatores, contribuir para o desenvolvimento tardio da esquizofrenia.

Palavras-chave: Brasil. Esquizofrenia. Sazonalidade. Estação do nascimento. Região subtropical.

Introduction

Recent studies have shown that environmental factors might be involved in the development of schizophrenia. The importance of these factors has been demonstrated by the fact that in monozygotic twins discordant for schizophrenia, environmental variations might have resulted in inter-individual differences[1]. Thus, current etiological models regarding the pathogenesis of this disease propose interactive effects between multiple genes and environmental factors[2].

Most risk factors associated with the development of schizophrenia occur during the prenatal and perinatal period of life. According to Torrey et al.[3], birth rates during the winter and spring months are 5 to 8% higher among individuals that later develop schizophrenia than in the general population during the same months.

Many of the studies investigating the relationship between schizophrenia and winter births have been conducted in the northern hemisphere where marked variations in temperature occur[3-4]. Studies carried out in tropical regions where no marked seasonal variation is present may contribute to the understanding of the influence of the winter period on the genesis of this disease. A study conducted on a tropical island in the southern hemisphere showed no correlation between seasonality of birth and schizophrenia[5]. The same was reported by McGrath and Welham[6] in studies conducted in the southern hemisphere, who observed no significant correlation between individuals with schizophrenia and winter births. However, another study carried out in an equatorial region demonstrated a significant number of patients with schizophrenia who were born during the colder period of the year[7].

Many studies have also reported a relationship between the period of birth of individuals who develop schizophrenia and prenatal exposure to viral agents such as the influenza virus when patients are exposed to this pathogen during the second trimester of gestation[8-9]. In addition, rain, humidity and temperature positively contribute to the

transmission of pathogens such as dengue and influenza, and rubella, diphtheria and poliomyelitis viruses have been suggested to be involved in the etiology of schizophrenia[10-13].

Suvisaari et al.[12] studied the relationship between the incidence of poliomyelitis and season of birth of individuals who later developed schizophrenia. In that study, the authors included place of birth, age, gender and seasonality as variables and investigated the incidence of the poliovirus epidemic during different gestational periods. A significant association between these factors was observed. Prenatal infections with poliovirus and enterovirus have been suggested to contribute to the development of schizophrenia as demonstrated by the decline in the incidence of this disease in many countries after the introduction of the poliomyelitis vaccine[14-15].

Individuals born in cities with a high demographic density are more likely to develop infections and this condition may therefore represent a significant risk factor when this exposure occurs during the embryonic or neonatal period or during childhood[16]. The effects of infections on the late development of schizophrenia have been confirmed in various epidemiological studies. Since the incidence of most infectious agents shows seasonal variations, different studies have suggested that patients with schizophrenia born during winter may have been under the influence of these agents. Increased birth rates in urban regions may increase the chance of infection during the gestational and neonatal period due to a high population density, thus representing a risk factor for schizophrenia[3-17-21]. Winter births in urban areas might be associated with a higher risk of schizophrenia than in rural areas, suggesting that infections increase the risk for this disease[22-23].

The study area includes one metropolitan city, Campinas, seven medium-sized cities in terms of economic development (Mogi Mirim, Mogi Guaçu, Araras, Rio Claro, Limeira, Piracicaba, and São João da Boa Vista), and four smaller towns (Espírito Santo do Pinhal, Aguaí, Itapira, and Cordeirópolis). This area was chosen based on the fact that it is part of a region of high economic development and is located in the transition area between the tropical zone (two well-defined seasons, dry winters and rainy summers) and temperate zone.

The objective of the present study was to investigate the correlation between seasonality (winter) and the number of births of patients with schizophrenia hospitalized at three psychiatric facilities in the towns of Araras, Itapira, and Espírito Santo do Pinhal, interior of the State of São Paulo, southeastern Brazil. This region is located in a transition area between the tropical and subtropical zone. The research was approved by the Uniararas Ethics Committee (Protocol number 075/2005).

Methods

Sampling

The patients analyzed in the present study were hospitalized in psychiatric hospitals in the towns of Araras, Itapira, and Espírito Santo do Pinhal, State of São Paulo, southeastern Brazil. Patients were selected according to the medical diagnosis made by the respective institutions, which provided a total of 461 medical records of patients with schizophrenia for the study, including patients of both sexes ranging in age from 17 to 37 years. Ethnic differences between the patients were not considered.

The data collected included the date and place of birth of the patients. These data were used to correlate number of individuals with schizophrenia and the month and season of birth. The clinical evaluation of these patients was performed by psychiatric institutions where the diagnoses were obtained based on the International Classification of Diseases (ICD).

Statistical analysis

The patients studied (n = 461) were grouped according to the month and sea-

son of their respective periods of birth for application of the chi-square test, which is appropriate for the analysis of differences in observed and theoretically expected frequencies, the same for all months and seasons of the year. This test was used to determine the correlation between season and the number of births of individuals with schizophrenia.

The dates of birth of the patients in relation to season of the year were distributed according to the dates of the beginning and end of each season in the southern hemisphere. In this hemisphere, spring starts on September 23 and ends on December 21, summer starts on December 22 and ends on March 20, autumn starts on March 21 and ends on June 21, and winter starts on June 22 and ends on September 22. This procedure could be applied because the exact days of birth were available for each individual.

Geographic setting

The study area comprised 12 cities in the interior of the State of São Paulo, Brazil (São João da Boa Vista, Espírito Santo do Pinhal, Aguaí, Itapira, Mogi Mirim, Mogi Guaçu, Araras, Rio Claro, Cordeirópolis, Limeira, Piracicaba, and Campinas), located between 22°54'46 S latitude and 47°38'45" W longitude and 21°58'8" S latitude and 46°47'24" W longitude, at the relief of the Paulista Peripheral Depression between the Eastern Crystalline Plateau and Western Plateau of São Paulo, at a mean altitude of 680 m .

According to the classification of Köppen adapted for Brazil, the climate of the study areas is of the Cwa type (humid mesothermal climate, with hot and rainy summers). Rainfall and temperature are two climatic parameters that vary between the winter and summer seasons in the tropical zone.

Temperature and rainfall data for the 1952 to 1986 series, corresponding to the years of birth of the patients studied, were obtained from ESALQ, USP (2006)*.

Results

Analysis of the data revealed a lack of temperature data for some months in 1971, 1972 and 1973. Thus, in the present study the series from 1952 to 1970 and from 1974 to 1986 were considered for climatological analysis. As shown in Figures 1 and 2, the mean maximum annual temperature varied, with temperatures higher during summer (approximate mean of 30°C) than during winter (approximate mean of 26°C). As can be seen in Figure 1, mean monthly and seasonal (autumn and winter) rainfall indices for the 1952 to 1970 and 1974 to 1986 series varied between the summer season (December, January and February) and the end of autumn (May) and winter (June, July and August). Higher rainfall indices were observed during summer, with a mean of 188 mm, and the lowest indices were observed during winter, with a mean of 29 mm.

Figure 2 shows the distribution of the patients studied along the months of the year by birth period comprising the years from 1952 to 1986. A larger number of births was observed in June (n = 52), which corresponds to one of the periods with the lowest median temperature and rainfall index (Figures 1 and 2). As can be seen, more patients with schizophrenia were born during the winter season (n = 147).

Analysis of the data by the chi-square test (X^2 = 18,245 for 3 degrees of freedom) showed a non significant difference in the distribution of births when classified according to month (p = 0.0761), but this difference became significant when births were grouped according to season (p = 0.0044). In this case, the chi-square was 13,091 for 3 degrees of freedom.

Discussion

The present results showed a higher frequency of births during the winter season, with this period being characterized by lower mean temperature and rainfall

* ESALQ.USP.DadosMeteorológicos. http://esalq. usp.br/departamentos/lce/posto.html. [Accessed October 24, 2006]

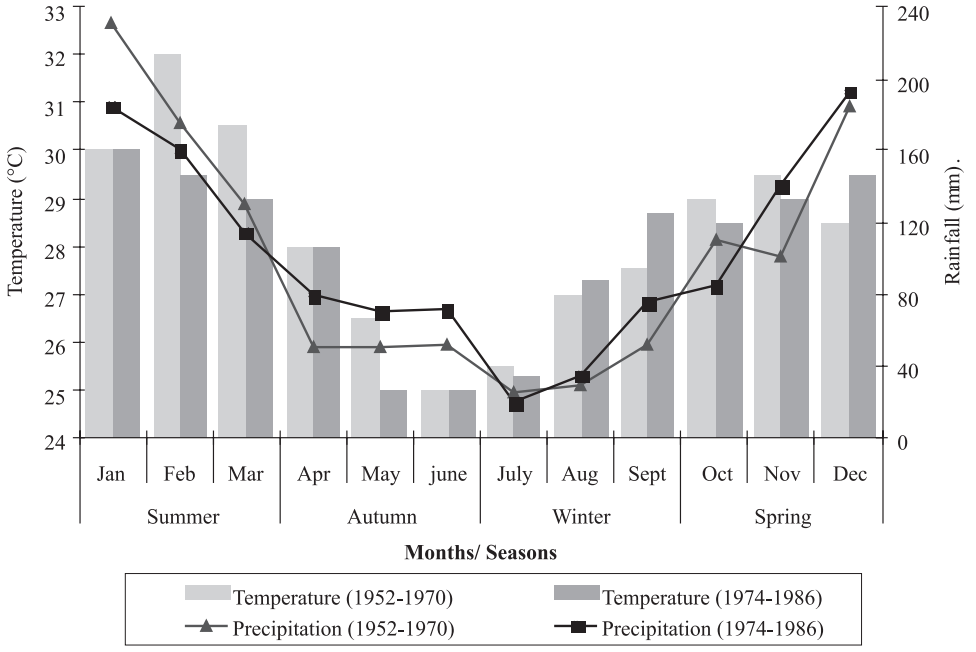

Figure 1 – Mean maximum temperature and rainfall (1952-1970 and 1974-1986) according to month of the year, highlighting the different seasons.
Figura 1 – *Médias máximas de temperatura e precipitação (1952-1970 e 1974-1986) de acordo com o mês do ano, destacando-se as diferentes estações.*

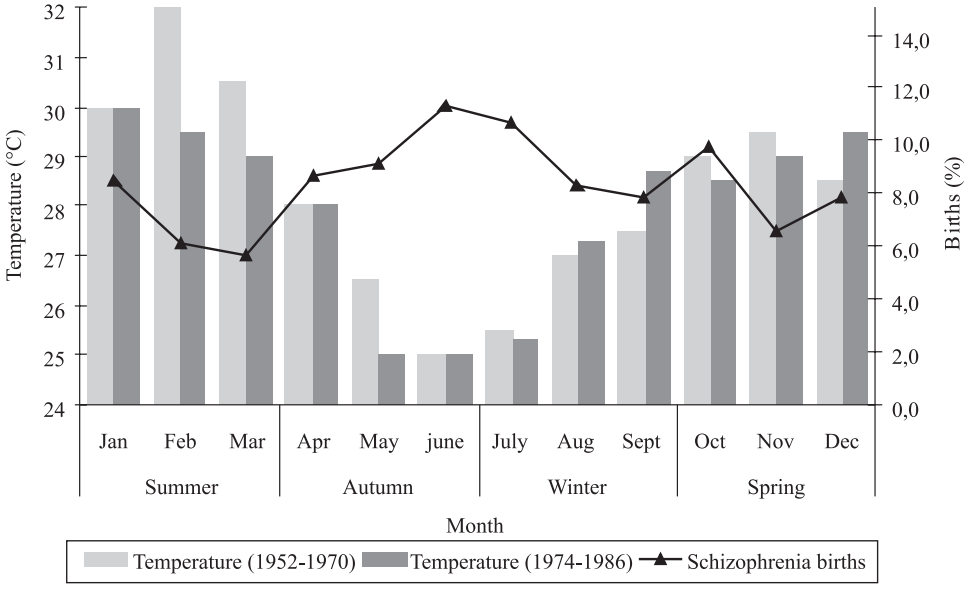

Figure 2 – Mean maximum temperature and percentage of schizophrenia births according to month of the year, highlighting the different seasons.
Figura 2 *– Temperatura média máxima e porcentagem de nascimentos de indivíduos que apresentam esquizofrenia de acordo com o mês do ano, destacando-se as diferentes estações.*

indices in the cities of birth of the patients included in this study (southeastern Brazil in the tropical zone and in the transition zone to subtropical climate). Similar results have been reported by Carrion-Baralt et al.[24] (2004) who studied the effects of seasonality

as a risk factor for schizophrenia in a tropical region. The authors found that the risk of development of this disease was 36.48% higher for individuals born in February (lowest temperatures in this region) compared to those born in other months of the year.

In the northeastern region of Brazil which is characterized by distinct dry and rainy seasons, de Messias et al.[25] observed a significant number of individuals born between May and June who later developed schizophrenia and a significant correlation between these births and a high rainfall index 3 months before birth. In this region, a small decline in temperature also occurs during the rainy period. De Messias et al.[26] also studied the relationship between season of birth and schizophrenia comparing a group of patients with schizophrenia with multiple control groups presenting other disorders such as non-specified psychosis and other psychiatric diagnoses. The authors observed that patients with schizophrenia had a significantly greater risk of being born during the risk period than any of the control groups. In addition, the authors found a significant association between rainfall in a month and schizophrenia births 3 and 4 months later, thus indicating a significant influence of seasonality and birth period in northeastern Brazil.

However, in the present study, the month presenting the lowest mean temperature and rainfall was June, a month during which a significant number of winter births was observed among patients with schizophrenia.

Most studies correlating seasonality and schizophrenia conducted in North America and Europe reported a higher concentration of births of individuals with this disease during winter (or winter-spring) compared to summer[3-19]. These observations agree with the present results. Our climatic analysis revealed a significant correlation between the number of births of individuals who developed schizophrenia and the winter period. However, a meta-analysis of 12 southern hemisphere studies found a non significant excess in winter schizophrenia births[6].

According to McGrath[27], low temperatures and rainfall indices provide the ideal conditions for propagation of viral agents, and seasonal changes such as a shorter duration of sunlight during the day, i.e., longer nights in winter is another positive factor that contributes to the contraction of viral diseases. Dowell[28] also suggested that physiological variations related to annual light-dark periods and the melatonin secretion rate reduce the resistance of humans to infectious diseases.

Urashima et al.[29] observed that the incidence of influenza was significantly associated with a decline in temperature during winter in Japan. Hope-Simpson[30] proposed that the influenza virus shows a latent behavior and manifests according to adequate environmental conditions such as photoperiodicity or temperature. In a study carried out in southeastern Thailand (Southeast Asia, tropical zone), Chumkiew et al.[31] showed that variations in temperature and rainfall are associated with incidence of the influenza virus.

In addition to the influenza virus, other factors vary throughout the year and might be associated with the genesis of schizophrenia. These factors include level of sunlight, vitamin D synthesis and nutritional changes[27-32]. Altamura et al.[33] suggested that genetic and environmental factors might play a role in the pathogenesis of schizophrenia and raised the hypothesis of the involvement of infectious agents associated with immunological alterations. Carrion-Baralt et al.[34] found a significant number of winter births among individuals who later developed schizophrenia on a tropical island in Puerto Rico, a region characterized by the lack of marked seasonal variations. These authors suggested that cold temperatures are not sufficient to determine this disease unless they are associated with a genetic predisposition. The viral hypothesis of schizophrenia has found support in studies in which an increase of winter births, prenatal exposure to epidemic viral infections and specific geographic conditions were observed [8-3-35-36].The region studied here is a

transition zone from tropical to subtropical climate, where there are seasonal variations in climatic parameters such as temperature and rainfall.

The limitation of this study is the size of our sample of patients with schizophrenia. The objective of the present study was to investigate whether there is a significant seasonal influence on the patients with schizophrenia analyzed. This fact explains the modest number of cases when compared to other similar studies that correlated the number of schizophrenia births with data of the general population.

In conclusion, statistical analysis showed a significant increase in the number of individuals born in the initial months of winter (June and July) among the patients with schizophrenia studied. Thus, the results suggest that the winter period in this region characterized by low rainfall indices and a decline in temperature, together with other factors, may contribute to the late development of schizophrenia.

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