Season of birth in schizophrenia: no latitude at the equator

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Background   If the established winter excess in births of people who subsequently develop schizophrenia is an effect of 'seasonality', this would be testable by examining the pattern of births in an equatorial region with no formal seasons.

Aims   To investigate whether there is any variation in month of birth among patients from equatorial Singapore with a diagnosis of schizophrenia.

Method   All 9655 patients discharged from Singapore's national psychiatric hospital with a diagnosis of schizophrenia were included (year of birth range 1930–1984). We analysed aggregated data, as well as the data of subsamples grouped according to birth-year periods, in order to examine secular trends. One patient subsample (those born 1960–84) allowed exact matching against the general population data set and close testing of any seasonal influence.

Results   Monthly variation in births was evident for both patients and controls; the patterns were very similar, apart from the patient sample showing a trough in March–April.

Conclusions   In an equatorial region, where 'seasons' are absent, no seasonal excess in births of those later developing schizophrenia was evident.

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Seasonal birth patterning in those with schizophrenia has been extensively studied, principally in order to identify determinants and 'preventable causes' (Hare *et al*, 1974). Published epidemiological studies reviewed by Torrey *et al* (1997) identified a winter–spring birth excess, of the order of 5–8% in virtually all 76 northern hemisphere studies. A recent meta-analysis of 12 southern hemisphere studies (McGrath & Welham, 1999) suggested that a non-significant winter excess exists. The seasonal excess is unlikely to be trivial on a population basis – while a family history of schizophrenia was associated with the highest risk of having schizophrenia in a Danish general population cohort (Mortensen *et al*, 1999), degree of urbanisation and season of birth accounted for more cases on a population basis. Multiple explanations for seasonality include, according to Torrey *et al* (1997), seasonal parental procreation habits, genetic factors, prenatal and birth complications, seasonal variation in external toxins, nutritional deficiencies, infectious agents and numerous meteorological variables. One epidemiological approach to clarification is to undertake studies in equatorial regions, where formal 'seasons' are absent; such a study is reported here.

METHOD

Regional nuances

Singapore is situated only 137 km (or 2 degrees) north of the equator, occupies only 641 km² , and is highly urbanised, with a population of more than three million. The warm tropical weather is relatively consistent throughout the year; data obtained from the Changi Meteorological Station for the last 10 years (i.e. 1989–98) show mean monthly temperatures ranging across a narrow band of 26.4–28.4 °C. There is no distinct 'wet' season, although rainfall is higher during the north-east monsoon season from November to December.

Subjects

The subjects were obtained from computerised records of all patients from Woodbridge Hospital (Singapore's national psychiatric hospital) who were discharged with a recorded diagnosis of schizophrenia (ICD codes of 295.0–295.4 and 295.9) (World Health Organization, 1992). Subjects with multiple discharges were counted only once, while those without a national identity card number were excluded (in order to minimise the chance of including those not born in Singapore). Region of birth was not recorded on the computerised record and we therefore undertook a record review of one in four of the selected cases in an attempt to establish place of birth. Monthly general population birth data were only available from 1960 onwards.

Statistical analyses

Adjustment for varying numbers of days per calendar month and for leap years was made. A χ^2 test examined for goodness of fit between observed and expected monthly births in the patient sample, but it is a limited test for cyclic data. Following earlier suggestions by Mardia (1972), Machin & Chong (1998) described a method for estimating the peak date of birth with grouped data. This technique requires establishing the magnitude of this peak (termed the mean resultant or R). If all the data are concentrated at a particular date the resultant will equal unity, whereas, if the distribution is uniform over the year, the resultant will equal zero (although values of zero are also possible if the distribution has two peaks six months apart). It is important to note that quoting the peak 'day' when using monthly data as the unit of analysis risks spurious accuracy, so any such identified 'day' should be interpreted with caution. Once the peak is calculated, approximate confidence intervals can be obtained, while the Mardia statistic (which has two degrees of freedom) tests specifically for the presence of a single peak in the data.

RESULTS

Of the 9655 patients identified with a discharge diagnosis of schizophrenia, 514 (5%) had no date of birth recorded in the computer, leaving a definitive sample for analysis of 9141 subjects, all of whom were born between 1930 and 1984. A review of 2415 cases (about a quarter) showed that place of birth was not recorded for 876.

Where place of birth was recorded, it was Singapore for 1531 patients and other regions for 23 patients – five from Malaysia and Thailand, three from India, Pakistan or Sri Lanka, and 15 'others'.

The monthly distribution of births is shown in Table 1, both for the whole sample of subjects with schizophrenia and for subsamples from three intervals (1930–49, 1950–59 and 1960–84) comprising 2702, 3046 and 3393 subjects respectively. Subsample analyses examined for consistency in any birth pattern in the subjects with schizophrenia over time. The pattern in the raw (and adjusted) distributions was relatively consistent across the subsamples, with, in essence, the lowest birth rates occurring in March or April, and the highest in September or October. For the 1960–84 sub-sample (where we possessed matched general population year of birth data), we calculated the number of schizophrenia sufferers expected to have been born in each month by using the season of birth pattern in the general population and then made a comparison against the observed distribution. Observed and expected births showed the most distinct difference in March (with a decrement of 12%), but the overall distributions of observed and expected births across all 12 months did not differ.

Analyses of the data in Table 2 estimating the peak date of births of people later diagnosed with schizophrenia identified the peak months as October for the 1930–49 subsample and September for both the 1950–59 and 1960–84 subsamples. In the first and third subsamples, the values of P are small, indicating the presence of a single peak, but these peaks were of little epidemiological importance as the corresponding values of this mean resultant are so small. A similar pattern is evident in two subsamples of the general population birth data (subdivided again in order to examine for any secular trend), with the peak occurring at the beginning of October.

Returning to Table 1, key data are the adjusted monthly birth data for the 1960–84 patient subsample, the general population data for the same period, and the monthly ratio of patient to control births for that matched period. The adjusted data (see Table 1) showed peaks in each group in mid-October (and within one week of each other), indicating that if there is any seasonality in birth patterns, it is remarkably similar in both patients with schizophrenia and the general population. Figure 1 plots the monthly birth rates for the two groups.

As the scale on the y-axis does not include zero, fluctuations are graphically exaggerated. The figure nevertheless offers strong impressionistic support to the analyses, with both samples showing fairly variable rates across the year, a strikingly consistent peak in October, and a generally similar pattern (albeit with a more distinct March–April trough in the patient group).

We also examined the distribution of monthly births for those whose case file did not formally record birth in Singapore. Both in comparison with the whole sample of those with schizophrenia and in comparison with the general population, their monthly distribution was not significantly different.

DISCUSSION

Methodological issues

Torrey *et al* (1997) note a number of problems in seasonality studies. We addressed the accuracy of birth data by excluding subjects where no birth date was recorded, and ensured against duplication in counting subjects. The issue of ensuring a valid diagnosis of schizophrenia is more problematic as, while ICD diagnoses were recorded, no formalised diagnostic measures were used, so reliability was subject to the degree of clinical sophistication involved in the diagnosis (as in most studies). Concern about the sample being distorted by inclusion of immigrants from a non-equatorial region was addressed by including only those with a national identity card, and the one-in-four sample of all file data ensured that this strategy largely limited inclusion to those born in Singapore. In that analysis, of those with an identified region of birth, 98% were born in Singapore. While the region of birth was not recorded for a substantial percentage of subjects, we believe that our other strategies, particularly that of including only those with a national identity card (which is rarely provided to those born elsewhere), minimised the chance of non-regional subjects being included. The last concern would, of course, only create an interpretive problem if the patient and control data differed in their yearly pattern – which turned out not to be the case. Finally, we examined the monthly distribution of births in those whose file failed to record the region of birth, and established that it did not differ from the monthly birth distributions in the overall schizophrenia sample and in the Singapore general population.

General population control data were used (not always the case in the seasonality literature) and, in case there had been any variation in birth patterns across the decades (for either the patients or the general population), we focused on monthly birth data for patients and general population subjects born over the same interval (1960–84). Nevertheless, subsamples of patients born over other periods (and of the general population data) revealed relative consistency over time. We analysed by month, as opposed to the quarters or half years used in many other studies, and had a larger sample than the estimate (by Hare, 1975) of 4500 required if monthly distributions are to be examined. Our principal analytic strategy focused on determining peaks in the patient and general population samples – and any peak in the excess of patients over the general population.

Absence of seasonality

While there was a monthly variation in the births of those later developing schizophrenia, the variation was largely parallel to the seasonal pattern found in the general population. The study has therefore delivered a highly suggestive finding – that in a 'season-less' equatorial region where there is monthly variation in birth patterns, those later developing schizophrenia fail to show any monthly excess of births relative to the general population. These results contrast with a previous equatorial study undertaken in the Philippines (Parker & Balza, 1977), where an extremely large December–February excess of 15% was found. However, the Philippines is less 'equatorial' than Singapore (being 15 degrees north of the equator), and has relatively distinct wet and dry seasons; moreover, matching of patient and general population data was limited in that study.

Why is there any birth peak?

The reason for there being any September–October birth peak in Singapore (as evidenced in both groups) – and for it being such a consistent one – remains unclear but, if it relates to variation in procreation, some variable must operate across the December–January period. Christmas is in this period, and Chinese New Year usually falls in January or February; it is a two-day public holiday in Singapore and many businesses close for several days. There is, however, no known significance in becoming pregnant at such times, at least to the

Table 1 Monthly distribution of births of patients subsequently diagnosed with schizophrenia across three periods (1930–84) together with monthly distribution of all general population live births in Singapore, 1960–84

Period	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
Patients with schizophrenia													
1930–49	245	194	208	187	224	197	218	227	237	290	242	233	2702
1950–59	256	223	252	230	276	250	259	253	270	242	248	287	3046
1960–84	291	262	246	247	281	291	293	299	285	322	289	287	3393
Total	792	679	706	664	781	738	779	779	792	854	779	807	9141
All live births 1960–84													
Total	96 185	86 925	96 969	94 305	97 858	97 234	100 164	102 825	104 574	111 234	104 747	101 987	1 195 007
Adjusted births 1960–84[1]													
Patients	285.8	281.8	241.6	250.6	276.0	295.3	287.7	293.6	289.2	316.2	293.3	281.8	3393
All births	94 467.8	93 584.4	95 237.8	95 708.8	96 110.9	98 681.4	98 375.8	100 989.3	106 130.6	109 248.1	106 306.2	100 166.2	1 195 007
Ratio (per 1000)	3.03	3.01	2.54	2.62	2.87	2.99	2.92	2.91	2.72	2.89	2.76	2.81	2.84

1. 'Adjusted' refers to adjustment in raw data for varying number of days in a month and allowing for leap years.

Table 2 Date identified as peak date of birth (with 95% CI estimates)

	Period	n	Date of peak	95% CI	R	χ^2 (Mardia[1])	P
Patients with schizophrenia	1930–49	2701	28 Oct	30 Sep to 17 Nov	0.065	22.8	<0.001
	1950–59	3046	30 Sep	—[2]	0.010	2.4	0.2
	1960–84	3393	28 Sep	16 Aug to 3 Nov	0.038	9.8	<0.01
Total	1930–84	9141	14 Oct	19 Sep to 8 Nov	0.035		
All live births	1960–69	55 197	3 Oct	28 Sep to 9 Oct	0.020	441.0	<0.001
	1970–84	643 810	1 Oct	30 Sep to 4 Oct	0.032	1135.7	<0.001
Total	1960–86	1 195 007	2 Oct	30 Sep to 4 Oct	0.032		

1. See Mardia (1972).
2. The approximation for the CI is inapplicable as R is too small.

majority Chinese population; the Chinese astrological calendar gives more importance to auspicious and inauspicious years, rather than months, of birth.

Do the results reflect absence of seasonality in virus infections?

The extent to which seasonality may be a proxy for environmental risk factor has encouraged previous researchers to pursue a range of factors, particularly seasonal variation in viral illness. We therefore sought such data for Singapore. Doraisingham *et al* (1988) reported on influenza surveillance data for the period 1973–86 in Singapore. Despite being equatorial, Singapore showed the same seasonal pattern in viral illnesses as that found in temperate zones (i.e. a bimodal pattern, with a 'major seasonal increase' occurring from April to June, and usually extending into July, and a second increase during the last quarter of the year and extending into the beginning of the next year). Doraisingham *et al* (1988) speculated that patterns might

reflect temperature changes, noting that the major seasonal peak in influenza occurred during the 'warmest' period of the year (when mean monthly temperatures ranged from 26.4 °C to 28.2 °C), while the second peak occurred during the coldest months (mean temperature 24.8–

26.6 °C). Both periods preceded the periods of the greatest daily temperature fluctuations, which, the authors suggested, might indicate vulnerability effected by the "host's defence mechanisms". The alternative explanation (one considered by the authors) points to Singapore's busy
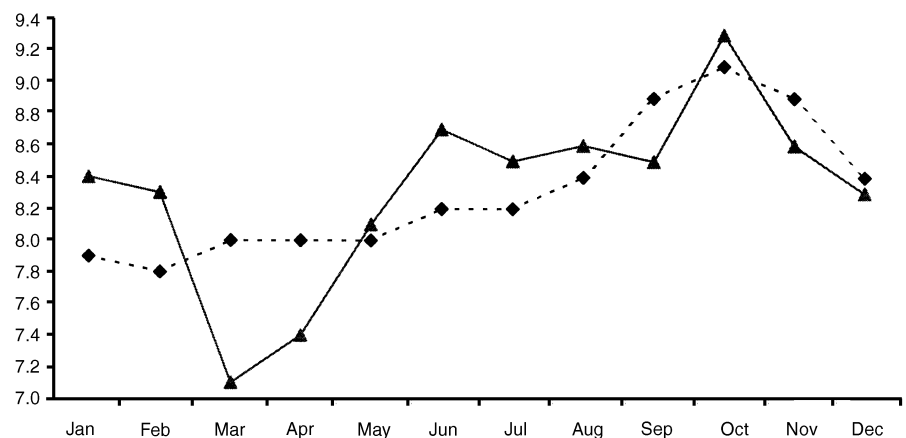
Fig. 1 Adjusted mean monthly percentages of births for patients with schizophrenia and general population subjects born 1960–84. --◆--, general population; —▲—, patients.

airport, which would facilitate the rapid spread of influenza from less temperate regions which have marked seasons – so 'imposing' or 'importing' a seasonal pattern to Singapore's temperate region.

Torrey *et al* (1997) concluded that the seasonal birth factor in schizophrenia is more likely to affect those "born in, or raised in, urban areas". In the equatorial region of urbanised Singapore, however, the monthly distribution of births in those with diagnosed schizophrenia appears consistent with the pattern recorded in the general population, while monthly peaking was identical. Such a finding suggests that in the absence of 'seasons', there is no evidence of a distinctive seasonal birth pattern in schizophrenia. If valid, the importance of such a negative result lies in reducing the list of putative risk factors that have been postulated over a lengthy period.

CLINICAL IMPLICATIONS

■ In an equatorial region (Singapore) there does not appear to be any increased risk of developing schizophrenia associated with being born at a particular time of year.

■ In the absence of any such environmental influence, schizophrenia may have a different phenotypic expression in equatorial regions.

■ These results argue against a link between any seasonal variation in schizophrenia and the subjects born in an urban area.

LIMITATIONS

■ The diagnosis of schizophrenia was a clinical one, not one generated by the use of a standardised diagnostic measure.

■ Reasons for an October excess in births in both the subjects with schizophrenia and the general population remain to be established.

■ The suggested slight trough in March and April births of those later developing schizophrenia is not explored.

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