OBSTETRICS

Seasonal variation in pregnancy hypertension is correlated with sunlight intensity

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OBJECTIVE: To examine seasonality of pregnancy hypertension rates, and whether they related to sunlight levels around conception.

STUDY DESIGN: Data were obtained for 424,732 singleton pregnancies conceived from 2001 through 2005 in Australia. We analyzed monthly rates of pregnancy hypertension and preeclampsia in relation to monthly solar radiation.

RESULTS: Pregnancy hypertension rates, by month of conception, were lowest in autumn (7.3%) and highest in spring (8.9%). Higher sunlight intensity before delivery, but not around conception, was associated with decreased pregnancy hypertension ($r = -0.67$). Increased sunlight around conception may correlate with decreased rates of early-onset preeclampsia ($r = -0.51$; $P = .09$).

CONCLUSION: The correlation between sunlight after conception and pregnancy hypertension was opposite to that hypothesized; however, sunlight levels before delivery did correlate with lower hypertension rates. For sunlight or ambient temperature to explain seasonal variation, the plausible exposure window is the period before delivery, but this may not apply to early-onset preeclampsia.

Key words: preeclampsia, pregnancy hypertension, seasons, sunlight, vitamin D

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Pregnancy hypertension is a leading cause of morbidity and mortality for both mother and infant.[1] It includes a spectrum of disorders characterized by the de novo onset of hypertension after 20 weeks of gestation and ranging from hypertension alone (gestational hypertension) through proteinuria and/or multiorgan dysfunction (preeclampsia) to seizures (eclampsia).

Previous studies have looked at seasonality of preeclampsia but only a few have examined the broader category of pregnancy hypertension.[2,3] Most studies have been based in a single hospital.[2,4-7] In the few population-based or large multicenter studies, preeclampsia rates were reported to be lower for summer births[3,8,9] and autumn conceptions.[10] Seasonal variation is also known to affect cardiovascular mortality rates in general populations and possible explanatory factors that have been suggested include sunlight intensity (due to resultant variations in vitamin D levels) as well as temperature and humidity.[11] Concurrently, there is interest in a possible role for vitamin D insufficiency in early pregnancy as a risk factor for preeclampsia. One study reported that low serum vitamin D in early pregnancy was associated with an increased risk of preeclampsia.[12] Another study reported a reduced risk of preeclampsia with higher intake of vitamin D supplements.[13]

We used a maternal population database, which can longitudinally link women's antenatal records and delivery records, to follow cohorts of pregnancies by month of conception. Our purpose was not just to quantify the monthly variation, but also to examine the implications of using conception, rather than delivery, as the basis for calculating pregnancy hypertension rates. We hypothesized that any seasonality in preeclampsia and pregnancy hypertension rates could be related to variation in early pregnancy exposure to sunlight intensity, as synthesis from sunlight is generally the source of 80-90% of vitamin D in humans.[14] We used Bureau of Meteorology data to look for any plausible correlation between pregnancy hypertension rates and sunlight levels in early pregnancy or in the period before delivery.

Materials and Methods

Data on all women giving birth in hospital (>99% of births) in New South Wales (NSW), Australia, were available from anonymized linked population databases. The Midwives Data Collection (MDC) is a legislated surveillance system of all births in NSW. The Admitted Patient Data Collection (APDC) has discharge summaries of all hospital admissions (public and private) and includes International Classification of Disease-10 (ICD-10) diagnostic codes related to the admission. A MDC delivery

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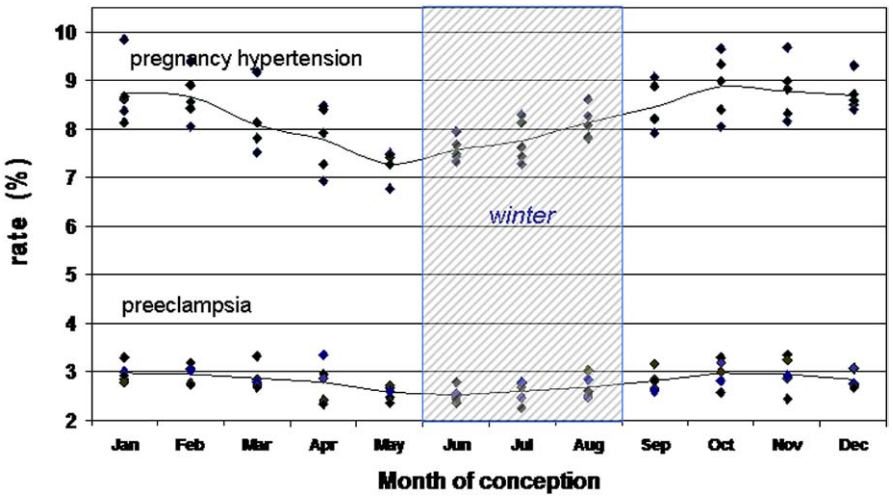
FIGURE 1
Distribution of monthly pregnancy hypertension and preeclampsia rates, by month of conception, 2001-2005



Pregnancy hypertension includes MDC code OHYPER.

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record was linked to a hospital admission for 99.1% of births in the study population. Multiple pregnancies were excluded because of their unique risk factors.

Date of conception for each pregnancy was estimated by subtracting the gestational age from the date of birth, but adding 2 weeks as an average for time from last menstrual period to conception. Gestational age is well reported on the MDC (85% perfect agreement) and only 57 birth records (0.01%) in the study population were missing a gestational age. The primary outcome of pregnancy hypertension (hypertension [≥140 mm Hg systolic and/or ≥90 mm Hg diastolic] arising after 20 weeks) included gestational hypertension (hypertension alone), preeclampsia (hypertension with proteinuria and/or multiorgan disease) and eclampsia (seizures),[15] and was determined by a diagnosis in any hospital record (including antenatal admissions) or by check-off box notification on the MDC birth record. Superimposed preeclampsia (on preexisting hypertension) was not included in either outcome, as the cause may differ. Pregnancy hypertension ascertainment is greatest when cases are identified from either data source and when the broader category of pregnancy hypertension is used (sensitivity 82%, positive predictive value 92% compared with clinical criteria extracted from medical records).[16] A diagnosis of preeclampsia (including eclampsia) was only available from the hospital discharge summaries and was a secondary outcome. Because it has been suggested that the pathology of early-onset preeclampsia may differ from late-onset preeclampsia, we also examined preeclampsia rates subdivided into 2 categories: early-onset (delivery by ≤34 weeks) and later-onset preeclampsia (delivery after 34 completed weeks).[17]

NSW is in the Southern Hemisphere and the seasons are reversed from the Northern Hemisphere; winter occurs in June-August and summer in December-February. The NSW population is geographically concentrated; 75% of the population live in the coastal areas centered on Sydney, which lies at 34° latitude (similar to Los Angeles in distance from the equator). Monthly means of daily solar radiation as measured by the Bureau of Meterology's Sydney airport station were used to represent the exposure for the state's maternal population by month. Solar radiation (sunlight energy) is reported as a daily average in units of megajoules per square metre (MJ/m^2) of land surface, available on the bureau's website (www.bom.gov.au). The daily solar radiation is affected by cloud cover as well as by sunlight intensity and length of the day.

Rates of pregnancy hypertension and preeclampsia were calculated for monthly conception cohorts of singleton pregnancies. Estimated conception dates for the study population ranged from January 2000 through December 2005. To investigate the nature of any association between hypertension rates and solar radiation levels, we calculated Pearson correlation coefficients (r) for different sunlight exposure "windows": month of conception, 1 month before conception, 1 month after conception, etc. The correlation coefficient has a value of zero if there is no correlation, a value of +1.0 if the exposure and outcome are perfectly and positively correlated and a value of −1.0 if perfectly and inversely correlated. We also used least squares linear regression to model the slopes of the associations between average solar radiation for each month (for all 5 years) and the hypertension outcomes.

RESULTS

There were 424,732 singleton pregnancies included in the monthly conception cohorts in the study period (January 2001 to December 2005) that were delivered at ≥20 weeks' gestation. The mean annual pregnancy hypertension rates and preeclampsia rates were 8.2% and 2.8%, respectively. The mean monthly pregnancy hypertension rate peaked at 8.9% for conceptions in October (mid-spring in the Southern Hemisphere); whereas, mean monthly preeclampsia rates were high for conceptions from October through February (spring and summer). The rate of pregnancy hypertension was lowest for conceptions in May (autumn) at 7.3% and preeclampsia was lowest for conceptions in May-July (late autumn to midwinter) at about 2.6%. Figure 1 shows the distribution of monthly rates of pregnancy hypertension and preeclampsia based on the month the pregnancy was conceived. Most women who had pregnancy hypertension diagnosed still delivered at term (≥37 weeks): 88.3% of those with any pregnancy hypertension (relative risk

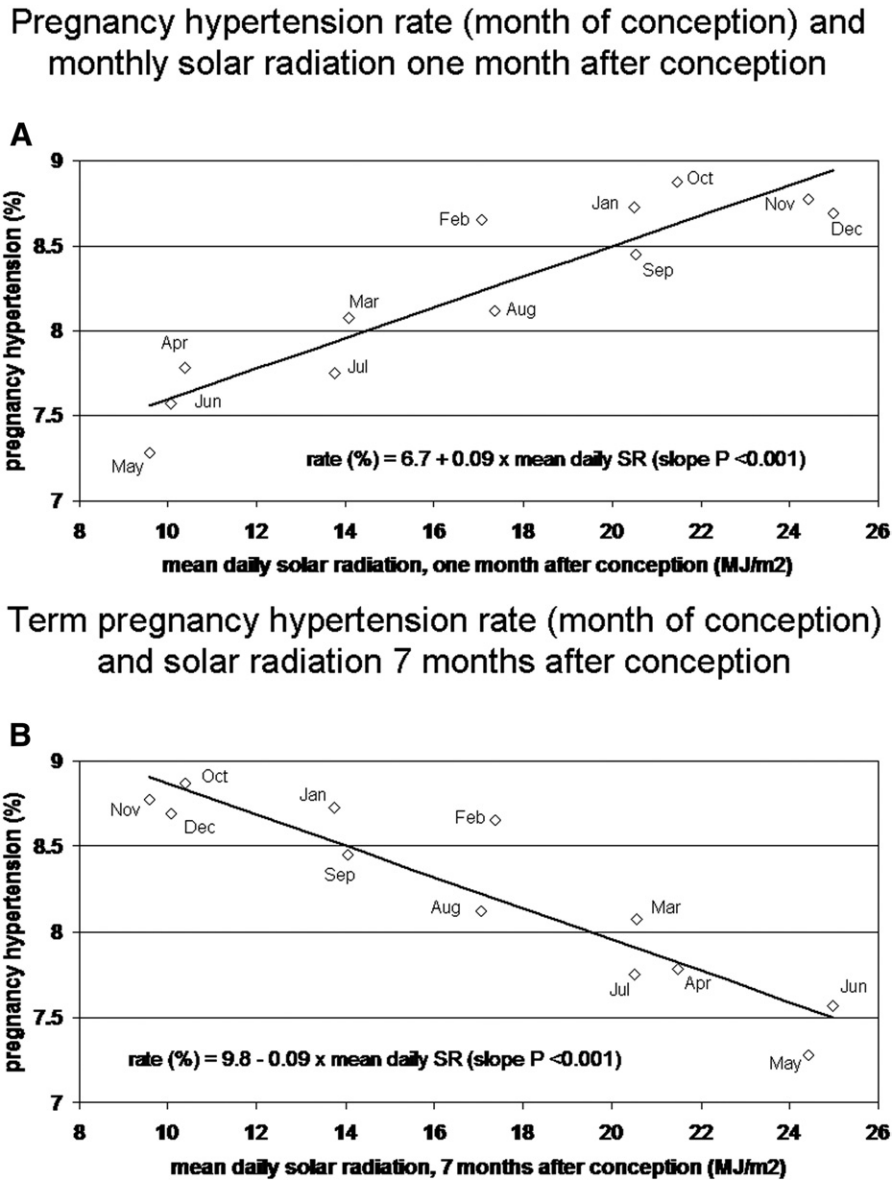
[RR] of preterm birth, 2.20; 95% confidence interval [CI], 2.13–2.28) and 78.2% of those diagnosed with preeclampsia (RR of preterm birth, 4.12; 95% CI, 3.98–4.27).

As an alternative, pregnancy hypertension rates were also calculated by month of delivery. This made little difference to the magnitude of seasonal variation, although the month of incidence was necessarily offset by about 8 months. Calculated by month of delivery, the peak pregnancy hypertension rate was 8.9% (August/September-late winter/early spring) and the nadir was 7.4% (January/February-summer).

Among the preeclampsia cases, there were 1339 (0.32%) with early onset, and 10,571 (2.5%) with late onset. The pattern of seasonality was different for early-onset preeclampsia: the lowest rate was for pregnancies conceived in November/December (0.26%) and the highest rate was for pregnancies conceived in April (0.39%). For later-onset preeclampsia, the seasonal pattern was the same as for the overall rate: lowest was for conceptions in May/June (2.2%) and highest October-February (2.6%).

There was correlation between pregnancy hypertension rates and solar radiation, but the correlations around conception were opposite in sign to what was hypothesized. Pregnancy hypertension was strongly and positively correlated ($r = +0.67$) with solar radiation at 1 month after conception. This signifies that an increased level of sunlight around conception was associated with an increased rate of pregnancy hypertension. However, solar radiation intensity at 7 months after conception was inversely correlated ($r = -0.67$) with pregnancy hypertension rates. That is, more intense sunlight in the period before delivery was associated with lower levels of pregnancy hypertension. The associations between pregnancy hypertension and ambient temperature were similar, except that the strongest correlation was with ambient temperatures 8 months after conception ($r = -0.69$). Only early-onset preeclampsia appeared to be inversely correlated with sunlight levels in early pregnancy ($r = -0.51$ for mean solar radiation in the month after conception), but this did not reach the level of statistical significance ($P = .09$).

FIGURE 2
Pregnancy hypertension rate



A, Mean pregnancy hypertension rate (month of conception cohorts) vs mean solar radiation 1 month after conception. **B**, Mean pregnancy hypertension rate (month of conception cohorts) vs mean solar radiation 7 months after conception.

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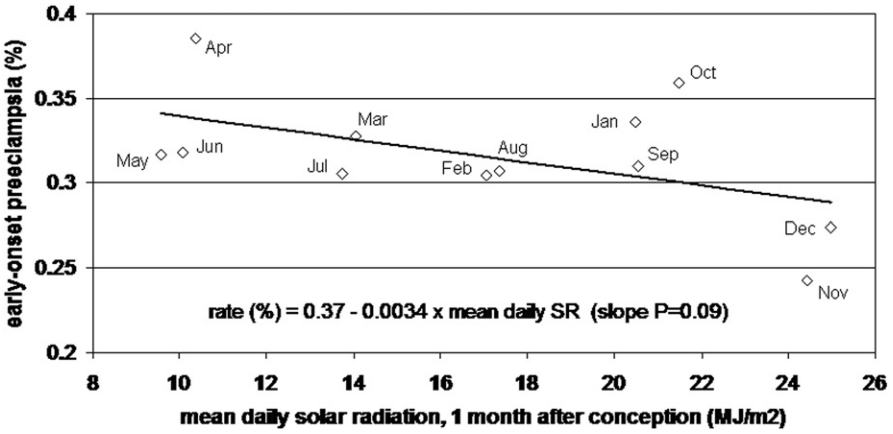
The association between mean solar radiation in the month after conception and the ensuing pregnancy hypertension rate is illustrated in Figure 2, A, a plot of mean monthly pregnancy hypertension rates (averaged over the entire 5 years) against monthly solar radiation levels (5-year averages). The positive slope shows that increased sunlight in this exposure window was associated with increased rates of hypertension. Figure 2, B shows pregnancy hypertension rates plotted against mean monthly solar radiation 7 months after conception. In this plot, increased sunlight in the month or so preceding delivery is associated with decreased rates of pregnancy hypertension. Figure 3 shows the association between

FIGURE 3
Mean rate of early-onset preeclampsia (month of conception cohorts) vs mean solar radiation 1 month after conception



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mean monthly solar radiation 1 month after conception and mean monthly rates of early-onset preeclampsia. There is an inverse correlation between sunlight levels and early-onset preeclampsia but the slope of the association was not statistically significant ($P = .09$).

Comment

We found a definite seasonality to the rate of pregnancy hypertension in our study population. Seasonality existed whether pregnancy hypertension rates were calculated based on cohorts by month of conception or month of delivery. Both increased sunlight and increased ambient temperature in the month(s) before delivery were associated with decreased rates of pregnancy hypertension; whereas, increased sunlight and temperature around conception were associated with increased rates of pregnancy hypertension.

To make sense of this seasonality, it needs to be related to a plausible exposure at some gestational period or periods in pregnancy. There are several potential mechanisms that might explain an association between increased sunlight intensity and reduced hypertension rates. One is seasonal variation in vitamin D levels, because synthesis from sunlight is the main source of vitamin D.[14] Population levels of vitamin D are low from midwinter to early spring (July-October in the southern hemisphere),[18,19] and low levels of vitamin D are associated with an increased risk of hypertension.[20] A second potential explanation could be that increased sunlight levels lead to decreased hypertension rates via the resultant increase in ambient temperature. One study reported that a 10°C increase in daily minimum outdoor temperature is associated with a 2.5 mm Hg drop in systolic blood pressure (SBP) in pregnant women,[21] perhaps due to temperature-related vasodilation.[22] A third possible explanation is that ultraviolet radiation may have a direct effect on blood pressure.[23] Finally, seasonal infections could play a part, as preeclampsia may be an excessive maternal inflammatory response[24] and could be exacerbated by respiratory tract infections that typically peak in winter. All of these explanations would be consistent with an inverse correlation between sunlight intensity and pregnancy hypertension rates, and would point to the relevant exposure period to explain seasonality being the month or months before delivery. As pregnancy hypertension may commonly initiate in early pregnancy, periods of more intense sunlight, or higher ambient temperature may moderate the progression of the disorder, so that relatively fewer women are diagnosed with hypertension, and fewer might progress to severe disease.

In contrast, there is less basis to support a hypothesis that increased levels of sunlight could lead to increased rates of hypertension. Melatonin is a potentially plausible early pregnancy exposure because it is a scavenger of free radicals and can reduce placental oxidative stress which has been associated with early-onset preeclampsia,[25] and concentrations of melatonin are lower in summer than in winter. One study has reported that levels of melatonin were lower in women with severe preeclampsia; however, this was only statistically significant from ≥32 weeks' gestation.[26] An alternate explanation is that seasonal variation in pregnancy hypertension may be a marker or correlate for some other early pregnancy factor not yet discovered.

Our results were inconclusive with respect to early-onset preeclampsia as a separate outcome. Increased levels of sunlight in the month after conception did correlate with lower rates of early-onset preeclampsia but the slope estimated by linear regression did not reach the level of statistical significance ($P = .09$).

The seasonality of pregnancy hypertension in our study population is generally consistent with previous population studies of preeclampsia. A Washington State study of preeclampsia rates based on month of conception found a pattern similar to the results of this study: preeclampsia rates were lowest for conceptions in late autumn/midwinter (northern hemisphere) and highest for conceptions in spring/summer.[10] A Norwegian population study of rates based on month of delivery found that preeclampsia was lowest for deliveries in July and August and highest in November and December,[9] implying that conceptions in late autumn had the lowest rate and conceptions in early spring had the highest rate of preeclampsia. A Swedish study of all nulliparas aged <35 years also reported that the preeclampsia rate was lowest for summer deliveries.[3]

A limitation of this study is that the measurement of sunlight exposure is at the population level. As a surrogate for individual vitamin D levels, ambient temperature exposures or other environmental factors would result in attenuation of any estimated effect. However, random misclassification of exposure would be unlikely to result in a reversal

of the nature of the correlation between sunlight exposure and pregnancy hypertension (from inversely proportional to proportional). Time lag could affect the correlations, because both vitamin D levels and ambient temperatures would lag changes in sunlight intensity, but there was no inverse correlation with solar radiation in any of the first 3 months after conception. An advantage to using month-to-month variation as the basis for comparison in our study is that most potential confounders are controlled for. Aggregate population characteristics such as mean maternal age, parity, body mass index, and proportion with dark skin change relatively little from month to month. Only factors which vary monthly are left as the explanation for variations in pregnancy hypertension rates. This does leave open the potential for confounding by factors such as maternal population physical activity levels, diet, and weight gain, which even in a temperate climate such as in this study can vary from month to month.

Another possible limitation is that case ascertainment is not complete, as the estimated sensitivity for pregnancy hypertension is 82% and milder cases are less likely to be reported in our databases.[16] This could mean that our results are more representative of the severe end of the pregnancy hypertension spectrum. In addition, the imprecision inherent in estimates of gestational age would likely have led to some underestimation of the true degree of correlation between monthly sunlight intensity and hypertension rates.

There was seasonality in pregnancy hypertension rates, and fluctuations in sunlight intensity (and ambient temperature) did correlate with variations in the rates of both pregnancy hypertension and preeclampsia. The nature of the correlation suggests that the most plausible hypothesis for sunlight and ambient temperature as sigificant exposure factors is in the period before delivery and the plausible exposure window for melatonin would be in early pregnancy. The association between sunlight around conception and early-onset preeclampsia may be inversely proportional and would be consistent with a hypothesis that early pregnancy sunlight exposure could affect the risk of early-onset preeclampsia. Further research is required to elucidate the underlying mechanisms behind seasonal variation in pregnancy hypertension. An important goal for such research is to measure the levels of factors such as vitamin D and melatonin at different stages in pregnancy and different seasons of the year, and analyze these in relation to pregnancy outcomes. ■

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