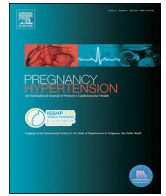




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Seasonality of hypertensive disorders of pregnancy – A South Australian population study



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ABSTRACT

Objectives: To investigate the seasonal variation of hypertensive disorders of pregnancy (HDP) in South Australia.

Study design: Retrospective population study including all 107,846 liveborn singletons during 2007–2014 in South Australia. Seasonality in incidence of HDP in relation to estimated date of conception (eDoC) and date of birth (DoB) were examined using Fourier series analysis.

Main outcome measures: Seasonality of HDP in relation to eDoC and DoB.

Results: During 2007–2014, the incidence of HDP was 7.1% (n = 7,612). Seasonal modeling showed a strong relationship between HDP and eDoC (p < .001) and DoB (p < .001). Unadjusted and adjusted models (adjusted for maternal age, body mass index, ethnicity, parity, type of health care, smoking and gestational diabetes mellitus) demonstrated the presence of a peak incidence (7.8%, 7.9% respectively) occurring among pregnancies with eDoC in late Spring (November) and a trough (6.4% and 6.3% respectively) among pregnancies with eDoC in late Autumn (May). Both unadjusted and adjusted seasonal modelling showed a peak incidence of HDP for pregnancies with DoB in August (8.0%, 8.1% respectively) and a nadir among pregnancies with eDoB in February (6.2%).

Conclusion: The highest incidence of HDP was associated with pregnancies with eDoC during late spring and summer and birth in winter, while the lowest incidence of HDP was associated with pregnancies with eDoC during late autumn and early winter and birth in summer. Nutrient intake, in particular vitamin D, sunlight exposure and physical activity may affect maternal, fetal and placental adaptation to pregnancy and are potential contributors to the seasonal variation of HDP.

1. Introduction

Hypertensive Disorders of Pregnancy (HDP), including gestational hypertension, preeclampsia and eclampsia, are common heterogeneous complications of pregnancy and important contributors to maternal and perinatal morbidity and mortality worldwide [1]. From 2007 to 2014, HDP affected 7.1% of the South Australian pregnant population [2]. The pathophysiology of HDP is not completely understood [1], but risk factors are primipaternity, multifetal gestation, chronic hypertension,

family or personal history of preeclampsia, gestational diabetes mellitus (GDM) and thrombophilias [3]. Environmental factors are also likely to play a role in the pathogenesis of HDP [3].

Seasonal trends in incidence of HDP have been investigated in an effort to contribute to the knowledge of environmental risk factors for HDP. Seasonal variability of antenatal blood pressure [4] and HDP [5,6] have been studied with conflicting results. There is a great diversity in studies on seasonality of HDP and dissimilarities between study populations, regions of the world, climates, environmental

Abbreviations: ATSI, Aboriginal or Torres Strait Islander; DoB, date of birth; eDoC, estimated date of conception; ePTB, early preterm birth; GDM, gestational diabetes mellitus; GTT, glucose tolerance test; HDP, hypertensive disorders of pregnancy; PTB, preterm birth; SAPSC, South Australian Perinatal Statistics Collection; SBR, supplementary birth record; SGA, small for gestational age; Tregs, T regulatory cells

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exposures and statistical methods make it hard to interpret and harmonize results [5–7].

The aim of this South Australian study was to assess the seasonal variation in the prevalence of HDP for women in a large population birth registry according to estimated date of conception (eDoC) and date of birth (DoB) for each pregnancy.

2. Materials and methods

This was a retrospective population study among all singleton live births of at least 400 g birth weight or 20 weeks of gestation in women without pre-existing hypertension, with a known body mass index (BMI) in South Australia from 2007 to 2014. Data was sourced from the South Australian Perinatal Statistics Collection (SAPSC), maintained by the Pregnancy Outcome Unit (POU) of SA Health. The SAPSC collects information regarding the characteristics and outcome of all births in South Australia, notified by hospital and homebirth midwives and neonatal nurses using a supplementary birth record (SBR). The majority of the South Australian population resides in the metropolitan area of Adelaide, the state capital. Adelaide is a coastal city at latitude 34° 55' South with a temperate climate, with long hot dry summers (December, January, February) and short cold rainy winters (June, July, August).

Hypertensive disorders of pregnancy included all types of clinically reported hypertensive disorders of pregnancy, defined as blood pressure $\geq 140/90$ on two occasions at least four hours apart, or $\geq 170/110$ on one occasion \pm proteinuria. The SAPSC does not record information on proteinuria, so preeclampsia reports could not be confirmed. The eDoC was based on DoB and gestational age at birth. Gestational age was determined by best obstetric estimation and based on the dating ultrasound (performed at 8–13 weeks' gestation) supported by the first day of the last menstrual period or by review of other ultrasonography. The database does not indicate how gestational age was determined for individual women, but in the studied time period 98.5% of the women had an antenatal ultrasound.

Other studied variables included maternal age, body mass index (BMI), ethnicity, type of health care, civil status, parity, gravidity, and smoking at conception and in the second half of pregnancy. BMI was calculated before 20 weeks' gestation with the formula $BMI = weight\ in\ kg / (height\ in\ m)^2$. Underweight was defined as $< 18.5\ kg/m^2$, normal weight $18.5\text{--}24.9\ kg/m^2$, overweight $25.0\text{--}29.9\ kg/m^2$, obese $30.0\text{--}39.9\ kg/m^2$ and morbidly obese $\geq 40.0\ kg/m^2$. BMI was recorded in the SAPSC since 2006 and was complete for 70.1% of cases between 2007 and 2014. Ethnicity was divided in Caucasian, Aboriginal or Torres Strait Islander (ATSI), Asian and other. Medical and obstetric conditions studied were pre-existing diabetes mellitus, asthma and GDM. GDM was listed in the SAPSC when the clinician documented that the woman had GDM. All patients had a glucose challenge test at 28 weeks'. Patients with an abnormal glucose challenge test ($\geq 7.8\ mmol/L$) underwent a glucose tolerance test (GTT); fasting glucose $\geq 5.5\ mmol/L$ and/or 2 h value $\geq 8\ mmol/L$ were the cut-off values used to diagnose GDM over these 7 years. Birth and fetal variables studied were fetal sex, birth weight in grams and gestation at birth. Term birth was defined as birth between 37 and 42 weeks of gestation. Early preterm birth (ePTB) was defined as birth before 34 weeks of gestation, and preterm birth (PTB) was defined as birth before 37 weeks of gestation. Small for gestational age (SGA) was defined as a neonate born with a birth weight below the 10th percentile of the expected birth weight for the Australian population [8].

2.1. Data analyses

Data analysis was performed with SPSS version 21.0 (SPSS inc, 2013). Differences were considered significant when the *p*-value was less than .05. Fisher's exact test and chi square test were used to compare categorical variables.

Seasonality of HDP in relation to eDoC and DoB was initially

investigated using an univariate regression analysis. The model was run with and without adjustment for potential confounders defined *a priori* (maternal age, BMI, ethnicity, parity, type of health care, tobacco use in second half of pregnancy and gestational diabetes using effects coding). The average of all months together was used as the reference in the model. Covariates were removed from the model via backward elimination if their inclusion was non-significant ($p > .05$). Subsequently, multivariate logistic regression models were fit by specifying a full model with all available data on potential modifiers and confounding variables defined *a priori* (see above).

In the primary analysis, seasonal patterns in HDP were investigated using Fourier series methods (single cosinor analysis) [9]. Fourier series are considered to be the natural mathematic models for seasonality. Borrowing the following equation [10,11] to model the underlying seasonality of eDoC and DoB the first *p* pairs of term of the Fourier series was employed:

$$Seasonality(\theta_i, p) = \sum_{r=1}^p \{\beta_r \sin(r\theta_i) + \gamma_r \cos(r\theta_i)\}$$

In this series θ_i is the point in the annual cycle that the i^{th} day on which conception/birth occurred. Denoting the number of days between 1 January 1950 and the i^{th} day of conception/birth as D_i , we calculated this angle in radians thus: $\theta_i = 2\pi (D_i \text{ mod } 365.25)/365.25$. Thus, seasonal effect of the eDoC and DoB on the binary pregnancy outcome is modelled by adding $S(\theta_i, p)$ to the linear predictor of a logistic regression model so that β_i and γ_i become parameters in a simple linear model. In these data, the first pair of Fourier terms (F1 model: sine and cosine) was significant based on a likelihood ratio test ($\alpha = 0.10$), permitting their use in the model. Akaike information criterion was used to compare models for best fit.

2.2. Ethics

The existence of personal identifying information in the SAPSC was eliminated to ensure that confidentially of all patient records was maintained. The study protocol was approved by the Human Research Ethics Committee of the South Australian Department of Health [HREC/13/SAH/97].

3. Results

3.1. Incidence of HDP and study characteristics

Between 2007 and 2014, South Australia had 107,846 live, singleton births of a gestation 20–42 weeks and a birthweight $\geq 400\ g$ in women without pre-existing hypertension, with a known body mass index (BMI). The incidence of HDP was stable throughout the study period at 7.1% ($n = 7,612, p = .890$, Table 1).

Compared to normotensive pregnancies, risk factors for HDP

Table 1
Incidence of pregnancy hypertensive disorders in South Australia from 2007 to 2014.

Year of birth	Births complicated with HDP		All births n
	n	%	
2007	563	7.1	7,961
2008	772	7.0	10,998
2009	925	7.2	12,876
2010	938	6.9	13,574
2011	1,055	7.2	14,597
2012	1,096	7.1	15,429
2013	1,122	7.1	15,710
2014	1,141	6.8	16,701
Total	7,612	7.1	107,846

HDP, Hypertensive Disorders of Pregnancy.

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