Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health 5 (2015) 198–204

Contents lists available at ScienceDirect

Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health

journal homepage: www.elsevier.com/locate/preghy

Original Article

Pre-eclampsia causes adverse maternal outcomes across the gestational spectrum

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ARTICLE INFO

Article history:
Received 16 January 2015
Received in revised form 3 February 2015
Accepted 14 February 2015
Available online 28 February 2015

Keywords:
Pre-eclampsia
Early onset
Maternal outcomes

ABSTRACT

Objective: To determine if women with early onset pre-eclampsia (EOP) have worse maternal outcomes than those who present later. Specifically, we aimed to determine whether term preeclamptic women and their infants have better outcomes than either their late pre-term or early onset counterparts.

Study design: Between 1991 and 2011, 4657 pregnancies complicated by hypertension were recorded in our database; 2148 (45%) had pre-eclampsia (PE). Six hundred ninety six cases (32%) that had accurate data for the gestation at which PE developed were analysed. Pre-eclampsia was defined as per the International Society for the Study of Hypertension in Pregnancy guidelines. Maternal outcomes included (1) episodes of severe hypertension, (2) proteinuria, (3) acute kidney injury, (4) abnormal liver function, (5) thrombocytopenia and (6) neurological complications. Perinatal outcomes were also analysed.

Results: Eighty seven (13%) of 696 cases had EOP; 226 (32%) had late pre-term PE and 383 (55%) term PE. Maternal age was similar amongst the three groups. Women with late pre-term and term PE had similar rates of maternal and foetal outcomes. Compared with term PE, women with EOP had similar rates of adverse maternal outcomes, however their babies had significantly increased rates of morbidity and mortality.

Conclusion: Pre-eclampsia causes significant maternal organ involvement regardless of gestation at onset. Outcomes for babies of women with EOP are significantly worse than for those who present later. Overall, women presenting with PE after 34 weeks have generally good maternal and foetal outcomes in a unit equipped to manage such cases.

Background

The International Society for the Study of Hypertension in Pregnancy (ISSHP) recommends that pre-eclampsia (PE) arising before 34 weeks be considered early onset [1,2]. Early onset pre-eclampsia (EOP) is considered a serious disorder for both mother and baby [3]. Definitions vary for EOP; sometimes it has been considered synonymous with 'severe' pre-eclampsia though 'severe' pre-eclampsia can occur at any gestation [4], or onset >24 weeks gestation but <34 weeks [5,6];others suggest <34 weeks is 'early' and after 34 weeks is 'late' pre-term pre-eclampsia [7]. There are uncertainties about maternal and foetal outcomes of EOP, however maternal outcome reporting may be affected by selection bias i.e. inclusion of only severe early onset cases giving the impression of more severe

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http://dx.doi.org/10.1016/j.preghy.2015.02.002
2210-7789/

maternal outcomes than for presentations after 34 weeks [4]. Additional uncertainty about maternal outcomes arises from the focus of previous studies on foetal outcomes, where the aim of management was to prolong the pregnancy in order to achieve foetal maturity and survival [8,9,10].

Historically, both foetal and maternal outcomes in EOP are reported to be poor. Of 303 severe PE cases described by Sibai et al. [11] a 100% perinatal mortality rate was found in the 27 cases presenting at <28 weeks gestation and maternal morbidity was also high. More recently, Sibai reported outcomes of severe PE before 34 weeks, suggesting that prompt delivery in EOP may not be necessary and advocating delaying delivery. Hall et al. reported good perinatal outcomes of EOP < 34 weeks in centres equipped to manage high-risk pregnancies and premature neonates [8].

We therefore sought to determine, amongst a large cohort of pre-eclamptic women, if EOP confers similar or worse maternal and foetal outcomes than in those who present later. Specifically, we aimed to determine whether term pre-eclamptic women and their infants have better outcomes than either their late pre-term or early-onset counterparts.

Methods

Patients were identified from the Hypertension in Pregnancy (HIP) database of patients with hypertensive disorders of pregnancy in St George Hospital, Sydney, Australia. This database includes data from three neighbouring hospitals: St George Public Hospital, St George Private Hospital, and Hurstville Private Hospital. A single management protocol is employed at all sites. St George Public Hospital is a metropolitan teaching hospital with full maternal obstetric and intensive care services, but not a neonatal intensive care unit (NICU). Women transferred to a Unit with NICU facilities were included in this study although subsequent maternal management may have differed. The three centres deliver approximately 5000 women in total each year, and this has been stable throughout the study period of 1991–2011 [12]. HIP data are collected during the woman's hospital admission and completed on discharge, with the final diagnosis verified by an Obstetric Medicine consultant. We defined EOP as PE diagnosed before 34 weeks gestation, late pre-term PE as that developing after 34 but before 37 weeks and term PE when diagnosed at or after 37 weeks [1]. Reported outcomes are those at the time of delivery.

Hypertensive disorders in pregnancy were defined according to the Society of Obstetric Medicine of Australia and New Zealand [13]. Similar to ISSHP [2], pre-eclampsia was defined as de novo hypertension after 20 weeks gestation with evidence of maternal liver, renal, neurological or haematological abnormalities; proteinuria was not required for diagnosis. Other outcomes of patients in this database have been published previously [14–17].

Management and data analysis

All women diagnosed with a hypertensive disorder of pregnancy were managed as per a single policy [18]. Newly diagnosed pre-eclamptics were admitted for monitoring and, if not delivered and stable, followed as outpatients in Day Assessment. Indications for delivery included inability to control maternal blood pressure, progressive maternal renal, hepatic, neurological or haematological abnormalities, pre-eclampsia after 37 weeks [19] and CTG or ultrasound-based concerns about foetal welfare.

To reduce confounding, multiple pregnancies, women with pre-existing hypertension and/or secondary hypertension, including underlying renal disease, and women with gestational hypertension, were excluded.

Baseline data included gestation at presentation, maternal age, parity and booking (usually 1st trimester) blood pressure. Maternal outcomes included (1) episodes of severe hypertension, defined as systolic blood pressure $\geqslant$170 mmHg and/or diastolic blood pressure $\geqslant$110 mmHg [13], (2) proteinuria, defined as spot urinary protein/creatinine ratio >30 mg/mmol [20,21], (3) acute kidney injury, defined by serum creatinine $\geqslant$90 μmol/L, (4) abnormal liver function, defined by elevation in transaminases, (5) thrombocytopenia (analysed both by platelet count <150 and <100 $\times$ 10^9/L) and (6) neurological involvement including eclampsia, severe headaches combined with hyper-reflexia, clonus, or repeated visual scotomata. Perinatal outcomes included: (1) gestation at delivery, (2) birth weight <10% of that expected for gestational age (SGA < 10th), (3) admission to neonatal intensive care (NICU) and (4) perinatal mortality, defined as stillbirth or neonatal death within 28 days of delivery. Term PE was used as the reference group.

Statistical analysis

SPSS version 21.0 was used for statistical analysis (SPSS, IBM Corporation). For continuous data, normally distributed data were analysed using Student's *t*-test and ANOVA and non-parametric data were analysed across groups using the Kruskal Wallis test. Categorical data were compared by the Chi-Square test.

Results

There were 4463 hypertensive pregnancies during the study period Jan 1, 1991–Dec 31, 2011 (Fig. 1). Pre-eclampsia developed in 1950 (44%) and 696 (32%) of these had accurate data for the gestation at which PE developed. Of these, 383/696 (55%) presented at term, 226 (32%) presented with late pre-term PE and 87 (13%) developed EOP.

Women with PE not included in the final analysis did not differ in demographics or outcomes from those included (Appendix Table A).

Maternal age, parity and booking blood pressure did not differ between groups, nor did blood pressure at the time of diagnosis (Table 1). However, significantly more women with EOP had severe hypertension (DBP > 110 mmHg) at diagnosis (Table 1).

Maternal outcomes (Table 1)

The major maternal outcomes of severe hypertension, acute kidney injury, liver impairment, thrombocytopenia and neurological involvement were similar between groups.