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Original Article

Prediction of recurrence of hypertensive disorders of pregnancy in the term period, a retrospective cohort study

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ABSTRACT

Objectives: To assess the recurrence risk of term hypertensive disease of pregnancy and to determine which potential risk factors are predictive of recurrence.
Study design: We performed a retrospective cohort study in two secondary and one tertiary care hospitals in the Netherlands. We identified women with a hypertensive disorder in the index pregnancy and delivery after 37 weeks of gestation between January 2000 and December 2002. Data were extracted from medical files and women were approached for additional information on subsequent pregnancies. Adverse outcome was defined as recurrence of a hypertensive disorder in the next subsequent pregnancy.
Main outcome measures: The absolute risk of recurrence and a prediction model containing demographic and clinical factors predictive of recurrence.
Results: We identified 638 women for potential inclusion, of whom 503 could be contacted. Of these women, 312 (62%) had a subsequent pregnancy. Hypertensive disorders recurred in 120 (38%, 95% CI 33–44) women, of whom 15 (5%, 95% CI 3–7) delivered preterm. Women undergoing recurrence were more at risk to develop chronic hypertension after pregnancy (35% versus 16%, OR 2.8, 95% CI 1.5–5.3). Body mass index, non-White European origin, chronic hypertension, maximum diastolic blood pressure, no use of anticonvulsive medication and interpregnancy interval were predictors for recurrence.
Conclusions: Women with hypertensive disorders and term delivery have a substantial chance of recurrence, but a small risk of preterm delivery. A number of predictors for recurrence could be identified and women with a recurrence more often developed chronic hypertension.

Introduction

Approximately 10% of all pregnancies are complicated by a hypertensive disorder, including gestational hypertension (GH), preeclampsia (PE) and HELLP (hemolysis,

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elevated liver enzymes and low platelets) syndrome. Ninety percent of women with mild or severe preeclampsia deliver at term (⩾37 weeks of gestation) [1–3]. Although less than in early-onset disease, these disorders contribute substantially to both maternal and perinatal outcome [4,5]. Late-onset hypertensive disorders do not have the same impact on particular neonatal outcome as do early-onset preeclampsia. Nevertheless, recurrent disease produces more pregnancy complications as preterm delivery, placental abruption and fetal death, than preeclampsia in nulliparous women [6]. Several studies have been published on recurrence rates of hypertensive disorders [3,7–12]. Most studies concentrate on recurrence rates in women who suffered early-onset severe hypertensive disorders, or are registry-based research lacking information on important risk factors.

The heterogeneity of hypertensive disease of pregnancy, both in cause as in symptomatology, leaves recurrence prediction of these disorders based on a single variable problematic [7]. Additionally, prediction models for recurrence have been unsatisfactory because the quality of reporting of studies is generally low and their clinical usefulness or generalizability suboptimal [7]. The psychological impact of hypertensive disorders of pregnancy can cause parents to refrain from future pregnancies [13–15]. Therefore, accurate knowledge of the risk of recurrence in future pregnancies underlying informed counseling is of the utmost importance.

Our primary aim was to calculate the absolute risk of recurrence of a hypertensive disorder in the next pregnancy after a hypertensive pregnancy with a delivery beyond 37 weeks of gestation. Our secondary aim was to identify independent risk factors for recurrence and to develop a prediction model for recurrence.

Materials and methods

Study population

We retrospectively identified patients from electronic databases in three hospitals in the Netherlands: two secondary care centers (Amphia Hospital, Breda and Atrium Medical Centre, Heerlen) and one tertiary care center (Academic Medical Center, Amsterdam). We included consecutive patients who delivered after 37 weeks of gestation of their index pregnancy between January 2000 and December 2002, and were diagnosed with GH, PE or HELLP syndrome.

Women carrying a pregnancy with fetal abnormalities were excluded. Chronic hypertension was not an exclusion criterion. Standard practice for determination of gestational age was ultrasound dating.

We collected demographic data including: age, body mass index (BMI), parity, and cardiovascular risk factors like: smoking, chronic hypertension diagnosed before pregnancy, thrombophilia and family history for cardiovascular disease. Of the index and subsequent pregnancy we collected data on: highest systolic and diastolic blood pressure, use of medication, hospital days and perinatal outcome including gestational age at delivery, birth weight and perinatal death.

Data were extracted from medical files. Information on subsequent pregnancies was gained first through medical files. A subsequent pregnancy was defined as an on-going pregnancy beyond 16 weeks of gestation. If this information was not available in the records of the institution, we tried to contact the individual patients. If the patient reported that she had had an on-going subsequent pregnancy, a written informed consent was obtained, after which her gynecologist or family doctor was contacted for additional data. All contacted patients were asked if they had developed chronic hypertension at time of data collection. All ethically available public resources were consulted if patients were lost to follow-up.

The outcome was: hypertensive disorders of pregnancy, a composite of PE, superimposed PE, GH and HELLP syndrome. Preeclampsia was defined as hypertension (diastolic blood pressure ⩾90 mmHg or systolic blood pressure ⩾140 mmHg on two occasions, 4–5 h apart) in combination with proteinuria (defined as 1+ (0.3 g/l) or more on proteinuria dipstick test, a protein/creatinine ratio of 30 mg/mmol or more in a random sample or an urine protein excretion of 300 mg or more per 24 h.) after 20 weeks of pregnancy [16]. Women with hypertension without proteinuria, or a significant rise in blood pressure (a rise of ⩾30 mmHg) if known chronic hypertension, were considered to have GH. Complementing the definition of GH with a significant rise of 30 mmHg or more in blood pressure was made to emphasize a distinction between chronic hypertension and a pathological process related to pregnancy. Chronic hypertension was defined as a history of preconceptional hypertension or hypertension detected in the first half of pregnancy. Superimposed preeclampsia includes de novo proteinuria, or a sudden increase in proteinuria if already present, in a woman with chronic hypertension [16]. HELLP syndrome was defined by hemolysis (elevated lactate dehydrogenase (LDH) levels ⩾600 U/L), elevated liver enzymes by levels of aspartate transaminase (ASAT) or alanine transferase (ALAT) ⩾70 U/L and low platelets <100,000/mm [17]. SGA was defined as birth weight below the 10th percentile, according to the ACOG practice bulletin [18] and adjusted for gestational age based on a local reference population.

Statistical analysis

We expressed continuous variables as mean with standard deviation (SD) or median with interquartile range (IQR) if not normally distributed. Differences in baseline characteristics or outcomes between groups were tested with parametric (unpaired *t*-test) or non-parametric (Mann–Whitney-*U* test) tests as appropriate. Categorical variables were compared with Chi square tests. *p* values less than 0.05 were considered to indicate statistical significance.

Missing data are often not missing completely at random, but rather selectively missing. Removing the women with missing values (complete case analysis) could result in a loss of precision and biased study results [19–21]. Imputation of selectively missing values can reduce bias and allows for the inclusion of all women in the analysis.