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Association between hypertensive disorders of pregnancy and third stage of labor placental complications



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ARTICLEINFO	A B S T R A C T
<i>Keywords:</i> Third stage of labor Placental complication Retained placenta Pregnancy induced hypertension Preeclampsia	Objective: To examine the association between hypertensive disorders of pregnancy and third stage placental complications.Methods:A retrospective cohort study based on Soroka Medical Center institutional computerized database. All vaginal deliveries of women between the years 1998–2013 were included. Rates of third placental complications and other adverse pregnancy outcomes were compared between parturients with and without hypertensive disorders of pregnancy. Multivariate analysis models as well as generalized equations models (GEE) controlling for potential confounders were constructed. <i>Results:</i> Of 263,053 deliveries included, 14,754 (5.6%) were complicated by hypertensive disorders of preg- nancy. Hypertensive parturients were older, had higher rates of: diabetes, previous cesarean section and in- duction of labor. Rates of third stage placental complications were significantly higher among hypertensive parturients (4.7% versus 4.0%, p value < 0.001). Preeclampsia was found independently associated with third placental complication in the logistic regression and the GEE models constructed. Adjusted odds ratio, 95% confidence interval, respectively: 1.11 (1.00–1.24); 1.11 (1.00–1.25). <i>Conclusion:</i> Our study was the first to demonstrate that an association between hypertensive disorders of pregnancy and third stage placental complications exists, suggesting a common pathological pathway. Further larger studies are needed in order to reinforce these findings.

1. Introduction

Hypertensive disorders of pregnancy is a term commonly used to describe a spectrum of disorders complicating 5%–10% of pregnancies [1,2]. These include: 1) chronic (pregestational) hypertension (HTN); 2) pregnancy induced hypertension (PIH); and 3) preeclampsia (PET). It is widely agreed that abnormal placentation, and more specifically pathological placental vascular remodeling, triggers a cascade of events that eventually lead to the development of PIH and PET [3,4]. Placental hypoperfusion and ischemia are fundamental components in the pathophysiology of PET [5–7], and are also the consequence of this altered placentation processes [8]. Hypertensive disorders are associated with placental insufficiency and hence maternal and neonatal morbidity and mortality [9] (e.g. placental abruption [10], intrauterine growth restriction [11] and perinatal mortality).

The third stage of labor normally lasts a few minutes with only 3.3% of women exceeding 30 min [12]. Prolonged third stage (delayed separation of the placenta) is a potential life threatening event that increases the risk of postpartum hemorrhage due to interference with

uterine postpartum contractions [12]. Third stage placental complications include among others: retained and adherent placenta, all may be a result of defective placentation [13,14]. These complications may result in interventions such as manual removal of the placenta or retained products of conception, revision of the uterine cavity, postpartum haemorrhage, blood transfusion and emergency peripartum hysterectomy [15-18]. The overall prevalence of placental complications varies across settings and over time and usually each of the components is handled separately in this term. Retained placenta has a reported incidence of 1:100-1:300 deliveries [15] and the incidence of adherent placenta has been reported to be 1:533 [19]. The pathophysiology of third stage placental complications is under debate; One of the proposed mechanisms is attributed to over-invasiveness of the trophoblast while another links it to primary deficiency of decidualisation [14]. Preeclampsia has been reported to be a risk factor for prolonged third stage of labor [20]. Retained placenta was associated with preeclampsia in several studies [21,22], while no studies have examined the association with adherent placenta. We hypothesized that both hypertensive disorders of pregnancy and third stage placental

https://doi.org/10.1016/j.preghy.2018.06.004

Received 11 January 2018; Received in revised form 20 March 2018; Accepted 9 June 2018 Available online 09 June 2018

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Given the increasing prevalence of hypertensive disorders of pregnancy, and the gap in knowledge regarding its association with third stage placental complications, we conducted this study in order to examine whether an association exists between these conditions.

2. Materials and Methods

2.1. Study design and setting

A population based retrospective cohort study was conducted at the Soroka University Medical Center (SUMC). SUMC is the largest and the single tertiary hospital in the southern district of Israel. Deliveries occurred between the years 1988–2013, and during the study period the annual average of deliveries was 12,500. Data was extracted from institutional computerized delivery database, which contains among others: demographical characteristics, pregnancy and perinatal outcomes and maternal complications. This database is tested and validated repeatedly by the Department of Epidemiology of the Ben-Gurion University of the Negev (Beer Sheva, Israel). Immediately after the delivery data are recorded by an obstetrician, and skilled medical secretaries examine the data before entering into the database.

2.2. Study population

Included in the study were all women that delivered vaginally during the study period. Multiple gestations, pregnancies complicated with known chromosomal or fetal malformations and those with lack of prenatal care [23] (defined as fewer than three visits to a prenatal care facility) were excluded. The study has been approved by the Institutional Review Broad (in accordance with Helsinki declaration).

2.3. Definitions

Though, both tested variables are hypothetically a result of the same abnormal placentation process, due to the fact that chronologically hypertensive disorders during pregnancy proceed third stage of labor, third stage placental complications was chosen to be the dependent variable in the multivariate regression models.

Hypertensive disorders of pregnancy includes two major forms, both require development of hypertension (systolic \geq 140 or diastolic \geq 90) [2]:

1. PIH: first detected after 20 weeks of gestation in the absence of proteinuria or other diagnostic features of preeclampsia [2]. 2. PET: new onset of HTN and proteinuria (\geq 300 mg in 24 h urinary collection, or 1 + in a urine dipstick) as well as superimposed PET which is defined as: new onset of proteinuria, significant end-organ dysfunction, or both after 20 weeks of gestation in a woman with chronic/preexisting hypertension [2]. 3. Severe PET: new onset of HTN and end-organ dysfunction with or without proteinuria. We included only hypertensive disorders that were diagnosed during pregnancy [2].

Third stage placental complications were defined as a composite of [13–15]: Retained placenta – lack of expulsion of the placenta within 30 min of delivery of the infant when third stage of labor is managed actively; adherent placenta – the placenta is adherent to the uterine wall, but easily separated manually; procedures of manual removal of the placenta or retained products of conception (manualysis), post-partum curettage and revision of the uterine cavity.

Stillborn was defined as all cases of antepartum or intrapartum fetal demise after 20 completed weeks of pregnancy [24]; preterm delivery (PTD) was defined as delivery prior to 37 weeks of gestation [25]; bad obstetric history is combined habitual abortions, previous infant demise and preterm deliveries [26]; small for gestational age (SGA) was defined as birth weight below the 10th percentile for gestational age in accordance with the regional Dollberg curve [27].

2.4. Statistical analysis

Data was analyzed using SPSS 21.0 (SPSS, Chicago, IL).

The initial analysis was performed by using descriptive statistics (mean, SD), followed by logistic regression models. Continuous variables with normal distribution are presented as mean \pm SD and compared between the study groups using *t*-test. Continuous variables which aren't normally distributed are presented as median with interquartile range and their statistical analysis was performed using the Mann-Whitney test. Categorical variables are presented in counts and percentages and their statistical analysis was performed using Chi-Square or Fisher Exact test when appropriate. All analysis with two-sided p-value of < 0.05 were considered significant. Variables that were found statistically associated with the composite outcome in the univariate analysis as well as known risk factors for third stage placental complications were adjusted for in the multivariate regression models.

Multivariate logistic-regression models were constructed to in order to assess the association between hypertensive disorders of pregnancy and the composite outcome, controlling for the following confounders: gestational age, parity, induction of labor, smoking and previous history of caesarean delivery. Allowing more than one pregnancy per women, generalized estimating equations (GEE) analysis was constructed in order to control for a correlation between pregnancies belonging to the same woman.

3. Results

During the study period there were 263,053 vaginal deliveries at the SUMC, 14,754 (5.6%) of them were complicated with hypertensive disorders of pregnancy. Demographic and clinical characteristics are presented in Table 1. Women who had hypertensive disorders of pregnancy were older (30.3 vs. 28.53, p < 0.001), had higher gravity and higher parity (p < 0.001). Higher rates of induction of labor were noted among women with hypertensive disorders of pregnancy (21.9% vs. 5.8%, p < 0.001). Significant differences were noticed with regard to obstetrical history, the rate of women with bad obstetrical history (5.4% vs. 3.8%), previous cesarean section (29.9% vs. 13.9%), were all significantly elevated (p < 0.001). In addition, higher rates of diabetes were found among women with hypertensive disorders of pregnancy (p < 0.001).

Table 2 summarizes different adverse pregnancy outcomes in the comparison groups. The rates of PTD (18.2% vs. 7.1%) and SGA neonates (10.0% vs. 5.0%) were higher among women with hypertensive disorders of pregnancy (p < 0.001). In addition, rates the rate of stillbirth was higher in the study group (1.2% vs. 0.7%, p < 0.001). Third stage of labor placental complications (retained placenta, manualysis, revision of uterine cavity and the composite outcome) were found to be increased among women with hypertensive disorders of pregnancy (4.7% vs. 4.0%, p < 0.001).

A multivariate logistic regression model was constructed to estimate independent risk factors associated with third stage placental complications (Tables 3a, 3b, 3c), controlling for: gestational age, parity, status post cesarean section, induction and smoking. Third stage of labor placental complications (aOR 1.11, 95% CI 1.00–1.24) were found to be independently associated with PET.

The independent associations with PET observed in the logistic regression model remained significant in the GEE model (Table 4). Third stage of labor placental complications remained independently associated with PET (aOR 1.11, 95% CI 1.00–1.24).

4. Discussion

In our population based retrospective cohort study we demonstrated a significant association between hypertensive disorders of pregnancy and third stage of labor placental complications, in addition to other Download English Version:

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