



Prior abortion history and pregnancy hypertensive disorders in primiparous gravidae



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ABSTRACT

Objectives: To explore the relationship between prior abortion history with incidence of pregnancy hypertensive disorders (PHD), including gestational hypertension (GH) and pre-eclampsia (PE), to determine whether the secular increases in GH and PE in developed countries could be related in part to the decreased incidence of abortion.

Study design: A single center retrospective cohort study on primiparous Chinese gravidae managed in 1997–2015 in our hospital.

Main outcome measures: The occurrence of PHD, GH and PE with respect to the presence or otherwise of prior abortions, with the analysis stratified for risk factors that include advanced age, high body mass index (BMI), history of medical disorders, birth before 34 weeks, and maternal hepatitis B virus (HBV) infection and rubella non-immunity which have been shown to influence the occurrence of PHD in our population.

Results: The 23,698 (39.3%) of the 60,335 gravidae in the cohort with \geq one prior abortion had higher incidence of advanced age, HBV infection, rubella non-immunity, and high BMI, but lower incidence of PHD, GH, PE and birth before 34 weeks gestation. The difference in the incidence of GH and PE between gravidae having one versus those with two or more abortions was minimal, and the effect of abortion on PHD was influenced by the other risk factors. On regression analysis, prior abortion reduced PHD (aRR 0.761, 95% CI 0.684–0.846), GH (aRR 0.660, 95% CI 0.563–0.773), and PE (aRR 0.857, 95% CI 0.745–0.987).

Conclusions: Prior abortion reduces the subsequent development of GH and PE in primiparous women.

1. Introduction

The pregnancy hypertensive disorders (PHD), including both gestational hypertension (GH) which is also described as pregnancy-induced hypertension (PIH), and pre-eclampsia (PE), occur mainly in primiparous gravidae, whereas multiparous gravidae not only have a much lower risk but also tend to have milder symptoms. The higher risk of PHD in primiparous gravidae is attributed to maternal first exposure to fetal cells, as primigravidity is the strongest risk factor [1,2], and a previous successful pregnancy confers a protective effect [2–7]. However, whether a previous abortion, which should also have exposed the mother to fetal cells, would produce a similar protective effect on primiparous gravidae remains controversial.

Several studies have found prior abortion to be protective against PHD. In one study, nulliparous gravidae with previous spontaneous or induced abortion were protected to the same extent against eclampsia as for multiparous gravidae without abortion [1]. In another study on gravidity-2 women involving 200 cases and 100 controls, no difference

in PE and eclampsia was found between gravidae with one previous abortion versus those with one previous term live birth [8]. As well, prior abortion decreased the risk of PE and PIH [6,9–11], an effect that appeared to be enhanced by increasing number of abortions [10]. However, while one study found no difference in the protective effect between spontaneous or induced abortion [9], another found that PE was significantly reduced only following an induced but not spontaneous abortion in gravidae carrying a first pregnancy to term [5], and prior induced abortion could mitigate the effect of maternal hypertension on preterm delivery [12]. Of note, prior abortion reduced the risk only if the index pregnancy was conceived with the same partner, and the risk was no different from women without abortion history in the case of a new partner [7].

Nevertheless, no reduction in the incidence of PE or PHD was also reported following previous abortions, whether induced or spontaneous [13,14], or with respect to the number [6], or whether it was recurrent [15,16]. At the other end of the spectrum, a first pregnancy miscarriage has also been associated with higher risk of PHD and PE in the

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following pregnancy [17,18], as well as for preterm birth induced for PE [19]. Indeed, the risk could be further increased with three or more prior miscarriages [19–21], which was also associated with increased severity of PE and chronic hypertension [21].

There have been secular increases in PHD [22]. Even with enhanced management of PE resulting in a reduction in eclampsia [22], there were still significant increases in the overall prevalence of PHD in developed countries like the USA [22–24] and Norway [22]. One unexplored factor is the impact of prior abortions. In the developed but not the developing world, abortion rates have declined significantly from 1990 to 2014 [25]. In terms of total pregnancies, it had decreased from 23% to 17% (1.6 million to 1.2 million) from 1990 to 4 to 2010–4 in North America, while in Northern Europe for the same period, it decreased from 22% to 19% (0.4–0.3 million). On the other hand, it had increased from 12% to 15% (4.6–8.3 million) in Africa and from 23% to 28% (31.5–35.8 million) in Asia for the same period. The changes in abortion rate could therefore have influenced the rates of PHD in different countries. In addition, race/ethnicity is an important confounding factor, for instance prevalence of PE is low in Chinese compared with Caucasians [26], which could in turn be related in part to the high prevalence of maternal chronic HBV infection that is associated with reduced PE and GH [27]. To clarify the impact of prior abortion on PHD, we studied the occurrence of PHD in primiparous Chinese gravidae managed from 1997 to 2015 in our hospital, taking into account the other known risk factors that include maternal HBV infection [27] and rubella non-immunity [28] which have been shown to decrease and increase respectively the incidence of PHD in our population.

2. Methods

In Hong Kong, the Hospital Authority (HA) provides free antenatal care and subsidized inpatient obstetric treatment and confinement to all local residents through eight public hospitals, one of which is our hospital with the largest number of annual deliveries (7000) and a level III neonatal intensive care unit, serving a population of 1.7 million or about one-quarter of that in Hong Kong. Obstetric management is based on medical indications and protocols. At the antenatal booking visit, a detailed history is taken, including past health and obstetric history, but the paternity of any prior pregnancies, successful or otherwise, is not elucidated unless hereditary traits and genetic conditions are encountered or suspected. Maternal demographic and anthropometrics factors are also ascertained, and routine antenatal screening include blood tests for hepatitis B surface antigen (HBsAg) to identify pregnancies in which passive-active immunoprophylaxis against the hepatitis B virus (HBV) is required for the newborn infant, as well as rubella immunity in which case postnatal rubella immunization is arranged for gravidae found to be seronegative for rubella. The results of the screening tests, the antenatal examination, admission details, and pregnancy complications and outcome as coded by the ICD coding, are captured in a computerized database set up by the HA for annual statistics. The data entry is made by trained midwives and obstetricians in the clinics and wards, and is doubled checked after delivery. The database has been validated before [27].

For this retrospective cohort study, eligible cases were primiparous gravidae carrying a singleton pregnancy beyond 24 completed weeks of gestation and delivered between 1997 and 2015 under the care of our department. Exclusion criteria were multiparous gravidae and gravidae who had booked but did not deliver in our hospital. Gravidae with and without previous abortions constituted the study and comparison groups respectively. We did not distinguish between spontaneous or induced abortion as the effect of these two conditions was found to be no different regardless of whether abortion increases or reduces the risk [1,9,14]. Information on the interval in months between the last abortion with the current conception was not available as only the year of abortion was entered into the database. We also had not

distinguished between medical or surgical treatment employed to evacuate the uterus, because natural conception rate, cumulative pregnancy rate, and subsequent live birth rate were found to be similar between either treatments [29]. Our society is still relatively conservative so that some women are reluctant to divulge the paternity of their previous pregnancies, successful or otherwise, and unless volunteered, we would not attempt to extract data on paternity of previous pregnancies in respect for patient confidentiality. For the diagnosis of PHD, we included GH (labelled as PIH in some studies), unclassified hypertension, and PE [22], and PE is defined as hypertension with proteinuria arising de novo, or superimposed on pre-existing hypertension. The diagnosis of GH and PE were according to the International Society for the Study of Hypertension in Pregnancy criteria as described before [30]. The diagnosis of GH and PE are mutually exclusive. The reported risk factors for PE [31,32] were examined, including nulliparity status, advanced age (≥ 35 years), high body mass index (BMI) at booking ($> 25 \text{ kg/m}^2$), and presence of significant medical history that included cardiovascular disease, renal and autoimmune disorders, and pre-gestational diabetes mellitus grouped together in one category owing to the low incidence of each of the individual disorders, together with maternal HBV infection [27] and rubella non-immune [28] status. The occurrence of all hypertensive disorders and presence of risk factors were compared between gravidae with and without history of abortion, and then the relationship between hypertensive disorders with abortion was analyzed stratified by the presence or absence of risk factors. As the study utilized the anonymized database for auditing purpose, patient consent was not required.

Comparison of continuous variables was performed with the *t* test, and categorical variables with the chi square test and calculation of the relative risk (RR) with 95% confidence intervals (CI). The trend between the numbers of abortions with hypertensive disorders was examined by Spearman's correlation. Multiple logistic regression analysis was performed to determine the independent association between abortion and other risk factors with PHD overall, and with GH and PE specifically, with the results expressed by the adjusted relative risk (aRR) with 95% CI. Statistical analysis was performed using a commercially available statistical package (IBM SPSS Statistics version 22.0).

3. Results

There were 120,658 women managed under the obstetric unit during this period, and 62,888 (52.1%) were primiparous gravidae, of whom 60,335 (95.9%) satisfied the inclusion criteria of, and were included in, the study. Overall, 99.1% ($n = 59812$) were Chinese and 39.3% ($n = 23698$) of the 60,335 gravidae had one or more prior abortion. This group was slightly but significantly older with higher incidence of advanced age, as well as a slightly but significantly higher BMI, but there was no difference in the incidence of significant medical history or chronic hypertension (Table 1). Nonetheless, this group had higher incidence of HBV infection and rubella non-immunity, but lower incidence of PHD, GH, PE and preterm birth at < 34 weeks gestation.

On further analysis, the number of gravidae with none, one, and two or more prior abortions was 36,637 (60.7%), 15,167 (25.1%), and 8531 (14.1%) respectively. The incidence of PHD was 3.1%, 2.6% and 2.4% for these three subgroups ($p < 0.001$ for difference and trend). For GH the figures were 1.4%, 1.2% and 0.9% respectively ($p < 0.001$ for difference and trend). For PE, the respective figures were 1.7%, 1.5% and 1.6% ($p = 0.065$ for difference and $p = 0.053$ for trend). For chronic hypertension, the figures were 0.3%, 0.3% and 0.2% respectively ($p = 0.331$ for difference and $p = 0.163$ for trend). In view of the minimal difference between gravidae having one versus those with two or more abortions, no distinction was made between gravidae with one or more abortions in the subsequent analysis.

Further comparison of the effect of prior abortion stratified for the

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