OBSTETRICS

Hypertension in pregnancy and long-term cardiovascular mortality: a retrospective cohort study

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BACKGROUND: There is growing evidence that hypertensive disorders of pregnancy are associated with increased long-term cardiovascular mortality in the mother. Hypertension in pregnancy, until recently, however, has been ignored largely as a risk factor for future cardiovascular disease and mortality because the link between the 2 is not fully understood.

OBJECTIVE: To determine the association between women with hypertension in pregnancy and long-term cardiovascular disease mortality.

STUDY DESIGN: All women who delivered at a metropolitan hospital between the periods of January 1, 1980, and December 31, 1989, were identified by use of the *International Statistical Classification of Diseases and Related Health Problems*, 9th Revision, Australian Modification.

RESULTS: The total number of deliveries in the given time period was 31,656, with 4387 (14%) of the women identified as having had hypertension in their pregnancy. Using information from the New South Wales Births, Deaths and Marriages Registry and the Australian Bureau of Statistics Death Registry, we identified a total of 651 deaths from this cohort (n = 31,656). There were 521 deaths among the women who remained normotensive in their pregnancy and 129 deaths for women who had hypertension during their pregnancy. Overall, the women with hypertensive disorders of pregnancy were at greater risk of death than the women who remained normotensive in their pregnancy (odds ratio 1.56; 95% confidence interval 1.28−1.89; $P < .001$).

CONCLUSION: Women with a history of hypertension in their pregnancy are at an increased risk of future cardiovascular mortality, and this work identifies a group of women who may benefit from early screening and intervention strategies to help decrease their risk of future cardiovascular disease.

Key words: cardiovascular disease, hypertension, mortality, preeclampsia, pregnancy

Women with a history of a hypertensive disorder of pregnancy (HDP) in their pregnancy have been identified as having an increased risk of adverse long-term cardiovascular outcomes compared with women who remained normotensive in their pregnancy.[1-3] It has been thought widely that the effects of hypertension in pregnancy reversed once the baby was delivered and hypertension values returned to their prepregnancy level; however, recent studies have demonstrated that the endothelial dysfunction remains in women who had hypertension in pregnancy and that it is this damage that increases the risk of developing cardiovascular disease (CVD) in later life.[4,5] The hypertensive disorders of pregnancy include gestational hypertension, preeclampsia/eclampsia, chronic hypertension, and preeclampsia superimposed on chronic hypertension.

In Australia and internationally, CVD is a major cause of death in women, accounting for 34% and 32% of all female deaths, respectively.[6,7] Women with a history of HDP provide a unique opportunity to primary healthcare providers to identify a group that is at an increased risk of CVD, which may allow for closer surveillance, optimization of other CVD risk factors, and the potential for intervention and CVD risk reduction with the introduction of preventative programs for these women. Despite the available evidence, a history of HDP is not included in the traditional CVD risk-assessment tools. This study looks to examine the association between HDP and CVD mortality and to assess the magnitude of effect of the different HDP categories on CVD.

Materials and Methods

All women who delivered at Royal Prince Alfred Women and Babies, Sydney Australia, between the periods January 1, 1980, and December 31, 1989 comprised the pregnancy cohort. A subcohort of these women, who were coded as having been diagnosed with HDP in the antenatal, intrapartum, or postnatal period, were identified via use of the *International Statistical Classification of Diseases and Related Health* Problems, 9th Revision, Australian Modification (ICD-9-AM codes). The ICD-9-AM coding for the diagnosis of hypertension in pregnancy was identified by clinicians at a major tertiary hospital with extensive experience in the field. The medical records of a 30% randomly selected proportion of the women with HDP women were examined manually by an experienced research midwife to determine the correct diagnosis of hypertension according to the definitions provided by the Society of Obstetric Medicine of Australia and New Zealand guidelines.[8] These women were categorized into the 4 different groups: gestational hypertension, preeclampsia, chronic hypertension, and preeclampsia superimposed on chronic hypertension.

Gestational hypertension was defined as an increase in systolic blood pressure ≥140 and/or diastolic blood pressure ≥90 mm Hg after 20 weeks' gestation with no previous history of renal disease

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or hypertension before the pregnancy or significant proteinuria. Preeclampsia was defined as an increase in blood pressure after 20 weeks' gestation associated with the involvement of at least 1 other organ manifestation, including proteinuria (>300 mg/24 hours), biochemical, neurologic, hematologic, hepatic impairment, acute pulmonary edema, fetal growth restriction, and placental abruption. Chronic hypertension was defined as an increased systolic blood pressure ≥140 and/or a diastolic blood pressure ≥90 mm Hg preconception or associated with renal disease, renovascular disease, cardiac disease, or endocrine disorders presented before 20 weeks' gestation and not associated with additional systemic features of preeclampsia, whereas chronic hypertension with superimposed preeclampsia was defined as 1 or more of the systemic features of preeclampsia that develops in women with chronic hypertension.

The cohort was then coded as to whether they had hypertension or remained normotensive in their pregnancy. The entire cohort was linked with the use of identifying variables by the Centre for Health Record Linkage to the NSW Registry of Births, Deaths and Marriages (Death data) and to the ABS Cause of Death database. The linkage period was between the years 1980 and 2009. Cardiovascular death was identified by the use of ICD-9-AM (390–459) and *International Statistical Classification of Diseases and Related Health Problems*, 10th Revision, Australian Modification codes (100–199) codes depending on the year of death. The subset of the women who had detailed pregnancy data collected was maintained on a separate dataset. This dataset also provided information on the severity of the disease. In this instance, severity of disease was categorized by the following parameters: severe blood pressure readings with a systolic blood pressure of ≥170 mm Hg and/or a diastolic blood pressure of ≥110 mm Hg,[8] gestation at delivery less than 34 weeks,[5] and intrauterine growth restriction (defined by less than the third centile[9]).

Student *t* tests and analysis of variance were used to compare baseline characteristics between the hypertensive and normotensive women and between the 4 diagnostic groups. For nonparametric data, Mann-Whitney *U* and Kruskal-Wallis analysis were undertaken and the median and interquartile range (25th and 75th percentiles) were reported. Contingency tables were compared with the χ^2 analysis and $P < .05$ was considered significant with Bonferroni correction made for multiple testing. All analysis used IBM SPSS v.20 statistical software (SPSS Inc., Chicago IL). Multivariate models included age, gestation at delivery, and parity. This study was approved by the institutional Ethics Committee.

Results

A total of 31,656 women delivered between the years 1980 and 1989, of which 4387 (14%) had hypertension in their pregnancy. Of the women who had hypertension in their pregnancy, a total of 1155 (26%) medical records were reviewed. The baseline characteristics of these women are shown in Table 1.

Of all the women (n = 31,656) a total of 651 (2%) deaths were reported in the period since delivery until 2009 (see Table 2 for mortality details). Of the 651 deaths, 129 (20%) had developed a HDP and 521 (80%) remained normotensive in their pregnancy, whereas the diagnosis of one is unknown (Figure 1 and Table 3). Of the total deaths in the women who had HDP, 39 medical records were reviewed. A total of 13 women had preeclampsia, 18 had gestational hypertension, 5 had chronic hypertension, and 3 had preeclampsia superimposed on chronic hypertension.

There was an increased risk of death in women who had more than 1 pregnancy affected by HDP compared with the women with HDP in 1 pregnancy (odds ratio [OR] 2.07; 95% confidence interval [95% CI] 1.09-3.94 $P = .019$). Using a logistic regression backward model, we found that age at delivery, gestation at

TABLE 1
Baseline characteristics of the women whose medical records were reviewed (n = 1155)

	Preeclampsia (n = 356)	Gestational hypertension (n = 625)	Chronic hypertension (n = 98)	Superimposed preeclampsia (n = 76)	*P* value
Age (at birth baby)[a]	30 (25–33)	30 (23.5–32.5)	33.5 (31–36)	29 (24–35)	<.001
Smoker (n)[b]	23% (81)	17% (107)	15% (15)	20% (15)	.005
Primiparous (n)[b]	73% (260)	63% (391)	39% (38)	58% (44)	<.001
Gestation at delivery[a]	35 (33–37)	37 (36–37.5)	36.5 (35–38)	35 (31.3–38)	<.001
Neonatal birth weight[a]	1930 (1480–2300)g	2650 (2322–2737)	2902 (2515–3290)	2055g	.07
Birth centile[a]	13.5 (4–48)	16 (12.5–55.5)	11 (7–15)	23 (8.3–47.5)	<.001
IUGR (<5th) (n)[b]	16% (56)	0	0	14% (11)	<.001

IUGR, intrauterine growth restriction.

[a] Median (interquartile range); [b] Percentage smokers (n), IUGR defined as gestation adjusted birth weight less than the 5th centile. Comparisons between the different diagnostic groups have been undertaken with Kruskal-Wallis tests.

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