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Postpartum physiology, psychology and paediatric follow up study (P4 Study) – Study protocol

Gregory K. Davis (A/Prof) [a,b,*], Lynne Roberts (Ms) [a,c], George Mangos (A/Prof) [a,b], Amanda Henry (Dr) [a,b], Franziska Pettit (Dr) [a,b], Anthony O'Sullivan (Prof) [a,b], Caroline S.E. Homer (Prof) [a,c], Maria Craig (Prof) [a,b,d], Samuel B. Harvey (A/Prof) [a,b,e], Mark A. Brown (Prof) [a,b]

[a] St George Hospital, Gray Street, Kogarah, NSW 2217, Australia
[b] University of NSW, Randwick, NSW 2031, Australia
[c] University of Technology Sydney, Broadway, Ultimo, NSW 2007, Australia
[d] Sydney Children's Hospital, Randwick, NSW 2031, Australia
[e] Black Dog Institute, Randwick, NSW 2031, Australia

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ABSTRACT

Background: Women who have had hypertension in pregnancy are at greater risk of long term cardiovascular disease (CVD). Little is known about their cardiovascular risk postpartum or the effects on the woman's mental health and the outcomes of their infants. In this project we will study the physiological and psychological health of women and the physical health and development of their infants six months, two years and five years after birth. We will establish normal blood pressure (BP) and metabolic function for women who were normotensive in pregnancy and use these to assess women who had gestational hypertension (GH) or preeclampsia (PE).

Design/methods: Women will be asked to participate if they have given birth in the preceding six months. They will be excluded if they had diabetes, hypertension, renal or other serious maternal disease prior to pregnancy or congenital anomaly in the pregnancy. We will recruit 292 women who were normotensive and their babies, 100 who had GH and 100 who had PE and their babies. They will be assessed at six months, two and five years after birth. At each assessment mothers will have their blood pressure (BP) assessed peripherally with a liquid crystal sphygmomanometer and 24 h ambulatory blood pressure monitoring (ABPM), and centrally with non-invasive applanation tonometry. Additional physiological testing will include: body composition; energy balance; vascular compliance; cardiac function; liver and renal function, lipids and biochemistry; glucose and insulin; and urinalysis. Psychological status will be assessed with validated self-report questionnaires for depression, anxiety, post-traumatic stress disorder (PTSD) and mother-infant bonding. The babies will have a medical examination by a paediatrician at each assessment. Their behavioural development will be assessed with an Ages and Stages Questionnaire completed by their mother at each assessment and a developmental assessment by a child psychologist at two and five years.

Conclusions: This study will re-define normal BP and other physiological parameters for young parous women thereby permitting a more sensitive assessment of post-partum BP and other cardiovascular risk markers in women who have had GH or PE. It will also determine the extent, if any, of psychological disorders in these women and developmental or other concerns in their babies.

Trials registration: Australian and New Zealand Clinical Trials Registry Number: ACTRN12613001260718.

Abbreviations: ABPM, 24 h ambulatory blood pressure monitoring; ASQ, Ages and Stages Questionnaire; BP, blood pressure; CVD, cardiovascular disease; EPDS, Edinburgh Postnatal Depression Scale; GAD-7, General Anxiety Disorder 7-item scale; MIB, mother infant bonding; P4 Study, postpartum physiology, psychology and paediatric follow up study; PDS, Posttraumatic Diagnostic Scale; PTSD, post-traumatic stress disorder; SD, standard deviation.

* Corresponding author at: St George Hospital, Gray Street, Kogarah, NSW 2217, Australia.
E-mail addresses: Greg.Davis@health.nsw.gov.au (G.K. Davis), Lynne.Roberts2@health.nsw.gov.au (L. Roberts), g.mangos@unsw.edu.au (G. Mangos), Amanda.Henry@unsw.edu.au (A. Henry), Franziska.Pettit@health.nsw.gov.au (F. Pettit), a.osullivan@unsw.edu.au (A. O'Sullivan), Caroline.Homer@uts.edu.au (C.S.E. Homer), m.craig@unsw.edu.au (M. Craig), s.harvey@unsw.edu.au (S.B. Harvey), m.brown@unsw.edu.au (M.A. Brown).

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1. Introduction

Hypertensive diseases in pregnancy are the most common medical complication of pregnancy affecting 10% of pregnant women [1]. GH is usually a benign condition with good maternal and fetal outcomes but 4% of pregnant women will develop PE, with increased maternal and fetal morbidity and mortality [2]. Cardiovascular disease is the leading cause of death for women in the western world [3]. Women who have had hypertension in pregnancy have a 2–3 fold increased risk of CVD in later life [5] and an increased risk for venous thromboembolism, diabetes, microalbuminuria, end stage renal disease [4] and mental health disorders [6]. The significant physiological demands of pregnancy are a stress test [7] that either unmasks a predisposition to CVD [8,9], or initiates a cascade of vascular changes which lead to later CVD [10].

2. Hypertension and metabolic syndrome after hypertension in pregnancy

Subgroups of women with hypertension in pregnancy and CVD share the features of the metabolic syndrome including obesity, hypertension, insulin resistance and dyslipidaemia, and preeclampsia has been described as the metabolic syndrome of pregnancy [11]. This common risk pattern is relevant to clinical practice in that, although women with early onset PE (prior to 34 weeks gestation) have a greater risk of subsequent CVD [12] and end stage kidney disease [13], the features of the metabolic syndrome are more common in women with late onset PE (after 34 weeks gestation) or GH [14,15].

Thus, women with any form of PE or even GH should be considered at risk for future CVD. The diagnosis of hypertension in pregnancy therefore provides a unique opportunity to identify a group of young women at risk of later disease and to institute measures to potentially lower their long term risk [16,17]. Interventional studies examining exercise and dietary modification in the postpartum period have been shown to be effective, particularly in women who know they are at increased risk [18,19]. However data are urgently needed to determine prevention strategies, screening and treatment schedules for the large number of women who have had hypertension in pregnancy [17]. Perhaps the biggest barrier to date is our need to rely on cardiovascular risk assessments that are designed for use in the general population, usually older people and often male predominant [20,21]. For example, we have shown previously that women who have had hypertension in pregnancy have higher BP several years post-partum than women who had a normotensive pregnancy [22]. Nonetheless their BP levels fall within the so-called 'normal' range and are therefore unlikely to be recognised as having a BP higher than that expected for a young woman who has had a previously normal pregnancy.

What is needed is a study to define normal parameters for blood pressure and metabolic function in: 1) normal postpartum women; and 2) women who had hypertension in pregnancy; to determine where women who have had hypertension in pregnancy fall in newly defined 'normal' ranges. This is a major knowledge gap: to the best of our knowledge there are no published data to provide guidance to clinicians. Definition of the group of women at risk, i.e. falling outside newly defined normal parameters for this age group of women, would allow the establishment of a follow up guidance to coordinate early intervention for modification of lifestyle factors and treatment of hypertension and insulin resistance/diabetes [23,24].

3. Psychological issues after hypertension in pregnancy

Our society generally assumes that the birth of a child should be an entirely positive experience. While on balance this is usually true, these expectations mean that women may find it difficult to discuss some of their negative experiences. This is important as childbirth can be difficult, with 20–48% of women reporting their birth experience as traumatic [25]. At one extreme, pregnancy complications and a difficult childbirth can lead to PTSD [26], although the exact prevalence of PTSD among new mothers is uncertain [27]. Not surprisingly, PTSD appears to be more common where there have been complications in pregnancy and/or the birth, such as PE [28] and co-existing maternal depression further increases the risk of PTSD [29].

PTSD is one of a number of mental disorders that can be seen following a complicated pregnancy and birth. Increased levels of anxiety and depression are also reported amongst postpartum women, although it is not clear whether these symptoms develop during or after the pregnancy [6].

Gaining a better understanding of the psychological consequences of complicated pregnancies is crucial for a number of reasons. Firstly, apart from the impact of these psychological disorders on the mother, maternal PTSD, anxiety and depression can affect the emotional and behavioural development of the infant and disturb mother-infant attachment [30]. Secondly, there is increasing evidence that if groups at high risk of mental disorder can be identified, targeted interventions can prevent around 25% of the cases of mental disorder occurring [31]. However, the success of such preventative interventions relies on a valid way of identifying those at increased risk.

4. Paediatric outcomes after hypertension in pregnancy

While it is accepted that PE increases perinatal morbidity and mortality [2], the effect on the subsequent health and development of the infants of women who have had hypertension in pregnancy has not been adequately addressed. Variable findings have been reported [32,33] . Minor cognitive differences at two years of age were noted in infants of mothers with hypertension in pregnancy born at less than 35 weeks gestation [34] and a significant developmental delay was reported in the children of women who had PE in a study of neurodevelopmental disability at two years of age [35]. In a study of developmental outcomes at two years of age in babies born at less than 32 weeks gestation, those infants whose mothers had PE were more likely to have mild cognitive impairment (OR 10.9, 95%CI 1.4, 84.9) [36]. Similarly, in a small study of growth restricted babies (<5th centile) at three years of age, infants of mothers who had PE were more likely to have a moderately impaired cognitive development (mean IQ 85.5 vs. 96.9, $p < 0.03$) [37]. However in a long term epidemiological study of recruits into the Israeli armed forces at 17 years of age there was no difference in mean intelligence scores between those whose mothers had PE and those who did not [38].

The study design is a longitudinal follow up of infants born to mothers with and without hypertension, which will provide sufficiently powered, controlled data to assess the effect of hypertension during pregnancy on growth and development, with adjustment for risk modifying variables, particularly gestational age.

With this study we will define for the first time what should be considered normal BP (ABPM, routine office and central BP), lipids, heart and kidney function and mental health scores in young women who have had a normal pregnancy and the health of their babies. Similarly we will determine which women who were hypertensive in pregnancy and/or their babies who are at increased later risk.

5. Methods/design

5.1. Study design and setting

A prospective, open, cohort study is being undertaken at St George Hospital, a large metropolitan teaching hospital that serves