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Title	Hypertensive diseases of pregnancy and risk of hypertension and stroke in later life: results from cohort study
Type	Article
URL	https://clock.uclan.ac.uk/25141/
DOI	https://doi.org/10.1136/bmj.326.7394.845
Date	2003
Citation	Wilson, B. J., Watson, M. S., Prescott, Gordon, Sunderland, S., Campbell, Doris Margaret, Hannaford, Philip Christopher and Smith, William Cairns Stewart (2003) Hypertensive diseases of pregnancy and risk of hypertension and stroke in later life: results from cohort study. British Medical Journal (BMJ), 326. pp. 845-849. ISSN 0959-8138
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<https://doi.org/10.1136/bmj.326.7394.845>

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Hypertensive diseases of pregnancy and risk of hypertension and stroke in later life: results from cohort study

Brenda J Wilson, M Stuart Watson, Gordon J Prescott, Sarah Sunderland, Doris M Campbell, Philip Hannaford, W Cairns S Smith

Abstract

Objective To examine the association between hypertensive diseases of pregnancy (gestational hypertension and pre-eclampsia) and the development of circulatory diseases in later life.

Design Cohort study of women who had pre-eclampsia during their first singleton pregnancy. Two comparison groups were matched for age and year of delivery, one with gestational hypertension and one with no history of raised blood pressure.

Setting Maternity services in the Grampian region of Scotland.

Participants Women selected from the Aberdeen maternity and neonatal databank who were resident in Aberdeen and who delivered a first, live singleton from 1951 to 1970.

Main outcome measures Current vital and cardiovascular health status ascertained through postal questionnaire survey, clinical examination, linkage to hospital discharge, and mortality data.

Results There were significant positive associations between pre-eclampsia/eclampsia or gestational hypertension and later hypertension in all measures. The adjusted relative risks varied from 1.13-3.72 for gestational hypertension and 1.40-3.98 for pre-eclampsia or eclampsia. The adjusted incident rate ratio for death from stroke for the pre-eclampsia/eclampsia group was 3.59 (95% confidence interval 1.04 to 12.4).

Conclusions Hypertensive diseases of pregnancy seem to be associated in later life with diseases related to hypertension. If greater awareness of this association leads to earlier diagnosis and improved management, there may be scope for reducing a proportion of the morbidity and mortality from such diseases.

Introduction

Cardiovascular disease is a major public health problem in women in developed countries. Each year in the United Kingdom over 150 000 women die from vascular causes (mainly ischaemic heart disease and stroke).¹ Many die prematurely² or experience a non-fatal event, often leaving them with permanent

disability. In Britain angina may be as common in women as in men.³ Most of the aetiological research in women has concentrated on risk factors that are shared by men—for example, smoking, social class, family history, obesity, and lipid and clotting factors. Women, however, are exposed to several possible risk factors that are sex specific, including pregnancy, menopause, hysterectomy, and the use of exogenous hormones. Vital statistics collected in England and Wales between 1938 and 1960 suggest that pregnancy has an effect as parous women have higher mortality from hypertension, ischaemic and degenerative heart disease, and cerebrovascular disease than nulliparous women.⁴

During pregnancy, many women are affected by hypertensive problems, especially in the first pregnancy.⁵ Such problems fall into four categories: chronic (pre-existing) hypertension, gestational (transient) hypertension, pre-eclampsia/eclampsia, and pre-eclampsia superimposed on chronic hypertension.⁶ While the exact prevalence of each condition is difficult to determine, almost 10% of all pregnancies are thought to be complicated by high blood pressure.⁵ Nearly 30% of first pregnancies are thought to be affected by gestational hypertension, pre-eclampsia, or eclampsia.⁶

Despite their frequent occurrence, relatively little research has been conducted into the long term effects of hypertensive problems in pregnancy. Both gestational hypertension and pre-eclampsia or eclampsia may be associated in later life with raised blood pressure⁷⁻¹¹ or hypertension¹²⁻¹⁵ and cardiovascular disease.^{16 17} Many of the reported studies have examined only hypertension as an outcome and have been limited by small sample sizes,^{7 9-13 15} inappropriate comparison groups,^{8 12 15 18} or relatively short follow up.^{7 8} There is also evidence to suggest that self reported exposure is more prone to recall bias with increasing time.¹⁹⁻²¹ As information on pregnancy related exposures is often sought more than 10 years later^{20 22} recall bias is of particular concern.

We designed a retrospective cohort study using the Aberdeen maternity and neonatal databank, a computerised database which has collated validated data on all obstetric events in women attending the Aberdeen

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bmj.com 2003;326:845

maternity hospital since 1951.²³ The hospital and associated units provide obstetric care for a population of about 400 000 people. The databank used standardised diagnostic criteria during the study and linkage to the individual original obstetric case notes. We determined whether a recorded history of gestational hypertension or pre-eclampsia or eclampsia predicted cardiovascular disease in later life, as indicated by measures of mortality and morbidity.

Methods

Identification and tracing of women

From the databank we identified a cohort of women who were living in Aberdeen city at the time of delivery. The cohort comprised all women who had a diagnosis of pre-eclampsia or eclampsia during their first singleton pregnancy in the years 1951 to 1970; an individually matched sample of women with a diagnosis of gestational hypertension during their first singleton pregnancy and matched for age to the nearest year and year of delivery with the previous group; and an individually matched sample of women with no history of raised blood pressure during their first singleton pregnancy likewise matched with the first group. Gestational hypertension was defined as diastolic pressure ≥ 90 mm Hg on two occasions at least four hours apart or a single reading of ≥ 110 mm Hg from 20 weeks' gestation onwards in a previously normotensive woman. Pre-eclampsia was defined as gestational hypertension plus proteinuria of ≥ 0.3 g/24 hours. Eclampsia was defined clinically as convulsions occurring in the presence of pre-eclampsia. Women with chronic hypertension were separately categorised on the databank and excluded from this study. No other exclusion criteria were applied.

We carried out two tracing exercises for the cohort. The first, carried out in 1996, was at the local level using the Grampian community health index (a comprehensive regional primary care register²⁴) to identify the current name and address of all cohort members still alive and resident in the Grampian area. From this exercise we were able to contact the current general practitioners of women in the original cohort who were still living in the area. The second tracing exercise was at national level and was undertaken in 1999. The information and statistics division (ISD) of the NHS in Scotland, Edinburgh, used probability matching to identify any women from the cohort who were admitted to hospital from 1980 to 1999. In collaboration with the NHS central registry in Southport, the division also ascertained the vital status of women in the cohort and obtained death certificates for any who had died, including those who died in the United Kingdom but outside Scotland. We retrieved the original databank records of women who could not be traced through either exercise to check whether additional information was available to maximise tracing rates.

Ascertainment of outcomes

Questionnaire and clinical examination—We contacted the general practitioner of each woman still living in Grampian and sought consent for us to contact her. We sent those for whom consent was given a self completion questionnaire, with questions covering general

health, lifestyle and wellbeing, and obstetric history, including illnesses related to pregnancy. The questions were taken from previously validated questionnaires. The study hypothesis was not disclosed to prevent bias in reporting current health status. Non-respondents received two reminder questionnaires together with reply paid envelopes. The questionnaire included an invitation to contribute further by attending for a medical examination. Each medical examination was conducted by one of two trained research nurses in accordance with an examination protocol developed for the project. The nurses were blind to study group status of the women they were examining, and appointments were scheduled in a random manner so that no batching of groups occurred, which would undermine blinding. All women had blood pressure measured twice with a random zero sphygmomanometer with the appropriate cuff size in the seated position after a period of rest, and the mean of the two readings was taken. Height and weight were measured and an electrocardiogram produced.

Hospital discharges—In collaboration with the information and statistics division (ISD) of the NHS in Scotland we conducted a data linkage exercise²⁵ to obtain details of all hospital discharges in cohort members. The division holds data on hospital discharges and cancer registrations of individuals who have been resident in Scotland at any point. Probability matching was based on first name, surname, previous surname, and date of birth, and any obvious mismatches were checked manually by the division.

Deaths—We obtained details of the dates and causes of death from the UK NHS central register.

Sample size

The expected frequency of outcome measures varies for different cardiovascular conditions in women in Scotland, from 0.5% for electrocardiographic evidence of myocardial infarction to over 8% for angina defined by Rose questionnaire criteria.³ The frequency of hypertension varies depending on the definition used. One study of women aged 40–59 years in Scotland identified 7% with a diastolic pressure greater than 100 mm Hg.²⁶ For an outcome present in 5% of the control group, a sample size of 932 subjects per group would detect a doubling of risk, with 80% power at the 5% level of significance. On this basis, we included all women with pre-eclampsia or eclampsia (likely to be the group with fewest potential members) in the cohort and randomly sampled control and gestational hypertension groups (matched for age and year of delivery) of the same size as this group.

Statistical analysis

We used χ^2 and t tests as appropriate to test for baseline differences between the three groups, and, for all analyses, we used the control group as reference for comparisons with each of the two “exposed” groups (gestational hypertension and pre-eclampsia or eclampsia). For the questionnaire and clinical examination data, we computed odds ratios and used logistic regression methods to adjust for the influences of age, body mass index, and smoking behaviour at follow up. For the mortality and hospital discharge outcomes, we constructed diagnosis groups using international classification of diseases (ninth/tenth edition) codes: “hypertension” (401-4/I10-14); “ischaemic heart

Table 1 Baseline characteristics of study cohort at booking unless stated otherwise

	Group		
	Control	Gestational hypertension	Pre-eclampsia/eclampsia
Total	1197	1197	1199
Mean (SD) age at delivery (years)	24.2 (4.69)	24.2 (4.64)	24.2 (4.68)
No (%) ≤ 20 weeks' gestation	736/1007 (73.1)	908/1155 (78.6)†	935/1140 (82.0)†
Mean (SD) BMI (kg/m ²)*	21.3 (2.7)	22.3 (3.1)†	22.2 (3.1)†
No (%) in social class I-III non-manual	384/947 (40.6)	370/1130 (32.8)†	291/1084 (26.8)†
No (%) who had ever smoked	140/325 (43.0)	124/349 (35.5)†	118/346 (34.1)†

*Corrected for gestation, excludes women over 20 weeks' gestation at booking; data missing for 10 women.

†P<0.05 compared with control group.

disease" (410-4, 428/120-25, I50); "cerebrovascular disease" (430-8/I60-9); "kidney disease" (580-99/N00-39); "other circulatory disease" (390-8, 405, 415-27, 440-59/ I00-9, I15, I26-8, I30-49, I51-2, I70-99). We counted only first admissions in a diagnosis group, using the date of first admission as the incident date, but women could appear in more than one diagnosis group. We computed incident rate ratios for deaths and hospital discharges and used logistic regression to adjust for potential confounders.

Social class (UK registrar general) at time of follow up was used for analyses of questionnaire and clinical examination outcomes. This was allocated on the basis of the woman's own social class, unless this fell outside classes I-V, in which case the spouse or partner's social class was used if available. Social class at the time of the

index pregnancy, based on the occupation of the spouse or head of household, was used for analyses of hospital admissions and deaths.

Results

The total cohort comprised 3593. Table 1 summarises the baseline characteristics of the three groups. The similarity of the mean ages at delivery reflects the initial age matching. Compared with the control group, women in the gestational hypertension and pre-eclampsia or eclampsia groups were less likely to be in occupational classes I-III non-manual (professional/administrative) but more likely to have booked for antenatal care before 20 weeks' gestation. They were also less likely to ever have been smokers

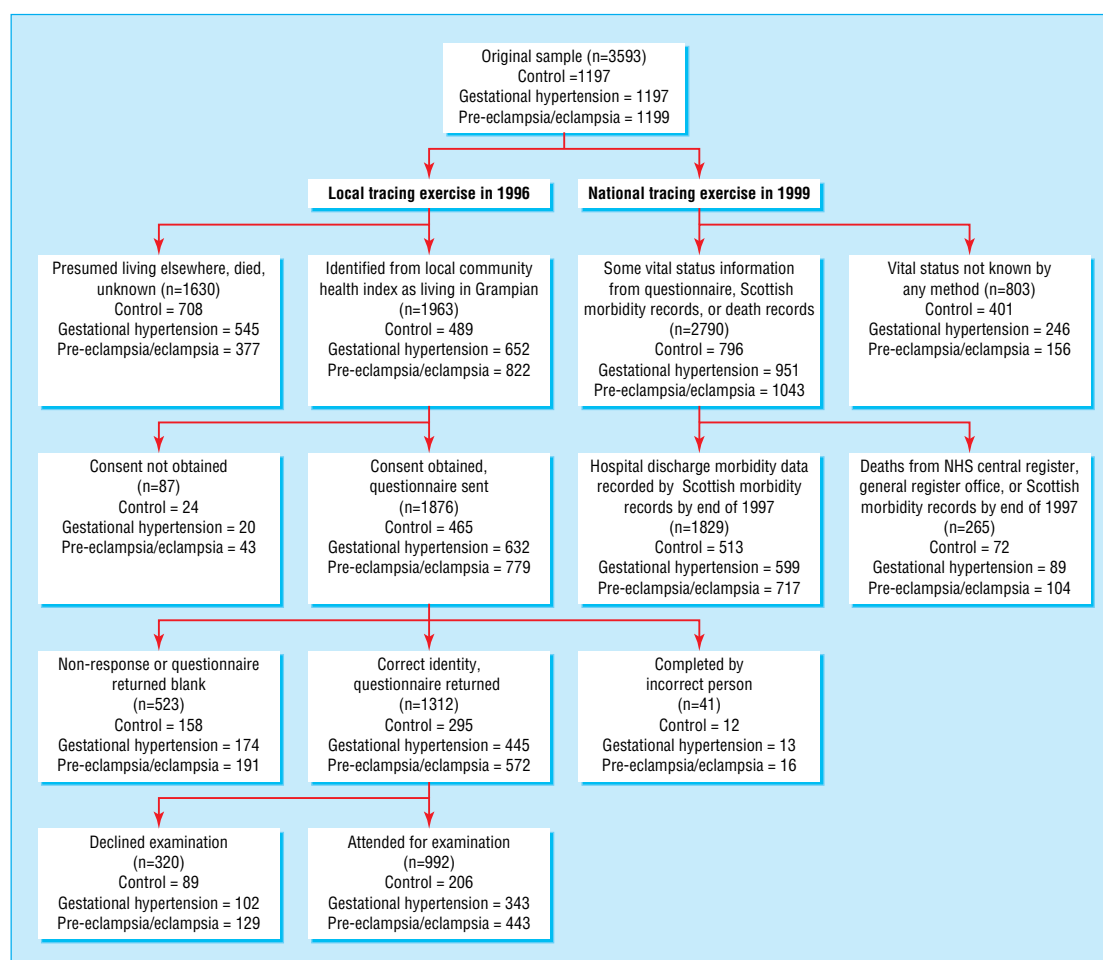


Fig 1 Cohort tracing in two different exercises including events up to 1997 (death and hospital discharge frequencies are not mutually exclusive; many women who died also had hospital discharges)

Table 2 Baseline and follow up characteristics of questionnaire respondents. Figures are numbers (percentage) of women unless stated otherwise

	Group		
	Control	Gestational hypertension	Pre-eclampsia/eclampsia
Total respondents	295/453 (65.1)	445/619 (71.9)	572/763 (75.0)
Attended for clinical examination	206 (69.8)	343 (77.1)	443 (77.4)
Mean (SD) age (years)	59.9 (8.0)	60.7 (7.5)	60.4 (7.6)
≤20 weeks' gestation at booking	183/253 (72.3)	348/430 (80.9)‡	472/548 (86.1)‡
In social class I-III non-manual at follow up	181/287 (63.0)	279/437 (63.8)	350/562 (63.3)
Attained higher education	109/293 (37.2)	134/438 (30.2)	173/563 (30.5)
Mean (SD) BMI at follow up (kg/m ²)*	25.4 (4.5)	26.6 (4.7)§	26.9 (4.8)§
Alcohol intake (units/week):			
0	146 (49.5)	233 (52.4)	303 (53.0)
1-14	139 (47.1)	199 (44.7)	258 (45.1)
>14	10 (3.4)	13 (2.9)	11 (1.9)
Took regular exercise†	80/286 (28.2)	109/427 (25.5)	176/556 (31.7)
Had ever smoked at follow up	158/295 (53.6)	210/445 (47.2)‡	227/572 (39.7)‡
Ever used oral contraceptive	128/294 (43.5)	172/438 (39.3)	240/563 (42.6)
Ever used hormone replacement therapy	95/291 (32.6)	115/436 (26.4)	154/562 (27.4)

*Data missing for five respondents.

†≥20 minutes ≥ three times per week.

‡P<0.05 compared with control group.

Table 3 Odds ratios (control group=1.0) for measures of hypertensive and other cardiovascular disease in questionnaire respondents

Outcome	Control*	Gestational hypertension				Pre-eclampsia/eclampsia			
		No*	Odds ratio (unadjusted)	Adjusted† odds ratio (95% CI)	P value	No*	Odds ratio (unadjusted)	Adjusted† odds ratio (95% CI)	P value
Hypertension, doctor diagnosis	76/277	215/428	2.67	2.47 (1.74 to 3.51)	<0.001	327/542	3.02	3.98 (2.82 to 5.61)	<0.001
Currently taking anti-hypertensive medication	43/295	113/442	2.01	1.89 (1.23 to 2.88)	0.003	151/565	2.14	1.90 (1.27 to 2.86)	0.002
Stroke, doctor diagnosis	3/266	10/404	2.23	2.42 (0.59 to 9.98)	0.22	19/511	3.39	3.41 (0.95 to 12.2)	0.06
Angina, doctor diagnosis	24/273	40/413	1.11	1.02 (0.58 to 1.81)	0.94	69/518	1.59	1.61 (0.95 to 2.73)	0.08
Angina, Rose criteria	22/290	34/441	1.02	0.93 (0.52 to 1.65)	0.80	47/559	1.12	0.90 (0.52 to 1.55)	0.69
Possible MI, doctor diagnosis	14/268	16/408	0.74	0.73 (0.32 to 1.63)	0.44	20/512	0.74	0.76 (0.35 to 1.63)	0.48
Possible MI, Rose questionnaire	22/292	19/444	0.55	0.48 (0.25 to 0.95)	0.03	36/569	0.83	0.84 (0.47 to 1.50)	0.56
Intermittent claudication, Rose criteria	3/292	7/440	1.56	1.54 (0.38 to 6.19)	0.55	9/565	1.56	1.57 (0.41 to 6.05)	0.51
DVT, doctor diagnosis	22/269	25/404	0.74	0.65 (0.35 to 1.20)	0.17	33/510	0.78	0.75 (0.42 to 1.34)	0.32
"Kidney disease", doctor diagnosis	7/267	9/398	0.85	0.64 (0.22 to 1.82)	0.40	28/508	2.17	2.39 (1.01 to 5.65)	0.05

MI=myocardial infarction; DVT=deep vein thrombosis.

*Denominator excludes missing responses.

†Adjusted for age, BMI, social class, and smoking habit.

(although smoking data at the time of pregnancy were incomplete), and there were small significant differences between the groups in mean body mass index.

Tracing

Local tracing identified 1963 women (54.6%) who were still alive and resident in Grampian (figure). General practitioners gave consent for a questionnaire to be sent to 1876 (95.6%) of these women. The information and statistics division ascertained the current vital status of 2790 (77.7%) of the original cohort, of whom 265 (9.5%) were known to have died. Linkage with hospital discharge data identified 1829 (65.6%) women of the original cohort who had been admitted at least once to a Scottish hospital between 1980 and 1999. Compared with these untraced women, on average the traced women were a year older at delivery, the mean body mass index at the time of the index pregnancy was 0.6 kg/m² higher, and fewer were from non-manual social classes (31% (778/2481) *v* 39%

(267/680)). The success of the tracing differed across the three comparison groups (figure).

Of the 1876 questionnaires, 1312 (71%) were returned with usable responses. Forty one were incorrectly identified as being eligible for the study by the Aberdeen neonatal and maternity databank. Table 2 summarises the self reported demographic and health characteristics of the questionnaire respondents at follow up. Respondents were more likely to be in manual social classes at baseline than the starting cohort. Respondents in gestational hypertension and pre-eclampsia or eclampsia groups had higher mean body mass index at follow up and were less likely to be former or current smokers, as they were at baseline. There were no clinically significant differences in alcohol intake, regular exercise, or use of exogenous hormones across the groups. A much higher proportion of the women were of non-manual social classes at follow up, using the woman's own profession,

Table 4 Odds ratios (control group=1.0) for measures of hypertensive and other cardiovascular disease at clinical examination

	Gestational hypertension					Pre-eclampsia/eclampsia				
	Control	No	Odds ratio (unadjusted)	Adjusted* odds ratio (95% CI)	P value	No	Odds ratio (unadjusted)	Adjusted* odds ratio (95% CI)	P value	
Currently taking anti-hypertensive drugs	25/206	80/343	2.20	1.95 (1.18 to 3.24)	0.009	129/443	2.97	2.77 (1.72 to 4.47)	<0.001	
Not on anti-hypertensive drugs but raised blood pressure at time of examination†	30/206	61/343	1.26	1.13 (0.69 to 1.86)	0.63	87/443	1.43	1.40 (0.87 to 2.26)	0.16	
Provisionally fulfilling WHO criteria for hypertension	55/206	141/343	1.90	1.70 (1.13 to 2.56)	0.01	216/443	2.60	2.62 (1.77 to 3.86)	<0.001	
Changes on ECG (any abnormality)‡	20/205	32/342	0.95	0.96 (0.52 to 1.77)	0.90	61/437	1.50	1.96 (0.96 to 2.98)	0.07	

*Adjusted for age, BMI, social class, and smoking habit.

†Mean diastolic ≥ 95 mm Hg or mean systolic ≥ 160 mm Hg or both.

‡Minnesota coding.

Table 5 Incident rate ratios (control group=1.0) for hospital admissions for specific conditions for all traced women

Discharge diagnosis*	Admissions in control group (n=796)	Gestational hypertension (n=951)				Pre-eclampsia/eclampsia (n=1043)			
		No of admissions	Incident rate ratio (unadjusted)	Adjusted† incident rate ratio (95% CI)	P value	No of admissions	Incident rate ratio (unadjusted)	Adjusted† incident rate ratio (95% CI)	P value
All causes	513	599	0.97	0.96 (0.84 to 1.09)	0.53	717	1.09	1.07 (0.95 to 1.22)	0.28
Hypertension	7	28	3.36	3.72 (1.43 to 9.65)	0.007	31	3.39	3.19 (1.21 to 8.39)	0.019
Cerebrovascular disease	13	22	1.42	1.53 (0.72 to 3.27)	0.27	34	2.00	2.10 (1.02 to 4.32)	0.043
Ischaemic heart disease	38	52	1.15	1.06 (0.68 to 1.65)	0.79	48	0.96	0.89 (0.56 to 1.40)	0.61
Other circulatory	64	108	1.42	1.51 (1.06 to 2.14)	0.021	121	1.45	1.49 (1.05 to 2.11)	0.024
Kidney disease	38	34	0.75	0.76 (0.47 to 1.28)	0.29	67	1.35	1.27 (0.81 to 1.98)	0.30

*First admission only for diagnosis group.

†Adjusted for age at delivery and social class.

Table 6 Incident rate ratios (control group=1.0) for mortality for specific conditions all traced women

Cause	Deaths in control group (n=796)	Gestational hypertension (n=951)				Pre-eclampsia/eclampsia (n=1043)			
		Deaths	Incident rate ratio (unadjusted)	Adjusted* incident rate ratio (95% CI)	P value	Deaths	Incident rate ratio (unadjusted)	Adjusted† incident rate ratio (95% CI)	P value
All causes	72	89	1.03	1.03 (0.74 to 1.45)	0.85	104	1.13	1.17 (0.84 to 1.65)	0.36
Cerebrovascular disease	5	13	2.18	2.87 (0.81 to 10.2)	0.10	16	2.44	3.59 (1.04 to 12.4)	0.044
Ischaemic heart disease	10	17	1.42	1.21 (0.53 to 2.75)	0.65	26	1.98	1.95 (0.90 to 4.21)	0.091

*Adjusted for age at delivery and social class.

than at baseline using husband/partner's profession. There was no gradient in social class at follow up across the groups using this measure.

Questionnaire assessed outcomes

After adjustment for known risk factors for hypertension, women in both the gestational hypertension and pre-eclampsia or eclampsia groups had higher odds ratios for indicators of hypertension (table 3). This was not seen for the other conditions of interest, except for kidney disease in the pre-eclampsia or eclampsia group, which may have related to the original episode in pregnancy. Similar results were observed in the clinical examination data (table 4), with increased risk of hypertension defined by WHO criteria in both gestational hypertension and pre-eclampsia or eclampsia groups. In total, 41.1% of the former and 48.8% of the latter provisionally fulfilled the WHO criteria for hypertension compared with 26.7% in the control group.

Hospital admissions

Women in the gestational hypertension group were more likely to have been admitted to hospital for cerebrovascular disease, ischaemic heart disease, hypertension, and "other" circulatory disease, although this reached significance only for hypertension and other circulatory disease (table 5). Women in the pre-eclampsia or eclampsia group were also more likely to be admitted for hypertension, cerebrovascular disease, and other circulatory disease.

Mortality

Over 90% of the traced cohort were alive at the time of analysis, and there were 265 deaths available for analysis (table 6). By the time of follow up, there were 72 deaths in the control group, 89 in the gestational hypertension group, and 104 in the pre-eclampsia or eclampsia group. No deaths were coded to hypertension per se. After adjustment, mortality for all causes, stroke, and ischaemic heart disease was higher

in both the gestational hypertension and pre-eclampsia or eclampsia groups. The pattern was consistent, though only the increased risk of stroke in the pre-eclampsia or eclampsia group was significant.

Discussion

Women with a history of gestational hypertension or of pre-eclampsia or eclampsia are at increased risk of hypertensive and associated diseases in later life. Our findings are consistent with those of previous work.^{7–15} We found an increased risk of admission to hospital for stroke and mortality from stroke but no significant increased risk of morbidity and mortality from coronary heart disease as has previously been reported.^{16–17} This may be because we used a study design that did not depend on recall and used standardised criteria to distinguish gestational hypertension and pre-eclampsia from chronic pre-existing hypertension. This is of importance in counselling women about their future health risks after delivery and in designing healthcare interventions to minimise avoidable morbidity and mortality.

Our design minimised the information bias that may occur with retrospective studies and quantified the absolute risk of adverse outcomes. It has two key advantages over many other investigations into the associations of interest: the underlying cohort design and the use of different data sources to ascertain the outcomes of interest, which permitted assessment of the consistency of the findings.

Influence of social class

Social class differed between the three study groups in the original cohort. This might be a result of chance or might indicate an association between social class and hypertensive diseases in pregnancy. Though such associations have been reported,^{27–28} there is no clear social class gradient. Pre-eclampsia or eclampsia is less common in smokers than in non-smokers^{27–28} and currently smoking is associated with social class, though in 1961 UK survey data showed little social class gradient in smoking in women.²⁹ We found a modest gradient in smoking across social class at the time of pregnancy but smoking information was recorded for only 28%. If there is a true inverse association between pre-eclampsia or eclampsia and smoking, and if recorded smoking habit during first pregnancy is an indicator of likely smoking habit in later life, then the pre-eclampsia or eclampsia group should in theory be at a lower than average risk of smoking related disease in later life. If so, this would operate against the hypothesis and might suggest that our results underestimate the association between pre-eclampsia or eclampsia and circulatory diseases.

Several studies have shown a risk of coronary heart disease associated with pre-eclampsia, though our findings were not significant. Retrospective studies of coronary heart disease that used patient recall of pre-eclampsia are subject to recall bias, while other cohort studies have combined coronary heart disease outcomes into a single cardiovascular disease group.³⁰

Tracing and investigation

The tracing rates varied across the three groups. Those who were normotensive during their first full term pregnancy were least likely to still be living in

What is already known on this topic

Much is known about the effect of cardiovascular risks factors that are shared by men and women, but less on those specific to women

Retrospective studies, based on patient recall, suggest that hypertension in pregnancy may be associated with increased risk of cardiovascular diseases in later life

What this study adds

Prospective recording of blood pressure and proteinuria shows that women who experienced raised blood pressure in pregnancy have a long term risk of hypertension

Women who experience raise blood pressure in pregnancy have an increased risk of stroke and, to a lesser extent, an increased risk of ischaemic heart disease

Long term cardiovascular risks are greater for women who had pre-eclampsia than those who experienced gestational hypertension (hypertension without proteinuria)

Grampian at follow up, suggesting selective migration from the area by the control groups. The national tracing exercise, however, was more successful and provided vital status and hospital discharge data for a larger proportion of women in each comparison group. Broadly similar patterns of cardiovascular sequelae were observed in the different groups, irrespective of whether the outcome measure used was obtained through the local or national tracing. Another important potential bias could have occurred if there were important differences in the response rates of those traced locally. There were in fact only small differences in the response rates to the survey by the three comparison groups (70%, 77%, and 77%) as shown in table 2, suggesting that response bias is unlikely to have materially affected our results. There were more women from higher social classes in the control group (table 1). Such women were more likely to emigrate from Grampian, resulting in a lower response rate in the control group.

Consistency of findings

There was consistency of the findings across the different methods of ascertaining outcomes. The association between gestational hypertensive disease and hypertension in later life was seen in the questionnaire and clinical examination data and also in the hospital diagnosis data and the mortality data. We suggest that our observations cannot be explained by chance or bias. The findings have implications for the aetiology and pathogenesis of circulatory disease, both in pregnancy and in later life. They also suggest that interventions that might minimise the risk of such conditions in later life should be identified and evaluated.

We acknowledge the contribution of Dean Phillips for tracing and data management; Amanda Cardy for review of the original case notes; Nicola Torrance for assistance with the data collection and the operation of clinics; Linda Harrigan and Wendy Aiken for entering the data; Tracy Mapp for assistance

with the study design; Isobel Ford and Ian Ross at Department of Clinical Biochemistry, Aberdeen, for assistance with the laboratory analysis; Val Angus of practitioner services at Grampian Health Board for tracing women; information and statistics division for record linkage; and the staff of the MONICA project at Queens University Belfast for assistance with Minnesota coding of ECGs.

Contributors: MSW, DMC, BJW, PH, and WCSS conceived the study and contributed to the analysis and interpretation. MSW also managed the implementation of the study. GJP did the statistical analysis and contributed to the interpretation of the findings. SS contributed to the development of the clinical measurement procedures and was responsible for the clinical examinations. The report was written with contributions from all authors. WCSS is the guarantor.

Funding: British Heart Foundation, grant number PG/95130. The guarantor accepts full responsibility for the conduct of the study, had access to the data, and controlled the decision to publish.

Competing interests: None declared.

Ethical approval: The study protocol was approved by the Joint Grampian Health Board and University of Aberdeen ethics committee, the information and statistics division privacy advisory committee and the Grampian Health Board general practice subcommittee.

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(Accepted 6 March 2003)