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Maternal and fetal morbidity following discontinuation of antihypertensive drugs in mild to moderate chronic hypertension: A 4-year observational study

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ABSTRACT

Objective: To assess maternal and fetal morbidity in women with mild to moderate chronic hypertension on antihypertensive drug therapy compared to cessation of therapy.
Methods: This was a prospective observational study included 222 women with mild to moderate chronic hypertension (systolic blood pressure of 140–159 mmHg or diastolic blood pressure of 90–109 mmHg) who were divided into two groups based on antihypertensive drug intake, treatment group (n = 104) who received methyl dopa, and non-treatment group (n = 118) who used only low dose aspirin. Patients were followed to assess maternal and fetal outcome.
Results: There were significant differences between the two groups regarding the development of severe hypertension ($p < 0.001$), renal impairment ($p < 0.001$), ECG changes ($p < 0.001$), placental abruption ($p < 0.05$), repeated hospital admissions ($p < 0.001$), preterm delivery ($p < 0.05$) and neonatal ICU admission ($p < 0.05$) with higher occurrence in the non-treatment group. There were no significant differences between the two groups in terms of the development of preeclampsia, hepatic impairment, mode of delivery, venous thromboembolism, small for gestational age, intrauterine fetal demise or neonatal mortality ($p > 0.05$).
Conclusion: Maternal and fetal morbidity is increased following cessation of antihypertensive drug use in patients with mild to moderate chronic hypertension. Further larger studies are warranted to confirm or refute our findings.

1. Introduction

Chronic hypertension complicates between 1% and 5% of pregnancies. It is associated with poor outcomes of pregnancy and, together with hemorrhage, was of the major contributors to maternal morbidity and mortality in developed and developing countries [1–3].

Women with chronic hypertension had high pooled incidences of superimposed pre-eclampsia, cesarean section, preterm delivery, birth weight <2500 g, neonatal unit admission and perinatal death [4,5].

Mild to moderate chronic hypertension was defined as a pregnancy with systolic blood pressure of 140–159 mmHg or diastolic blood pressure of 90–109 mmHg. Treatment of such cases may adversely affect fetal growth [6].

Most of previous studies focused on the fetal outcome with little attention to maternal morbidity from discontinuation of antihypertensive drug therapy in mild to moderate chronic hypertension upon occurrence of pregnancy.

The aim of this study was to assess maternal and fetal morbidity in women with mild to moderate chronic hypertension on antihypertensive drug therapy compared to cessation of therapy.

2. Materials and methods

This was a prospective observational study carried out at the Department of Obstetrics and Gynecology in collaboration with Cardiology and Internal Medicine Departments at Menoufia University Hospital, Menoufia, Egypt in the period between March 2012 and March 2016.

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The institutional review board approved the study protocol and an informed consent was obtained from all participants prior to commencing the study.

Pregnant women diagnosed with mild to moderate chronic hypertension, with systolic blood pressure of 140–159 mmHg or diastolic blood pressure of 90–109 mmHg [6], at the beginning of pregnancy were included in the study.

Women with multiple pregnancies, women with proteinuria at less than 20 weeks' gestation, women having other associated medical disorders as diabetes mellitus, bronchial asthma & epilepsy and pregnancies complicated by fetal malformations were excluded from the study.

Patients were divided into two groups according to antihypertensive drug intake as some mothers choose not to take the prescribed antihypertensives due to the worries of possible hazards for their babies.

Group 1 (treatment group): included 104 pregnant women who choose to take α-methyl dopa tablets (Aldomet, 250 mg tab Kahira Pharma. & chem. ind. co. Egypt) instead of their pre-pregnancy antihypertensive medications. Alpha-methyl dopa was started in doses of 500 mg every 12 h per day with modification of the dosage according to blood pressure readings with 2 gm as a maximal daily dose together with low dose aspirin (Jusprin 81 mg tablets, Future Pharmaceutical industries, Egypt) throughout pregnancy.

Group 2 (non-treatment group): included 118 pregnant women who choose to stop intake of antihypertensive drugs but agreed to take low dose aspirin (Jusprin 81 mg tablets, Future Pharmaceutical industries) throughout pregnancy.

Enrolled women were followed up via regular antenatal care visits every 1–3 weeks (minimum 6 visits) to be seen every time by an obstetrician and cardiologist from the start of pregnancy till the end of the puerperium and received the standard management at the hospital. Patients who developed severe hypertension were admitted to hospital for blood pressure control. Patients diagnosed with severe pre-eclampsia were managed by termination of pregnancy according to local hospital protocol.

2.1. Outcome measures

Maternal outcome: development of severe hypertension (systolic blood pressure ⩾160 mmHg and/or diatolic blood pressure ⩾110 mmHg), superimposed preeclampsia (a new onset proteinuria with 0.3 g of protein or more in a 24-h urine specimen after 20 weeks' gestation), eclampsia (generalized convulsions), renal impairment (elevated serum creatinine ⩾1.1 mg/dl), liver impairment (elevated liver enzymes twice the normal values), ECG changes (left ventricular heave and/or strain pattern), placental abruption, mode of delivery, hospital admissions for blood pressure control, venous thromboembolism (VTE) and maternal mortality.

Fetal-neonatal outcome: small for gestational age (SGA) defined as a birth weight <10th percentile, preterm labour (delivery <37 weeks), intrauterine fetal demise (IUFD), admission to neonatal intensive care unit (NICU) and neonatal death (defined as death during the first four weeks after delivery).

2.2. Statistical analysis

The data collected were tabulated & analyzed by SPSS (Statistical Package for the Social Science software) version 20.

Quantitative data were expressed as mean & standard deviation

(X ± SD) and analyzed by applying student *t* test for comparison of two groups of normally distributed variables and two groups of not normally distributed variables by applying Mann-Whitney Test.

Qualitative data were expressed as number and percentage (No & %) and analyzed by applying Chi-square test.

All these tests were used as tests of significance at:

- P value > 0.05 was considered statistically non significant.
- P value ⩽ 0.05 was considered statistically significant.
- P value ⩽ 0.001 was considered statistically highly significant.

3. Results

Out of 3642 pregnant women, 276 women with chronic hypertension were identified with exclusion of 34 women (not meeting inclusion criteria or declined to participate), and 20 patients dropped out, so 222 women completed in the study (Fig. 1: The flow diagram).

Table 1 shows the maternal characteristics. There were no significant differences between the two groups regarding the age, parity, body mass index or gestational age at inclusion ($p > 0.05$). There were highly significant differences between the two groups regarding blood pressure readings at inclusion and delivery and gestational age at delivery ($p < 0.001$) with higher blood pressure and earlier delivery in the non-treatment group.

Table 2 reveals the maternal outcome. There were significant differences between the two groups regarding the development of severe hypertension ($p < 0.001$), renal impairment ($p < 0.001$), ECG changes ($p < 0.001$), placental abruption ($p < 0.05$) and repeated hospital admissions ($p < 0.001$) with higher occurrence in the non-treatment group. There were no significant differences between the two groups regarding the development of preeclampsia, hepatic impairment, mode of delivery or venous thromboembolism ($p > 0.05$).

Table 3 reveals the fetal and neonatal outcome. There were no significant difference between the two groups regarding the development of small for gestational age, intrauterine fetal demise or neonatal mortality ($p > 0.05$). There were significant difference between the two groups regarding preterm delivery ($p < 0.05$) and NICU admission ($p < 0.05$) which were higher in the non-treatment group.

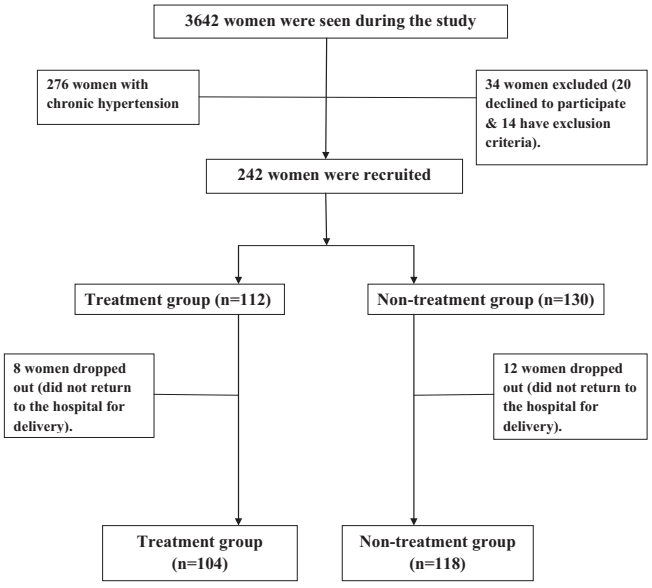

Fig. 1. Flow diagram of recruitment and retention of participants in the study.