Original Research

Ambulatory blood pressure monitoring during pregnancy: an Italian experience

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Summary

Objective: To describe the impact of a collaborative Italian diagnostic pathway offering ambulatory blood pressure (BP) monitoring (ABPM) in High Risk Antenatal Clinic (HRAC) pregnant women. The study included 395 pregnant women evaluated at HRAC between 2012 and 2016, while analyzing demographic, clinical characteristics, and prescription of ABPM. Pregnant women were firstly seen when gestational age was 19.6 ± 9.6 weeks. In at least one-third of cases, ABPM was followed by medical intervention aiming to modify the pre-existing therapeutic treatment. Hypertension and overweight were the main reasons for performing ABPM. WCH: white-coat hypertension.

Key words: High risk antenatal clinic; Pregnancy; Hypertension; Obesity; Ambulatory blood pressure monitoring.

Introduction

Hypertensive disorders in pregnancy are a leading cause of maternal morbidity and mortality worldwide. On one hand, a condition of hypertension developed during pregnancy impacts development of high blood pressure (BP) values increasing cardiovascular risk of women [1]. On the other, diagnosis and acute management of severe hypertension is crucial in order to reduce maternal mortality and screen for pre-eclampsia (PE) [2].

Data from the United States report that PE affects about 3% of pregnancies, and all other hypertensive disorders complicate approximately 5-10% of pregnant women.[3] PE represents common and dangerous complication of pregnancy, and causes maternal and perinatal illness. Moreover, it is responsible for a high proportion of maternal and infant deaths. Common findings during PE are increased BP and proteinuria, and generalized dysfunction of the maternal endothelium, secondary to exaggerated systemic inflammatory response mediated by cytokines [4].

Hypertension during pregnancy has been classified into four categories: 1) preeclampsia-eclampsia, 2) chronic hypertension (of any cause), 3) chronic hypertension with superimposed PE, and 4) gestational hypertension [1]. According to National Institute for Health and Care Excellence (NICE) guidelines, pregnant women should undergo more frequent BP measurements in the presence of the following risk factors: age 40 years or older, nulliparity, pregnancy interval of more than ten years, family history or previous history of PE, body mass index 30 kg/m^2 or above, pre-existing vascular disease such as hypertension, pre-existing renal disease, and multiple pregnancy [2]. For management of hypertension, ambulatory BP monitoring (ABPM) appears to be better than clinic BP, since around-the-clock BP values are strongly related to target organ damage, vascular risk, and long-term patient prognosis [5].

The aim of this study was to review the impact of a collaborative diagnostic pathway between the High Risk Antenatal Clinic (HRAC), Obstetrics and Gynaecology Unit, and the Hypertension Center, Clinica Medica Unit, at the General Hospital of Ferrara, Region Emilia-Romagna of Italy, offering ABPM in selected cases of pregnant women.

Materials and Methods

This retrospective study, conducted in agreement with the Declaration of Helsinki of 1975, revised in 2013, included all pregnant women evaluated at the local HRAC between January 1, 2012, and December 31, 2016, recorded in the database of the HRAC, and maintained by midwives. All subjects gave informed written

Table 1. — *Reasons for referral of pregnant women to high risk antenatal clinic.*

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Fetal growth restriction	27 (6.8%)
Diabetes mellitus	134 (33.9%)
Type I diabetes mellitus	24 (17.9% of diabetic women)
Type II diabetes mellitus	4 (3% of diabetic women)
Gestational diabetes	106 (79% of diabetic women)
Pre-eclampsia during a previous pregnancy	14 (3.5%)
Hypertension	77 (19.4%)
Overweight	97 (24.5%)
Excessive weight gain	11 (2.8%)
Rheumatological diseases	61 (15.4%)
Heart diseases	19 (4.8%)
Kidney diseases	14 (3.5%)

Figure 1. — Decision tree analysis evaluating patients who underwent ambulatory blood pressure monitoring (ABPM). Hypertension and overweight are the main reasons for performing ABPM.

consent for data recording and analysis.

The present HRAC functions as a referral center for a catchment area in North Eastern Italy. Pregnant women, who have risk factors according to a regional protocol, are referred from the local antenatal clinics. A senior Obstetrician would see each patient, perform ultrasound and Doppler studies, establishing the management.

The following parameters were recorded in the database: age, history of diabetes mellitus, hypertension, rheumatological diseases, heart diseases, kidney diseases, overweight that could be developed before or during pregnancy, PE, week of pregnancy at the time of every evaluation, presence of fetal complications such as fetal growth restriction, type of delivery, miscarriage or abortion, [6] gestational age and weight of the baby at the time of delivery (according to Italian birthweight charts), and week of pregnancy at the time of ABPM changes in anti-hypertensive treatment. Type of treatment was not analyzed, since only treatment variation happening after ABPM was taken into consideration. In agreement with national dispositions by law in terms of privacy, all potential identifiers from the database provided for this study have been removed. Every record corresponded to a single patient identified by a progressive number. Since HRAC is a hub center, some women had their deliver elsewhere, therefore data about the final weeks of their pregnancy could not be collected. Thus, these cases were excluded from the present analysis.

The University and General Hospital of Ferrara is provided with a Hypertension Center, an ambulatory setting being part of the Clinica Medica Unit, a 24-bed complex unit of internal medicine. This Center serves as the hub third-level facility for both the town of Ferrara and provincial area (around 350,000 inhabitants) and neighbouring areas, with a consolidated yearly activity of approximately 1,900 ABPM procedures and 1,500 visits.

ABPM was performed during 24 hours using a validated device validated for pregnancy by the British Hypertension Society [https://bihsoc.org/bp-monitors/for-specialist-use/]. BP was measured every 15 minutes or at intervals of not more than 30 minutes during daytime (06:00 - 23:00) and every 30 minutes or at intervals of no more than 60 minutes during night-time (23:00 – 06:00).

Data are expressed as absolute numbers, means, and percentages. Furthermore, the authors drew a decision tree analyzing conditions associated with prescription of ABPM. Statistical analysis was performed using SPSS 13.0, 2004, for statistical analysis of the demographic data.
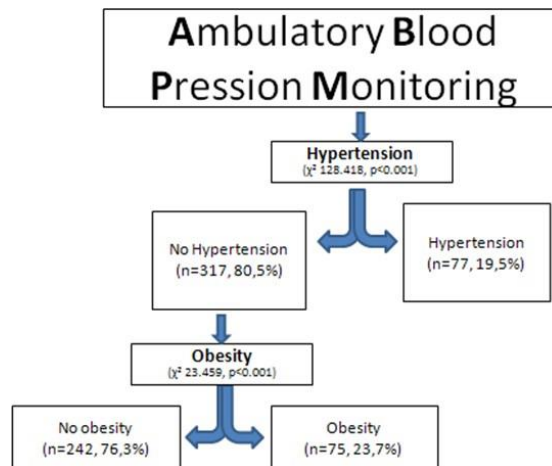
Results

The study included 395 pregnant women (87 in 2012, 101 in 2013, 64 in 2014, 67 in 2015, and 76 in 2016), considered at high risk. Their mean age was 33.9 ± 5.6 years, and they were mainly of Mediterranean origin (91%). They were firstly seen when gestational age was 19.6 ± 9.6 weeks.

Reasons for referral to HRAC were rheumatological diseases in 61 (15.4%) cases, heart diseases in 19 (4.8%), and kidney diseases in 14 (3.5%). Detailed information are reported in Table 1.

Fetal growth restriction was diagnosed in 27 (6.8%) patients. Diabetic pregnant women were 134 (33.9%) of whom 24 (17.9%) that had type I diabetes mellitus, four type II (3%), and 106 (79%) gestational diabetes. Pre-eclampsia during a previous pregnancy was reported in 14 (3.5%) cases, and hypertension was diagnosed in 77 (19.4%) cases. Overweight was present in 97 (24.5%) pregnant women, and excessive weight gain during pregnancy was observed in 11 (2.8%) cases.

A strong collaboration between HRAC and Hypertension Center is active for many years. Hypertension, but also overweight, represent the main causes for ABPM request and referral to Hypertension Center. The decisional tree analysis is shown in Figure 1. In the sample population object of the present study, ABPM was carried out at the following gestational age: 19 ± 8, 22 ± 8, 26 ± 8 weeks and beyond. A single ABPM procedure was performed in 87 (22%) cases, and multiple ABPM measures were necessary in 100 (25%) cases. In at least one-third of cases of single measurement, ABPM was followed by medical intervention aimed to modify the pre-existing therapeutic treatment. In details, range of variation to antihypertensive treatment

Table 2. — *Number of ABPM procedures and variation to antihypertensive treatment (AHT).*

ABPM	Women (n)	Women (%)	Variation to AHT (n)	Variation to AHT (%)
1	87	22	29	33.3
2	55	13.9	29	34.5
3	34	8.6	13	38.2
>3	11	2.8	10	90.9

was 33% to 91% (Table 2).

Three hundred and thirty-three (87.7%) women had successful delivery, and 41 (6.3%) women were lost during follow-up (delivery in other hospitals or other provinces). In details, among women with successful delivery, spontaneous delivery occurred in 186 (49%) cases and caesarean section in 147 (38.7%) cases. Mean birth weight of newborns was 3,225 ± 652 grams, and 14 newborns were considered underweight (4.7%) (less than the 10th centile). Miscarriages were 18 (4.7%), and abortions were 3 (0.7%).

Discussion

In this study, hypertension and overweight were the main factors determining prescription of ABPM in HRAC. The population of this study was characterized by a high risk for PE/eclampsia, and the result of careful management of high risk patients was that 87.7% of women had a baby, a percentage that could theoretically increase up to 94% if we remember that 6.3% of pregnant women were lost during follow-up. These findings are not so different from data shown by NICE guidelines, where perinatal mortality of infants without congenital abnormality in women with pre-eclampsia was 5% [7].

Evaluation of the role of ABPM in pregnancy associated hypertension has begun since the late nineties. In a study using ABPM on a limited sample of patients, accounting 73 controls, 48 patients with pregnancy-induced hypertension, 38 with PE, and 53 with mild to moderate chronic hypertension, Benedetto *et al.* concluded that ABPM during pregnancy enabled quantitative and qualitative evaluations of the hypertensive status [8]. Higgins *et al.* [9] evaluated ABPM in 1048 women at 18 to 24 weeks of gestation; of these 2.2% developed PE and 6.1% developed gestational hypertension. Values recorded during ABPM were higher in both the pre-eclamptic and gestational hypertensive group compared with the normotensive group, with no differences between the pre-eclamptic and the gestational hypertensive group for any of the BP parameters analyzed [9]. Bellomo *et al.* [10] assessed the prognostic value of white-coat hypertension (WCH) during pregnancy in a prospective cohort study. Duration of pregnancy was shorter in the hypertensive patients, but similar in the normotensive and WCH pregnant women. Incidence of PE was higher in hypertensive women, but similar in the normotensive and WCH groups. Frequency of cesarean delivery was lower in the normotensive than in the WCH and true hypertensive

groups. Neonatal weight was lower in the hypertensive pregnant women than in the normotensive and WCH groups. The authors concluded that in women with elevated BP during their third trimester of pregnancy, ABPM was superior to office BP, for prediction of the outcome of pregnancy. Outcomes in the normotensive and WCH group were comparable, but the increased incidence of cesarean delivery in the WCH group could reflect physicians' decision-making processes derived from office BP [10]. Waugh *et al.* [11] examined the relationship between ABPM during pregnancy and birth weight in a population of 237 women considered to have hypertension according to office BP. After adjustment for potential confounders, e.g., maternal age, maternal weight, smoking status, ethnicity, and gestational age at delivery, authors found a significant inverse association between daytime ambulatory diastolic BP measurement and birth weight. An increase of 5 mm Hg in daytime mean diastolic BP was associated with a fall in birth weight of 68.5 grams [11]. Brown *et al.* [12] found that night-time hypertension was detected in 59% of cases with PE and gestational hypertension, and night-time hypertensives also had higher routine sphygmomanometer BPs than women with normal sleep BP, and higher awake ABPM. However, the role of ABPM during pregnancy is still a matter of debate. The Society of Obstetric Medicine Australia and New Zealand (SOMANZ) guidelines for management of hypertensive disorders of pregnancy endorsed ABPM with the major role in identifying women with WCH, in order to avoid inappropriate treatment [13]. ABPM may be particularly useful in women before 20 weeks of gestation, since approximately one-third of pregnant women could show WCH or 'office' hypertension just in this period [13]. In fact, about fifty percent of pregnant women with WCH would not be treated with antihypertensive therapy, while the other fifty percent would become hypertensive, with ABPM confirmation. On the contrary, ABPM could be less useful in screening for WCH in the second half of pregnancy due to its poor sensitivity and specificity [13]. On one hand, Magee *et al.* [14] in their recent revision on diagnosis, evaluation, and management of hypertensive disorders in pregnancy, classified the relevant existing evidence related to the use of ABPM as of very low/weak quality. On the other, according to the 2013 recommendations for the diagnosis of adult hypertension, ABPM should be considered the gold standard for diagnosis of hypertension in pregnancy and the screening of pregnant women at high risk for other complications during

gestation [15].

Evidence-based data able to support recommendations about diagnosis and management of hypertension during pregnancy is limited by ethical and practical issues, in fact there are not homogenous and worldwide accepted cut-off thresholds for diagnosing and treating hypertension in pregnancy [7, 16]. In the present study, ABPM could be considered a helpful method able to help obstetricians not only in anti-hypertensive prescription, but also in establishing BP values in obese pregnant women. Obese women have been reported to have a significant increased risk of pregnancy induced hypertension [17].

Conclusions

Diagnosis and management of hypertension during pregnancy could sometimes be difficult, but evaluation of out-of-office BP by ABPM might help obstetricians in classifying hypertension during pregnancy. ABPM, in fact, is useful for diagnosis of WCH and masked hypertension, and for evaluation of night-time BP, the latter having an early prognostic value [18]. Precise definition of all aspects of hypertension could help investigation of novel prognostic factors, improve treatment, and have positive impact on both mother's and newborn's outcomes. Moreover, it has to be stressed that surveillance against hypertension and metabolic disorders begins, and does not cease, with delivery. A close interdisciplinary collaboration between obstetricians, midwifes, pediatricians, and hypertension specialists may represent first crucial point for prevention of metabolic syndrome at a later age. In this view, ABPM data analysis could favor tailored personalized therapeutic approach, suggesting the right time for hypertension treatment [19], to achieve better prognostic outcomes.

Acknowledgement

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