European Journal of Obstetrics & Gynecology and Reproductive Biology 216 (2017) 153–158

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

Preeclampsia is associated with increased ambulatory arterial stiffness index in type 1 diabetes mellitus

Hanine F.M. Al-Far[a,*], Ingvild H. Tjessem[a], Jens Fuglsang[b], Finn F. Lauszus[a,b]

[a] Department of Obstetrics/Gynecology, Herning Hospital, Denmark
[b] Department of Obstetrics/Gynecology and Clinical Institute, Aarhus University Hospital, Denmark

ARTICLE INFO

Article history:
Received 3 April 2017
Received in revised form 22 July 2017
Accepted 24 July 2017
Available online xxx

Keywords:
Arterial stiffness index
Birth weight
Diabetes mellitus
Preeclampsia
Pregnancy outcome
Pulse pressure

ABSTRACT

Introduction: Treatment of mild to moderate hypertension might not benefit maternal or fetal outcome. This pessimistic point of view may have come about by using non-validated methods for measuring blood pressure in pregnancy combined with inadequate methodology for diagnosis, treatment, and monitoring effects.
Aim: To determine the association between AASI in women with type 1 diabetes mellitus (T1DM) and preeclampsia, and to assess the ability of AASI to diagnose preeclampsia.
Material and methods: Repeated 24-h ambulatory blood pressure recordings were performed three times during pregnancy and once three months postpartum in 151 women with T1DM and 50 control women without diabetes. Circadian rhythm was evaluated as the night day ratio, night blood pressure divided by day blood pressure.
Results: Of the T1DM women, 33 developed preeclampsia, which was associated with AASI in the 3rd trimester ($p < 0.05$). The best predictor of preeclampsia in T1DM was an AASI of 0.35. The diurnal blood pressure was significantly higher in all trimesters in women who later had preeclampsia. A flattened circadian rhythm was present in T1DM women with preeclampsia compared to women without preeclampsia (night-day ratio: systole 2nd trimester: 0.94 ± 0.07 vs. 0.91 ± 0.05, women with and without preeclampsia, respectively, $p = 0.015$; diastole 2nd trimester: 0.89 ± 0.07 vs. 0.85 ± 0.07, $p = 0.003$). AASI was higher during pregnancy compared to postpartum in women with T1DM (0.31 ± 0.16, 0.31 ± 0.16 and 0.33 ± 0.18 vs. 0.25 ± 0.17; 1st, 2nd and 3rd trimester vs. postpartum).
Conclusion: Women with T1DM and preeclampsia demonstrate increased arterial stiffness and had early manifestations in the non-dipping of blood pressure.

Introduction

A recent Cochrane review concludes that treatment of mild to moderate hypertension might not benefit maternal or foetal outcome [1]. This pessimistic point of view may have come about by the occasional use of non-validated devices for measuring blood pressure (BP) in pregnancy combined with the use of such BP readings for diagnosis and for making other clinical decisions. For one, the BP methodology for diagnosis, was multiple measurements under non-standardized circumstances with semi-automatic monitors; these are most often non-validated [1,2]. (Secondly, on the consequence of the diagnostic thresholds, the largest studies to date of women with a history of preeclampsia and later life events find cardiovascular disease more prevalent; in case of women with diabetes, a 3–4 times increased risk of severe retinopathy and nephropathy was reported [3,4])However, the basis of these aggregated data was BP from history charts of all sorts. Similar short-comings are noted when monitoring antihypertensive treatment and its effect. Diurnal BP measurements were rarely used and, thus, monitoring is best described as sporadic. The analogue to glycaemic regulation in diabetic pregnancy comes to one's mind where previous underestimated glycaemic fluctuations and undetected hyperglycaemic fluctuations caused macrosomia and came to light by applying electronic home- and continuous glucometers [5]. In accordance, the macrosomia rate was reduced by continuous glucose monitoring and treatment in a randomized study [6].

We used a simple calculation of diurnal BP profile to further evaluate the elasticity of vascular walls, the ambulatory arterial stiffness index (AASI). This points to later aspects of life as detrimental cardiovascular outcome is more precisely predicted by

* Corresponding author at: Dept. of Gynecology and Obstetrics, Herning Hospital, Gl. Landevej 61, DK-7400 Herning, Denmark.
E-mail addresses: hanialfa@rm.dk, hanine84@yahoo.dk (H.F.M. Al-Far).

http://dx.doi.org/10.1016/j.ejogrb.2017.07.030
0301-2115/

the AASI than classical risk factors [7–9]. AASI has strong correlation with clinical outcome as well as other biometrical measurements like pulse pressure, augmentation index and vascular wall thicknesses [7–9]. Fatal cardiovascular death in normotensive individuals and stroke in hypertensive patients can be predicted by AASI: a 1 SD increase in AASI was associated with a 14% increased risk of cardiovascular mortality and a relative hazard ratio of 1.31 for cardiac disorders [8]. AASI is calculated from diurnal blood pressure measurements and associated with left ventricular hypertrophy, carotid artery abnormalities, and reduced renal function. Increase of AASI was shown to herald need for insulin treatment and predicted postpartum metabolic syndrome in women with gestational diabetes (GDM); similar was found in hypertensive pregnancies, too [10–12].

Antihypertensive treatment is essential in T1DM and can conserve renal function, modifying the risk of renal insufficiency. During pregnancy, renal insufficiency may lead to termination of pregnancy. Thus, accurate methodology with optimal sensitivity and specificity is preferred over fast-track and easy methodology, which are in common use [12].

The AASI and the pulse pressure (PP), both computed from repeated 24-h ambulatory BP recordings, are novel indirect measures of arterial stiffness and were reported in women with pre-gestational hypertension, GDM, and twin pregnancies [7–9,13,14]. It is obvious that preeclampsia increases along with retinopathy and nephropathy in T1DM women but has little to offer in term of prediction. We performed the study as a non-invasive diagnostic procedure for early diagnosis of hypertension and preeclampsia and the calculated indices of wall elasticity. We pondered that previous studies have found pregnancy and non-pregnancy AASI levels similar and that multiple and hypertensive pregnancies were no different from singleton and non-hypertensive ones in their relation to dipping and BP change. The increased prevalence of renovascular complications and of hypertensive disorders in pregnancies in T1DM women suggests that evaluation of AASI is relevant for further use in prediction of morbidity [10–12].

We present the results of a cohort of pregnant women with T1DM in which AASI and PP were analysed during pregnancy and compared to non-diabetic women. Pre-pregnant and postpartum measurements were compared to pregnancy values in T1DM women. We hypothesized that alterations in the stiffness of the arterial wall would display the functional changes associated with preeclampsia and the obstetrical outcome. The results regarding detailed associations of diabetic vasculopathy, BP variation patterns, coefficient of determination in measurements and their associations with AASI are presented elsewhere.

Material and methods

In an evaluation of morbidity in T1DM pregnancy with respect to nephropathy and retinopathy 151 T1DM women were recruited for repeat 24-h ambulatory BP recordings three times during pregnancy and three months postpartum. The study was approved by the local Ethics Committee (jr.nr.1992/2523, 1998/4147, and 2026-99) and The Danish Data Protection Agency (no. 1-16-02-92-16). Fifty non-diabetic women served as controls and had diurnal BP measured during 1st and 3rd trimester. The study performed in concordance with the Helsinki II declaration and all women gave their informed consent (Table 1). The study was performed at Aarhus University Hospital prospectively during six years until 1998.

A portable oscillometry monitor (Spacelab 90207, Redmond, WA, USA) was applied on the non-dominant arm and provided more than 60 readings in 24 h. The list of validated monitors is at the British Hypertension Society's website [15]. A random zero sphygmomanometer (Hawksley, Lancing, U.K.) was used to give three auscultatory BP and termed the clinical BP. Measurements were performed in gestational week 13, 25, and 33 and three months postpartum in women with T1DM. The non-diabetic women were included at their second visit to the department for ultrasound scan in week 18 and those who participated had diurnal BP measured again in 33.

The BP data were either initially stored to a data file or manually re-entered from a paper output and then processed statistically to calculate the regression slope of diastole on systole for each participant's BP measurements. AASI was defined as one minus the regression slope of diastolic BP on systolic BP from the diurnal

Table 1
1st trimester clinical and pregnancy data of 151 women with T1DM and 50 non-diabetic women.

	Non-diabetic women	All T1DM women	White Group of T1DM					
			B	C	D0	D+	R	F+F/R
No.	50	151	46	11	7	64	7	16
Normo-/micro-/macroalbuminuria	0	116/20/15	43/3/0	9/2/0	6/1/0	54/10/0	3/4/0	1/0/15
Age (yrs)	27 ± 3 [c]	28 ± 4	29 ± 4	27 ± 5	28 ± 6	29 ± 5	28 ± 3	28 ± 4
BMI (kg/m2)	26 ± 4 [d]	24 ± [e]	25 ± 4	24 ± 3	23 ± 1	25 ± 4	24 ± 2	24 ± 5
Duration of diabetes (yrs)	–	13 ± 8 [f]	4 ± 3	12 ± 4	20 ± 9	16 ± 7	20 ± 5	18 ± 5
Parity	1.3 ± 0.5 [d]	1.6 ± 0.8	1.7 ± 0.6	1.8 ± 0.8	1.9 ± 0.9	1.6 ± 0.8	1.9 ± 0.7	1.4 ± 0.8
HbA1c (%)	4.8 ± 0.3 [d]	7.4 ± 1 [f]	7 ± 1	7.4 ± 0.8	7.2 ± 0.4	7.5 ± 0.9	7.5 ± 1	8.3 ± 1.1
Creatinine clearance (ml/min)	–	127 ± 31 [f]	134 ± 26	120 ± 22	119 ± 23	130 ± 29	150 ± 30	88 ± 42
Gestational week at delivery	39.6 ± 1.6 [d]	35.5 ± 2.3 [f]	36 ± 1.6	36.3 ± 1.4	36.3 ± 1.6	35.7 ± 1.6	35.9 ± 1.1	32.6 ± 4.7
Birth weight (g)	3601 ± 483 [c]	3526 ± 905 [f]	3813 ± 803	3741 ± 703	3905 ± 714	3533 ± 729	3711 ± 635	2302 ± 1155
Birth weight ratio a,b	1.03 ± 0.12 [d]	1.3 ± 0.27 [f]	1.34 ± 0.24	1.31 ± 0.21	1.3 ± 0.29	1.31 ± 0.28	1.36 ± 0.36	1.05 ± 0.2
Preterm delivery <36 week (no. (%))	0 [d]	51 (34)	11 (24)	3 (27)	1 (14)	23 (36)	2 (29)	11 (69)
Pre-gravid/gestational hypertension (no./no.)	0/0 [d]	18/3	2/1	0/1	0/0	6/0	1/0	9/1
Preeclampsia (no. (%))	2 (4) [d]	33(22)	7 (15)	0	1	18 (28)	0	7 (44)

B: White group B, diabetes duration less than 10 years, C: White group C, diabetes duration between 10 and 20 years, D: White group D, diabetes duration more than 20 years; D0: White group D without retinopathy, D+: White group D with simplex retinopathy; R: White group R, diabetes with proliferative retinopathy; F: White group F, diabetes with nephropathy; F/R: diabetes with proliferative retinopathy and nephropathy.
a: Observed birth weight/expected birth weight for same gestational week and gender.
b: Birth weights of two twin pregnancies and one abortion in week 21 are excluded from calculations in birth weight and gestational weeks.
c: $p < 0.05$ and d: $p < 0.01$, test for difference, control vs. all T1DM women.
e: $p < 0.05$ and f: $p < 0.01$ test for difference between White groups in T1DM women (ANOVA).