Placenta 35 (2014) 639–644

Contents lists available at ScienceDirect

Placenta

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

Novel placental ultrasound assessment: Potential role in pre-gestational diabetic pregnancy

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ARTICLE INFO

Article history:
Accepted 6 March 2014

Keywords:
Pre-gestational diabetes
Novel ultrasound placental assessment

ABSTRACT

Objectives: Management of women with pre-gestational diabetes continues to be challenging for clinicians. This study aims to determine if 3D power Doppler (3DPD) analysis of placental volume and flow, and calculation of placental calcification using a novel software method, differ between pregnancies with type 1 or type 2 diabetes and normal controls, and if there is a relationship between these ultrasound placental parameters and clinical measures in diabetics.
Methods: This was a prospective cohort study of 50 women with diabetes and 250 controls (12–40 weeks gestation). 3DPD ultrasound was used to evaluate placental volume, vascularisation index (VI), flow index (FI) and vascularisation-flow index (VFI). Placental calcification was calculated by computer analysis. Results in diabetics were compared with control values, and correlated with early pregnancy HbA1c, Doppler results and placental histology.
Results: Placental calcification and volume increased with advancing gestation in pre-gestational diabetic placentae. Volume was also found to be significantly higher than in normal placentae. VI and VFI were significantly lower in diabetic pregnancies between 35 and 40 weeks gestation. A strong relationship was seen between a larger placental volume and both increasing umbilical artery pulsatility index and decreasing middle cerebral artery pulsatility index. FI was significantly lower in cases which had a booking HbA1c level $\geq$6.5%. Ultrasound assessed placental calcification was reduced with a histology finding of delayed villous maturation. No other correlation with placental histology was found.
Conclusions: This study shows a potential role for 3D placental evaluation, and computer analysis of calcification, in monitoring pre-gestational diabetic pregnancies.

1. Introduction

Pre-gestational maternal diabetes, which complicates approximately 1% of all pregnancies is associated with an increased incidence of fetal morbidity and mortality [1]. Women with type 1 diabetes who have only a slightly raised HbA1c (an indicator of glycaemic control) in early pregnancy have been shown to have an increased risk of major fetal malformations [2]. Abnormalities in placental development and function may be a contributory factor to poor outcome, as diabetes compromises the placenta, independent of glycaemic control [3–5]. There is an increase in the size of the villous stroma and the diffusion distance within the maternal and fetal systemic circulations in the placenta affected by diabetes, with capillary volume also increased [6,7].

Delayed villous maturation (DVM) of the placenta is a condition which is strongly associated with maternal diabetes and an increased perinatal mortality rate [8] and can also be related to abnormal placental calcification [9]. Delayed villous maturation ranges from mild to severe in type, however regardless of severity the tertiary placental villi will be immature for gestational age. The most recent study, analysing clinical and ultrasound markers which may indicate the development of DVM, failed to demonstrate any associated findings on ultrasound [10]. Grannum grading, which is

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http://dx.doi.org/10.1016/j.placenta.2014.03.007
0143-4004/

the only current method of assessing placental calcification, is felt by many clinicians to be unreliable and yet to date no other ultrasound method has been put forward as an alternative.

New ultrasound methods of placental assessment have been developed over the past decade or so [11]. One such method is three dimensional power Doppler (3DPD), which calculates volume, and blood flow according to three indices: vascularisation index (VI) or overall perfusion, flow index (FI) or blood flow intensity and vascularisation-flow index (VFI) or fractional moving blood volume. Recently a novel, 2D ultrasound imaging software tool, the 'placentometer' has been developed in the School of Medicine and Medical Sciences, University College Dublin. The placentometer can be used off-line for calculating the percentage of placental calcification, and involves accurate identification of the placenta and repeatable measurement of the extent of calcification.

This study aims to determine if 3DPD ultrasound assessment of placental volume and vascularity and computer analysis of placental calcification, using the placentometer, differ between pregnancies complicated with type 1 and type 2 diabetes and normal. This study also aims to determine if there is a relationship between these placental parameters, and glycaemic control, Doppler and placental histology results.

2. Material and methods

2.1. Patients

This was a prospective cohort study. With institutional ethical approval and maternal written consent thirty seven women with type 1 diabetes mellitus (T1DM) and thirteen women with type 2 diabetes mellitus (T2DM) were recruited to the study. Gestational age at the time of the scan ranged from 12 + 2 to 39 + 5 weeks. In the normal (control) group each woman underwent one scan, (gestational age 12 + 6 to 39 + 5 weeks).Criteria for normality were that there had been no pv bleeding at any stage in the pregnancy [12], that the patient had no medical disorder requiring treatment, e.g. diabetes, or any degree of hypertension. Women with a diagnosis of a fetal anomaly or a suspicion or diagnosis of intrauterine growth restriction were also excluded. The same exclusions, apart from diabetes, applied to the diabetic cohort.

All scans were performed transabdominally using a Voluson 730 Expert ultrasound machine (GE Medical Systems, Austria), equipped with curved array transducers. A 2–7 MHz transducer was used to acquire all two dimensional (2D) images, and a 4–8 MHz transducer was used to acquire the three dimensional (3D) images. The number of scans per diabetic patient depended on the gestational age at the time of recruitment, and ranged from one to six. Each scan incorporated assessment of placental site, fetal biometry and estimation of fetal weight (after 30 weeks gestation), Doppler studies of the umbilical artery (UA), middle cerebral artery (MCA) and uterine artery (UtA) were performed, with the pulsatility index (PI) calculated.

At the commencement of the study inter- and intra-observer agreement, between 3 observers, was assessed for 10 images [13,14]. Both inter-and intra-observer agreement in the calculation of placental volume, VI, FI and VFI was almost perfect (mean agreement index, AI, range 0.92–0.99). Inter-observer agreement was also close to perfect (mean AI 0.93) for the calculation of the percentage of placental calcification, with 2 clinicians having almost perfect intra-observer agreement (AI 0.91 and 0.92) and one clinician having good agreement (AI 0.83).

2.2. 3DPD placental analysis

A 3DPD placental image was saved at each scan with subsequent analysis of images to calculate volume, VI, FI and VFI flow using the Virtual Organ Computer-aided AnaLysis (VOCAL™) software (3 dimensional Sonoview, GE Healthcare). The method for saving and analysing images has been previously described [15]. Once each image was rotated 180O a shell contour was displayed in the lower right hand corner of the display, and the volume automatically calculated. Fig. 1 displays a volume of 371.709 cm^3. Once the contour was accepted as correct the vascular indices VI, FI and VFI were calculated.

2.3. Calculation of placental calcification

The initial step in calculating the percentage of placental calcification, using the placentometer, was to select the region of interest (ROI), by drawing an outline around the placenta using a pointing device controlled by the mouse. The pixels were recorded following the mouse movements, were then joined into line-

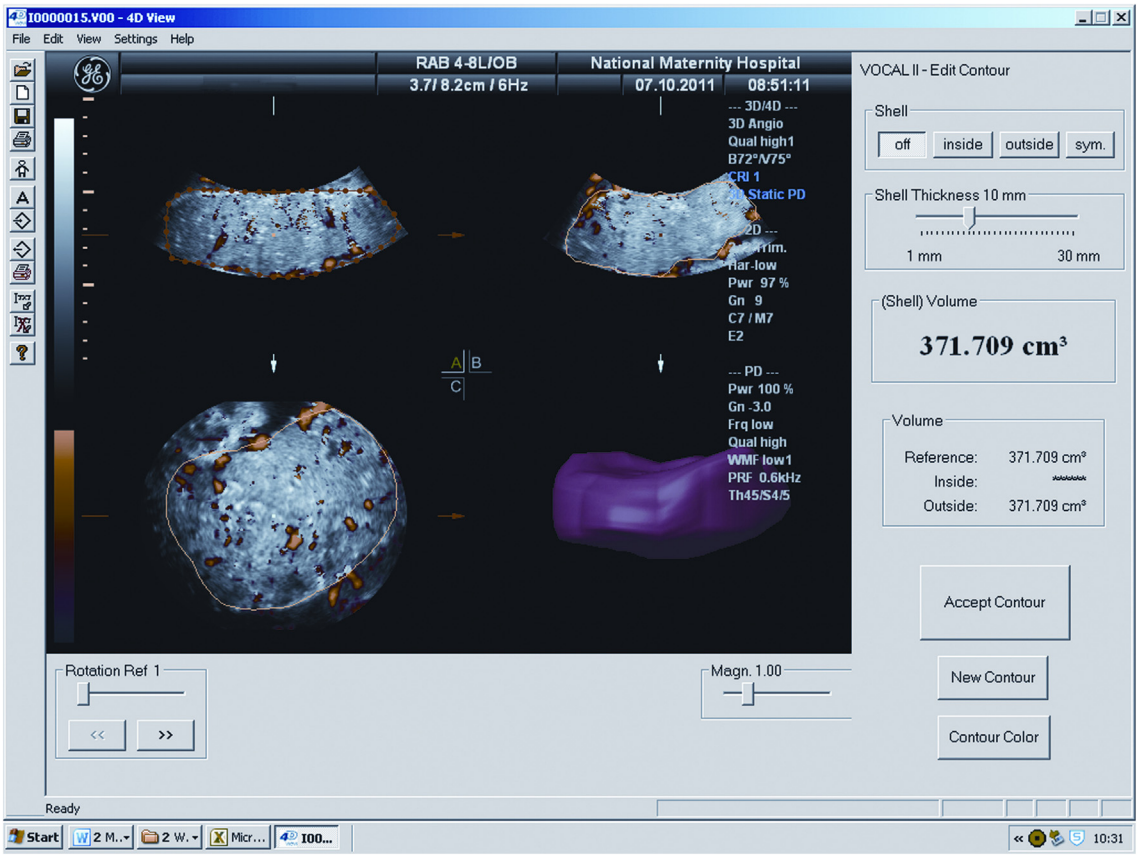

Fig. 1. 3D placental volume displayed as 371.709 cm^3.