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RESEARCH

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Placental perfusion imaging on 3Tesla magnetic resonance imaging using pseudo-continuous arterial spin labelling: an initial experience

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Abstract

Background During pregnancy, the placenta plays an important role in the development of the fetus by supplying it with oxygen and nutrition, eliminating waste, and acting as an immunological barrier. Pseudo-continuous arterial spin labelling (pCASL) MRI was recently shown to be a promising sequence for measuring perfusion in the placenta. The aim was to obtain the perfusion measurements of the placenta in normal pregnancies using 3 Tesla MRI from 19 to 38 weeks of gestational age.

Results This was a cohort observational study. One hundred and sixty (160) singleton pregnancies from 19 to 38 weeks of gestational age were included. A 3D pCASL sequence was performed in the axial plane for placental blood flow (PBF). Data post-processing was performed on a workstation using Ready View software for 3D ASL with automated generation of quantitative placental pattern-based morphometry (PBM). The mean values of placental perfusion were extracted by averaging the data obtained. A significant positive correlation was observed between the PBF and increasing GA using Karl Pearson's coefficient of correlation values (*r*-value 0.77, *p*-value < 0.001), respectively. Average PBF values from 19 to 38 weeks were (89.4 ± 13.5 to 155.3 ± 2.8 ml/100 g/min). According to our intra-class correlation coefficient (ICC), inter-observer reproducibility of placental blood flow shows good agreement between observers (0.98).

Conclusions Normal PBF values using ASL in 3 T MRI from 19 to 38 weeks of gestational age were provided. Statistical analysis revealed a significant positive correlation between gestational age and placental blood flow. In the future, it may help to identify placental perfusion abnormalities like placental insufficiency, preeclampsia, and fetal growth restriction (FGR).

Keywords Arterial spin labelling, ASL, Placenta, Placental blood flow, PBF, Placental MRI

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Background

During pregnancy, the placenta plays an important role in the development of the fetus by supplying it with oxygen and nutrition, eliminating waste, and acting as an immunological barrier. Early in pregnancy, remodelling of the spiral arteries develops such that blood flow in the maternal placental circulation increases in order to support rapid fetal growth and development. When this remodelling fails, placental insufficiency occurs when oxygen and nutrients are not adequately supplied to the fetus through the feto-placental circulation [1].

Ultrasound is the primary imaging modality in the assessment of placenta and fetal health due to its low cost, strong safety profile, and real-time imaging capabilities. Uterine artery (UA) Doppler has previously been deemed useful in detecting an abnormal increase in placental vascular resistance. However, the UA Doppler measures blood flow in the uterine artery and not in the placenta [2]. Unfortunately, ultrasound provides a limited number of image contrasts and thus may be insensitive to detecting early functional precursors to pregnancy complications [3].

Magnetic resonance imaging (MRI) is an emerging modality for the longitudinal monitoring of placental health in utero. It has an excellent safety profile and can acquire 3D volumes in any orientation [3]. Functional MRI allows the assessment of several functional aspects of the tissue, which include microvascular parameters, oxygenation, and metabolism [4]. Arterial spin labelling (ASL) is a powerful MRI technique that does not require contrast agents because it utilizes the water molecules in arterial blood as an endogenous contrast agent, making it optimal for examining placental perfusion in pregnancy [5]. The aim of this study is to find the perfusion measurements of the placenta in normal pregnancies using 3 Tesla MRI. There are few articles regarding placental perfusion using 3 T MRI.

Methods

Subject population

This prospective study was conducted in Department of Radiology. The study was approved by the institutional ethical committee (IEC) (NI/22/APR/82/58), and informed consent was obtained from all the patients. The data were collected from the MR imaging studies done between April 2021 and December 2022 (Fig. 1). Our study included 160 singleton pregnancies with gestational ages ranging from 19 to 38 weeks, with a mean of 26 ± 5 weeks. Maternal age ranged between 18 and 40 years, with a mean of 28 ± 4 years. Patients referred for the examination of MRI placenta or fetus to evaluate suspected placental abnormalities (predominately placental adherence) or fetal anomalies on ultrasound who were later found to be normal on MR imaging and prenatal follow-up were included in this study. Pregnancies with

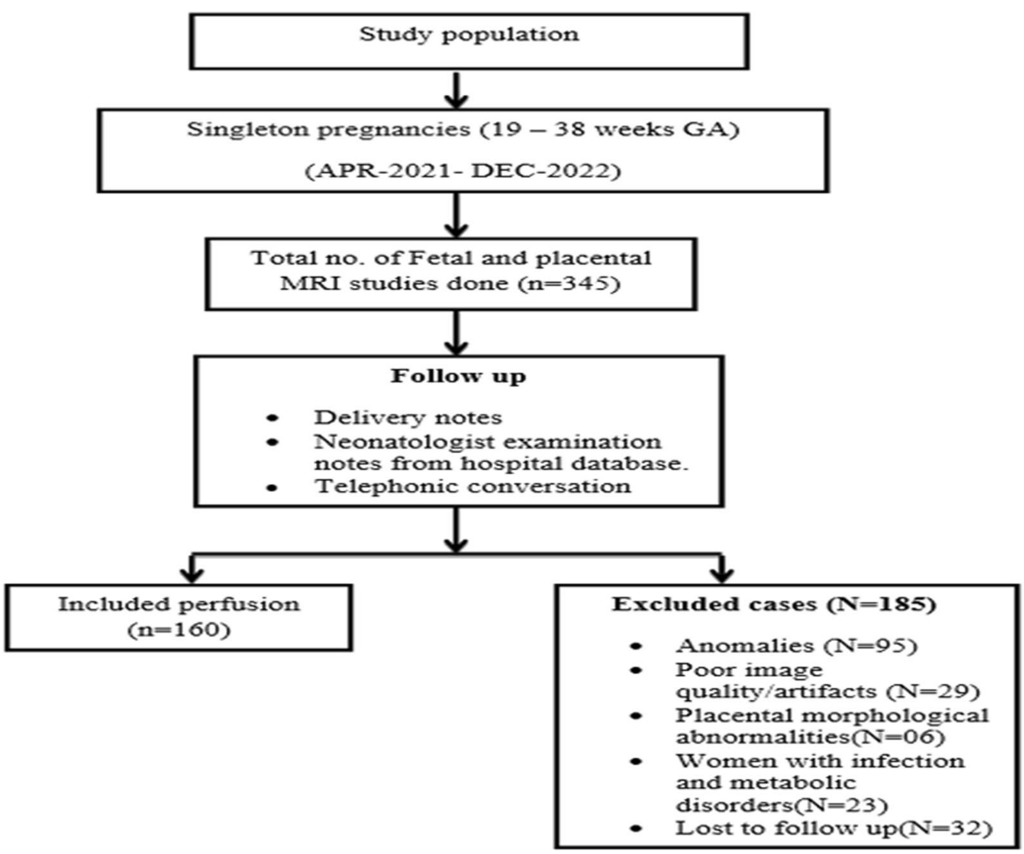

Fig. 1 Flow chart for determining study population included in the study

(1) severe anomalies (2) Poor image quality/artifacts (3) Placental morphological abnormalities (4) Women with infections and metabolic disorders (5) Contraindications to MRI like pacemakers, claustrophobia were excluded. The follow-up of these fetuses was obtained from the delivery notes and neonatologist examination notes in the hospital database. A telephone conversation with the parents provided further confirmation of the normalcy of the fetuses.

MR imaging

All the scans were performed on a Signa Architect GE 3 T MRI by using a phased array 16-channel body coil. The patients were positioned feet first in a supine position, and a body coil was placed over the abdomen. The localizer was centered over the anterior superior iliac spine. Our routine imaging protocol included a T2 weighted (T2W) single shot fast spin echo sequence (SSFSE) obtained in three planes and a T1 Weighted (T1W) fast-spoiled gradient echo sequence (FSPGR) obtained in the axial plane. These sequences were performed with the following parameters: T2W: TR: 1600–1900s, TE: 120 ms, matrix: 512 × 512, number of excitations: 1, slice thickness: 5 mm, FOV: 30 cm. T1W: TR: 100–150 ms, TE: 2–5 ms, matrix: 512 × 512, number of excitations: 1, slice thickness: 5 mm, FOV: 30.

A 3D pCASL sequence was performed in the axial plane for placental blood flow by using the following acquisition parameters: TR: 5000 ms, TE: 53 ms, matrix: 103 × 103, number of excitations: 1, spatial resolution: 3.6 × 4.2 × 4 mm2, slice thickness: 4 mm, post-labelling delay: 1525 ms. The scan time of the whole sequence was about 5 min. Respiratory gating was used to keep the acquisition time low and to reduce the effect of any motion artifacts.

Post-processing and data analysis

Post-processing of the data was performed on a workstation using Ready View software for 3D ASL with automated generation of quantitative placental pattern-based morphometry (PBM) maps. Multiple elliptical regions of interests (ROIs) (40–60 mm2) were placed on the placental pattern-based morphometry maps overlaid on T2-weighted images for each slice (Figs. 2 and 3). All placentae were measured in the same way. The mean values of placental blood flow were extracted by averaging the data obtained from multiple ROIs. A radiologist with more than 10 years of experience in interpreting fetal imaging first reviewed all MRI studies to identify normal placental studies. A trained research scholar obtained the measurements. To check the consistency of manually measured values, the radiologist and the research scholar evaluated the reproducibility of measurements from a

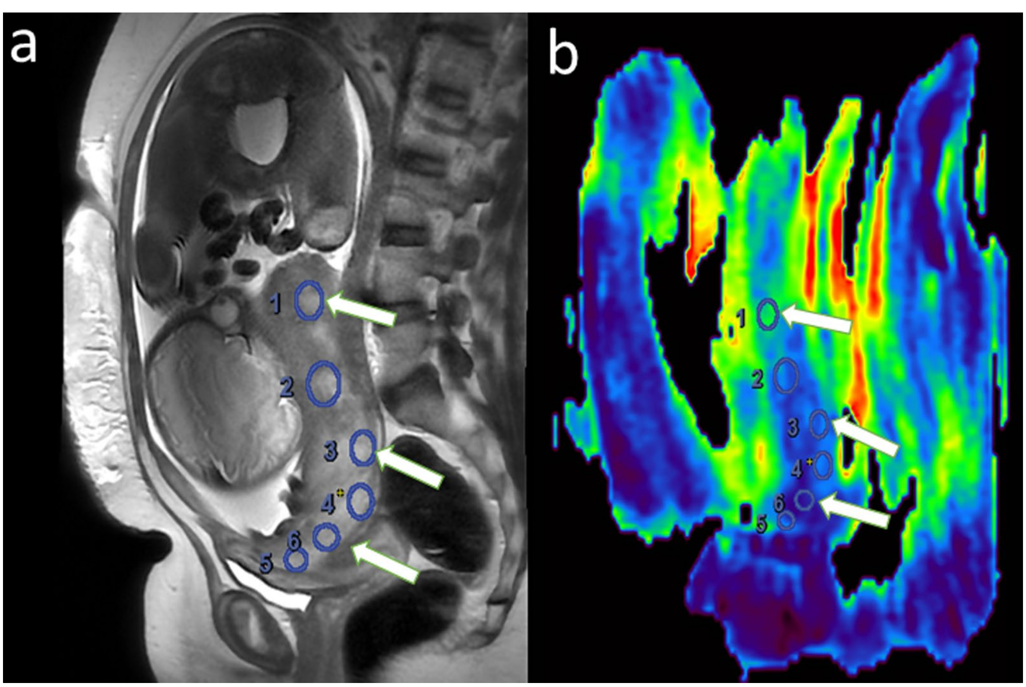

Fig. 2 A 25-year-old female with 31 weeks of gestation was referred for placental magnetic resonance imaging (MRI) in the evaluation of placenta previa and it showed normal placenta with placental blood flow value (191 ml/min/100 g) (arrows) **a**-T2 weighted SSFSE axial image. **b-**placental Pattern-based morphometry map (PBM) of placental image

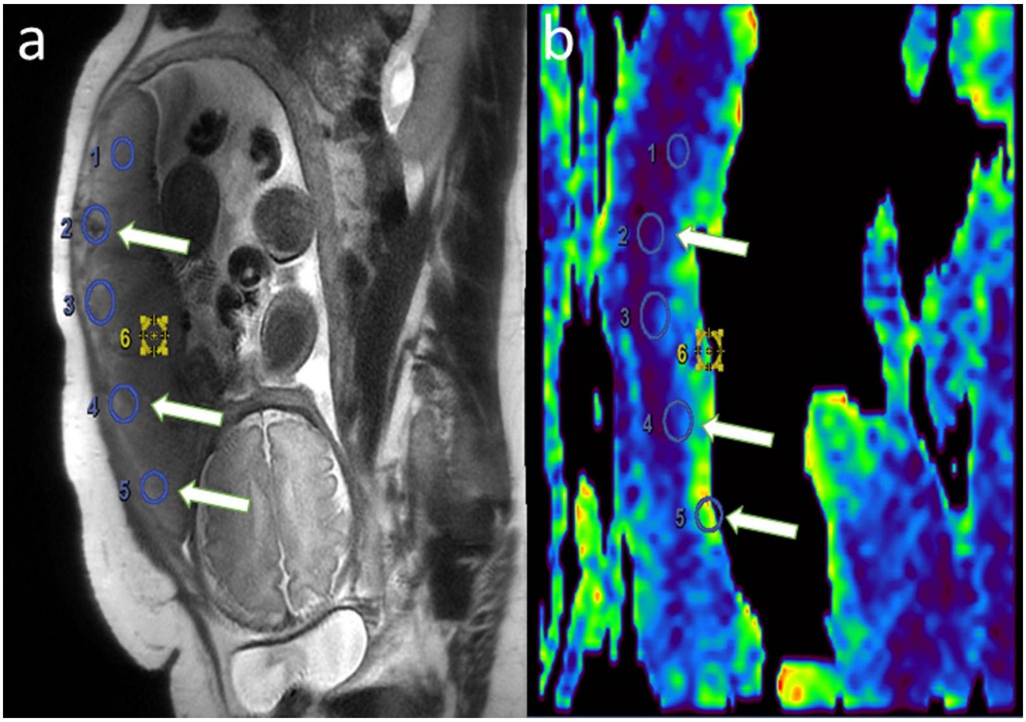

Fig. 3 A 28-year-old female with 35 weeks of gestation was referred for placental magnetic resonance imaging (MRI) in the evaluation of placenta accreta and it showed normal placenta with placental blood flow value (124 ml/min/100 g) (arrows) **a**-T2 weighted SSFSE axial image. **b**-placental Pattern-based morphometry map (PBM) of placental image

20% sample independently. Each observer was blinded to the results of the other observer.

Statistical analysis

The statistical analysis was performed using SPSS 19.0 (Armonk, NY: IBM Corp.) software. A one-way ANOVA was used to calculate the mean and standard deviation of quantitative variables. The correlation between parameter and gestational age was assessed using Karl Pearson's coefficient of correlation. Bland–Altman plots were used to assess inte-robserver agreement and mean difference, and the 95% limits of agreements are given. In addition, for inter-observer agreement, intra-class correlation coefficients (ICCs) were estimated; agreement was considered poor when $ICC \leq 0.2$, fair when $0.2 < ICC \leq 0.4$, moderate when $0.4 < ICC \leq 0.6$, good when $0.6 < ICC \leq 0.8$ and excellent when $ICC > 0.8$. $P \leq 0.05$ was considered to be statistically significant.

Results

A total of 160 singleton pregnancies between 19 and 38 weeks gestational age were included in our study out of 345 pregnancies and 185 fetuses who had anomalies were excluded. The mean PBF values were calculated for each gestational week (Table 1). The average means placental blood flow value ranged from 89.4 ± 13.57 at 19–20 weeks and increased to 155.3 ± 2.85 at 37–38 weeks. In normal pregnancies, thus the mean placental blood flow values estimated by pCASL MRI were found to be 106.4 ± 20.22 ml/100 g/min for gestational age ranging between 19–38 weeks. Placental blood flow (PBF) showed a positive and significant correlation with increasing gestational age with correlation values (*r*-value 0.77, p-value < 0.001) (Fig. 4). Bland–Altman analysis demonstrated that there was no significant bias between observers as the mean difference was near zero (Fig. 5), with upper limit (5.849) and lower limit (− 5.198) values, respectively. According to our intra-class correlation coefficient (ICC), inter-observer reproducibility of placental blood flow shows good agreement between observers (0.98).

Discussion

ASL is the only fMRI technique that gives a quantitative measurement of placental blood flow without any invasiveness. Some studies have shown the feasibility of measuring placental perfusion using pulsed ASL (PASL) [6, 7] and velocity-selective ASL (VSASL) [8]. Pseudo-continuous ASL (pCASL), which employs a train of discrete RF pulses to mimic flow-driven adiabatic inversion, is capable of labelling the maternal feeding aorta and distinguishing the source of perfusion [9].

Table 1 Showing the mean and standard deviation values of placental blood flow during 19–38 weeks gestation along with correlation(r) and *p*-value

Gestational weeks	*n*	Mean ± Std. Deviation	Correlation between PBF & GA (*r*-value)	*P* value (2 tailed test)
19–20 weeks	10	89.4 ± 13.57		
21–22 weeks	39	94.8 ± 12.44		
23–24 weeks	31	95.5 ± 6.13		
25–26 weeks	13	97.3 ± 4.17		
27–28 weeks	10	109.4 ± 8.00	0.77	0.000 < 0.001
29–30 weeks	17	113.2 ± 9.72		
31–32 weeks	11	121.0 ± 15.76		
33–34 weeks	14	127.2 ± 20.32		
35–36 weeks	09	129.9 ± 24.06		
37–38 weeks	06	155.3 ± 2.85		
Total	160	106.4 ± 20.57		

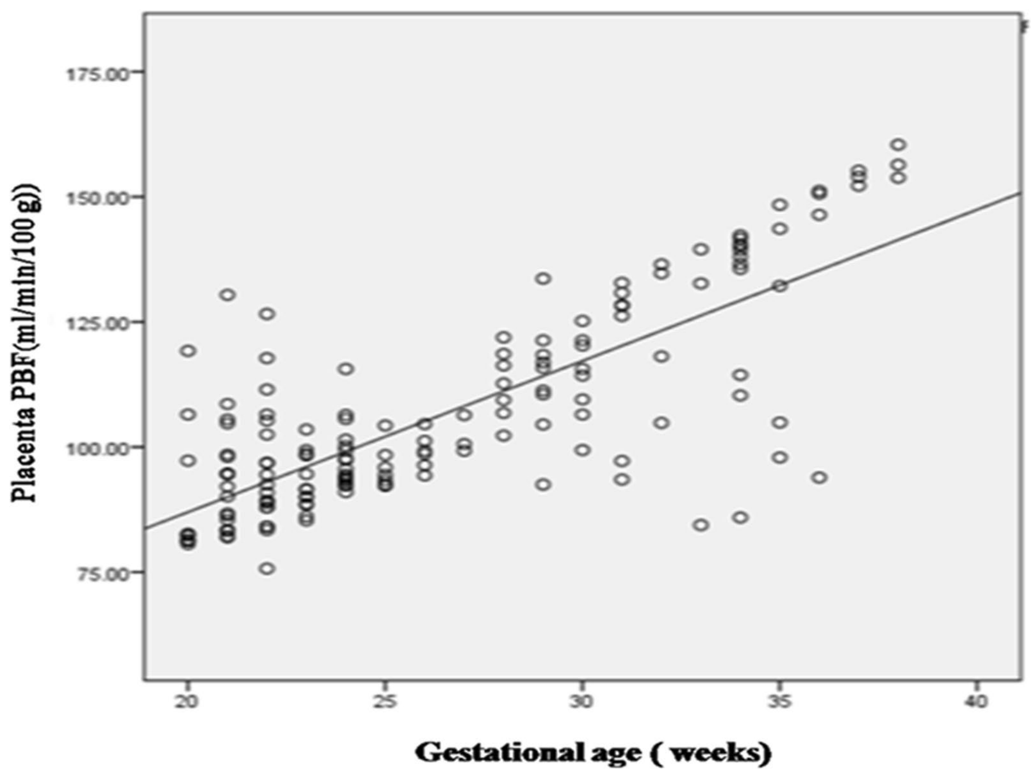

Fig. 4 Scatter diagram showing positive correlation between Placental blood flow values (PBF) & Gestational age ($n = 160$)

The aim of this study was to obtain the perfusion measurements of the placenta in normal pregnancies using ASL on 3 Tesla MRI from 19 to 38 weeks of gestational age. One hundred and sixty (160) pregnant women were included in this study, and the placental blood flow (PBF) obtained was expressed in ml/min/100 g of placenta.

Almost twenty years ago, placental ASL was first reported by a group that published three different studies. Gowland et al. [6] conducted a longitudinal study in which they used the FAIR (Flow alternative inversion recovery), a PASL sequence in a 0.5 T MRI to examine singleton pregnancies at 20–40 weeks and reported that placental perfusion did not change with gestational age and obtained a value for PBF of 176 ml/min/100 g. Duncan et al. [10] reported placental perfusion of 209 ml/100 g/min using a PASL technique at 0.5 T MRI

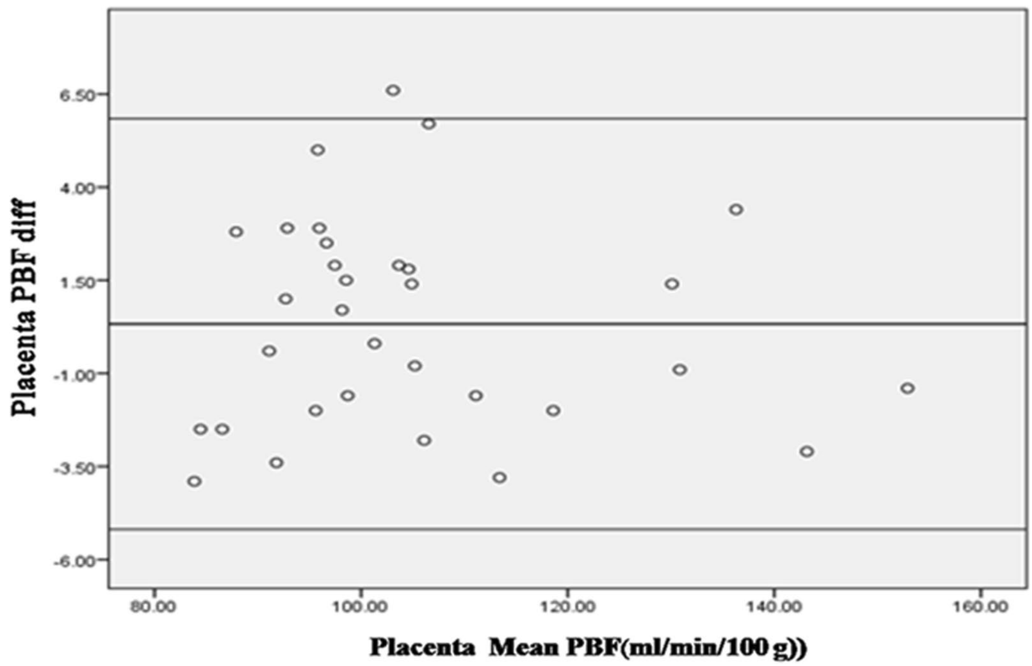

Fig. 5 Bland-Altman plot showing no inter-observer bias and good agreement between two observers for placental blood flow measurements

in normal pregnant women ($n=45$) with no correlation with GA.

Derwig et al. [11] reported placental ASL using FAIR, a PASL technique, in 1.5 T MRI from 24 to 29 weeks ($n=37$). They studied the association between placental perfusion (using MRI) and uterine artery Doppler ultrasound, and their relationship to pregnancy outcome. They concluded that small-for-age (SGA) foetuses exhibited reduced placental perfusion and increased impedance Doppler values. The FAIR ASL technique measures the movement of both maternal and fetal flow, which are around 600 ml/min and 360 ml/min at term [10]. As a result, an overestimation of placental perfusion complicates the understanding of maternal blood supply. Additionally, it requires a long scan time, has a low signal-to-noise ratio (SNR), and is susceptible to motion artifacts.

Liu et al. [2] reported that pCASL is promising for non-invasive assessment of PBF during pregnancy and provided average PBF values for 16 and 20 weeks (104.9 ± 31.4 and 111.3 ± 25.9 ml/100 g/min using 3 T MRI) and revealed a significant correlation between gestational age and placental blood flow. Perfusion-related image parameters for ischemic placental disease were significantly decreased compared to normal pregnancy during early gestation. Our values at 20-week gestational age were slightly lower than this study's reported value.

Shao et al. [9] demonstrated the feasibility of measuring volumetric placental blood flow using a multi-delay pCASL sequence at 3 T from 14 to 22 weeks during the second trimester (111.4 ± 26.7 ml/100 g/min) and showed a significant increase in placental perfusion. Compared to this study, our study provides average PBF values from 19 to 38 weeks (89.4 ± 13.5 ml/100 g/min to 155.3 ± 2.8 ml/100 g/min), normal PBF values in the second trimester from 19 to 22 weeks were 89.4 ± 13.57 ml/100 g/min to 95.5 ± 6.13 ml/100 g/min respectively. The PBF values obtained by our study at 19–22 weeks were slightly lower than the reported PBF values and showed a positive and significant correlation between increasing GA (Fig. 4). When the trophoblastic invasion and spiral arteries proceed, placental perfusion increases throughout pregnancy. Because of this, it might show a positive and significant correlation between increasing GA [1].

As compared to the previous studies, our study was conducted on 3 T MRI using pCASL from 19 to 38 weeks of gestation. This advancement has led to an increase in SNR and is good for clinical scans with limited scan time. The mean placental perfusion measured in normal pregnancies was found to be 106.4 ml/100 g/min for the second and third trimesters, which is slightly lower than the reported PBF values and shows a positive and significant correlation between increasing GA. These results are acceptable because our 3D pCASL sequence included the separation of the blood flow contributed from maternal and fetal sources. These results are related to the fundamental change in the nature of placental tissue perfusion during pregnancy. Based on the estimated maternal blood supply of 600 ml/min and the placental mass of 550 g, the normal placental perfusion rate was predicted to be 110 ml/100 g/min [10]. However, because maternal blood does not pass through the placenta in capillaries but rather collects in pools or lobes and combines with the tissue, there may be a systematic difference between PBF and the normal perfusion rate [6]. The absolute flow rate includes many assumptions (modelling, blood T1, blood tissue fraction, labelling efficiency, etc.), which may cause errors among different ASL techniques. We have demonstrated that inter-observer reproducibility of placental blood flow and our results are in agreement with those of previous studies [2, 9].

Flo et al. [12] and Rigano et al. [13] reported measurements of volume blood flow in the uterine arteries of normal pregnant women throughout the second and third trimesters (19–41 weeks) via Doppler sonography, and both groups also demonstrated a significant increase in uterine blood flow with increasing gestational age.

Assessment of normal PBF at different gestational age is a complementary approach to understanding the vascular structure and the potential pathological changes associated with observed perfusion variation and to increasing knowledge of placental insufficiency. It may permit a better characterization of placental perfusion in cases of genetic and developmental abnormalities, abnormal placental function, fetal growth restriction, preeclampsia, and fetal death in utero [14].

Limitations

This study has several limitations. First our preliminary study data involves a relatively small sample size. Second, though we used respiratory gating, there can still be movement due to maternal and fetal causes that is not compensated. The third limitation of our study is that the correlation between different BMI groups was not performed. Another limitation is that we have not evaluated pregnancies of normal volunteers for placental perfusion; rather, we have included pregnancies with suspected fetal and placental abnormalities that were later found to be normal. We did not correlate the MRI perfusion values with Doppler results, as many of the patients in our cohort did not have Doppler examinations.

Conclusions

This study provided the reference PBF values by using ASL in 3 T MRI from 19 to 38 weeks of gestational age. Statistical analysis revealed a significant positive correlation between gestational age and placental blood flow. The average means placental blood flow values ranged from 89.4 ± 13.57 at 19–20 weeks and increased to 155.3 ± 2.85 at 37–38 weeks. In normal pregnancies, thus the mean placental blood flow values estimated by pCASL MRI were found to be 106.4 ± 20.22 ml/100 g/min for gestational age ranging between 19 and 38 weeks. In the future, it may help to identify placental perfusion abnormalities like placental insufficiency, preeclampsia, and fetal growth restriction (FGR).

Abbreviations

MRI	Magnetic resonance imaging
GA	Gestational age
PBF	Placental blood flow
PBM	Pattern-based morphometry maps
ASL	Arterial spin labelling
FGR	Fetal growth restriction

Acknowledgements

Not applicable

Author contributions

Study conception and design: CP and RR. Data collection: CP. Analysis and interpretation of results: CP, RR, NP. Draft manuscript preparation: CP, RR, CA and NP. Critical revision of the article: CP, RR, CA and NP. Final approval of the version to be published: CP, RR, CA and NP.

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Availability of data and materials

The dataset used or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the institutional ethical committee (IEC-NI/22/APR/82/58) and informed consent was obtained from all the patients**.**

Consent for publication

Written informed consent for the publication of these data was taken from the patient.

Competing interests

Authors declare no competing interests.

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References

1. Sitepu M, Syahriza A, Sibuea D, et al. Placental perfusion in 3rd trimester pregnancy. In: IOP Conference Series: Earth and Environmental Science, 2018; Vol. 125, No. 1, p. 012191. IOP Publishing.
2. Liu D, Shao X, Danyalov A et al (2020) Human placenta blood flow during early gestation with pseudocontinuous arterial spin labeling MRI. J Magn Reson Imaging 51(4):1247–1257
3. Ludwig KD, Fain SB, Nguyen SM et al (2019) Perfusion of the placenta assessed using arterial spin labeling and ferumoxytol dynamic contrast enhanced magnetic resonance imaging in the rhesus macaque. Magn Reson Med 81(3):1964–1978
4. Siauve N, Chalouhi GE, Deloison B et al (2015) Functional imaging of the human placenta with magnetic resonance *Am*. J Obstet Gynecol 213(4):S103–S114

5. Harteveld AA, Hutter J, Franklin SL et al (2020) Systematic evaluation of velocity selective arterial spin labeling settings for placental perfusion measurement. Magn Reson Med 84(4):1828–1843
6. Gowland PA, Francis ST, Duncan KR et al (1998) In vivo perfusion measurements in the human placenta using echo planar imaging at 0.5 T. Magn Reson Med 40:467–473
7. Masselli G, Brunelli R, Bernieri M, et al. Arterial Spin Labelling in the Human Placenta: Mapping Perfusion. In: Radiological Society of North America Scientific Assembly and Annual Meeting, Chicago IL. 2014. http://archive.rsna.org/2014/14045638.html.
8. Zun Z, Zaharchuk G, Andescavage NN et al (2017) Non-invasive placental perfusion imaging in pregnancies complicated by fetal heart disease using velocity-selective arterial spin labeled MRI. Sci Rep 7(1):16126
9. Shao X, Liu D, Martin T et al (2018) Measuring human placental blood flow with multidelay 3D GRASE pseudocontinuous arterial spin labeling at 3T. J Magn Reson Imaging 47(6):1667–1676
10. Duncan KR, Gowland P, Francis S et al (1998) The investigation of placental relaxation and estimation of placental perfusion using echo-planar magnetic resonance imaging. Placenta 19(7):539–543
11. Derwig I, Lythgoe DJ, Barker GJ et al (2013) Association of placental perfusion, as assessed by magnetic resonance imaging and uterine artery Doppler ultrasound, and its relationship to pregnancy outcome. Placenta 34(10):885–891
12. Flo K, Wilsgaard T, Vårtun Å et al (2013) A longitudinal study of the relationship between maternal cardiac output measured by impedance cardiography and uterine artery blood flow in the second half of pregnancy. BJOG Int J Obstetr Gynaecol 117(7):837–844
13. Rigano S, Ferrazzi E, Boito S et al (2010) Blood flow volume of uterine arteries in human pregnancies determined using 3D and bi-dimensional imaging, angio-Doppler, and fluid-dynamic modeling. Placenta 31(1):37–43
14. Deloison B, Salomon LJ, Quibel T et al (2019) Non-invasive assessment of placental perfusion in vivo using arterial spin labeling (ASL) MRI: a preclinical study in rats. Placenta 77:39–45

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