

Progress Toward Reversed Uterine Diastolic Flow in the Third Trimester - An Inauspicious Sign

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ABSTRACT: Background. Increased uteroplacental resistance is associated with high uterine artery pulsatility and resistance indices and early diastolic notching. Evolution toward reversed diastolic uterine flow in the third trimester was scarcely reported previously. The feature was related to severe complications for both mother and fetus. Material and methods: Data were collected from 3638 pregnancies undergoing prenatal care in our hospital. In this study, we aimed to identify those pregnancies with development of a reversed diastolic flow at the spectral Doppler interrogation of uterine arteries later than 24 weeks of gestation. A secondary aim was to follow up and actively manage these pregnancies. Results: Previously, reversed uterine diastolic flow was reported during the third trimester in four cases only. In our study three pregnancies only developed reversed uterine arteries diastolic flow, none being associated with preeclampsia. All cases evolved with complications at birth. Conclusions: Progressive deterioration of uterine arteries flow is possible during pregnancy. Reversed diastolic flow is a rare occurrence in the third trimester of pregnancy. Based on current knowledge, it may be considered an ominous sign and should trigger a close follow-up. Future studies using routine investigation of uterine arteries flow late in pregnancy may prove informative.

KEYWORDS: Reversed uterine artery diastolic flow, third trimester, increased uteroplacental resistance, ultrasound.

Introduction

The increase in uteroplacental resistance causes high pulsatility and resistance Doppler indices, with or without notching.

Reversed diastolic flow in the uterine artery (UtA) in the third trimester (TT) is an uncommon finding.

This Doppler abnormality on ultrasound (US) was associated with fetal growth restriction (FGR), preeclampsia (PE), eclampsia, or placental abruption. Four cases were previously described [1-3].

Normal fetal growth and development are contingent on the normal development and function of the placenta.

In normal pregnancy, placental trophoblast cells invade the inner third of the myometrium and migrate the entire length of the maternal spiral arteries.

Remodelling of these high resistance arteries results in a low resistance and high flow state in

the intervillous space, which optimizes the delivery of oxygen and nutrients to the fetus.

Transformation of uterine spiral arteries and placenta trophoblastic invasion starts at around 8-10 weeks and continues until 24 weeks of gestation [4].

It has been described that the transformation of the uteroplacental vessels proceeds in two waves.

The first wave consists of an invasion of spiral arteries between the decidua and myometrium, and this occurs before 12 weeks.

The second wave involves invasion of the intra-myometrial segments of the spiral arteries and occurs between 12 and 16 weeks [5].

FGR and PE contribute significantly to neonatal and maternal morbidity and mortality.

Doppler of the uterine arteries allows the early study of the phenomenon of trophoblastic invasion and constitutes a useful tool for screening FGR and early preeclampsia.

These two entities arise from an alteration of the trophoblastic invasion of the uterine spiral arteries, which causes a deficient uteroplacental circulation [6].

Deficient uteroplacental circulation will modify the resistance that is reflected in uterine artery Doppler studies by a high diastolic velocity with continuous flow during diastole.

So, Doppler's interrogation of the uterine arteries provides important information on the conversion process of spiral arteries into uteroplacental arteries.

This remodelling, supposed to be complete at 23-24 weeks of gestation, narrow-lumen muscular spiral arteries convert into dilated, low-resistance uteroplacental vessels.

The presence of reverse diastolic flow in the UtA, has been poorly studied, but there is a hypothesis that this wave pattern in the TT could be the result of a progressive deterioration of the uteroplacental flow which would request maternal and fetal surveillance [1].

The aims of this study were first to identify those pregnancies that developed a reversed diastolic flow at the spectral Doppler interrogation of uterine arteries later than 24 weeks of gestation, and the secondary aim was to follow up and actively manage these pregnancies.

We describe below three cases evolving toward inverted UtA in the TT.

The first case was complicated with early-onset FGR, the reversed early diastolic flow occurred early (in the late second trimester-ST), had a low placental volume, and ended in stillbirth.

The second is a pregnancy complicated with early-onset FGR and maternal arrhythmia.

It resulted in a preterm prelabour emergency C-section, the live new-born having a favourable short-and long-term evolution.

The third case presented with isolated plateauing of the fetal growth curve and late occurrence of maternal hypertension.

This case was actively managed also and had a favourable outcome for the mother and the neonate.

Material and Methods

We performed a nested cohort prospective study, designed and conducted in the Prenatal Diagnosis Unit of the Emergency County Hospital of Craiova, a tertiary referral university-affiliated hospital in the southwest region of Romania.

The study was carried out over a period of three years (1 September 2019-1 September 2022).

We included 3638 women with singleton pregnancies, having normal and abnormal growth, with prenatal care and first trimester (FT) dating.

We excluded pregnancies lost to follow-up, with incomplete data, or the ones who withdrew informed consent.

The research hypothesis was as follows: we want to identify the pregnancies that maintain or develop reversed diastolic flow in the uterine artery (left uterine artery and/or right uterine artery) later than 24 weeks of gestation and to follow them up until birth.

For this purpose, we used for all cases a Voluson E10 (GE Medical Systems Chicago, IL, USA) US machine, equipped with a 4-8MHz curvilinear transducer.

The study protocol was approved by the university ethics committee and informed consent was obtained from all participants prior to enrolment.

All UtA Doppler measurements were performed following current recommendations, using an angle of insonation $<30^{\circ}$, in the absence of maternal and fetal movements, and using an automated trace, obtaining at least three consecutive waveforms.

Results

We found reversed diastolic flow in the uterine artery later than 24 weeks in three patients only in the study group.

Each of the presented cases has particularities.

Two of them had the nuchal scan performed in our unit.

We have proof that in these cases, although the early diastolic notch was present in the late FT, the UtA flow was bilateral positive during diastole (both UtA, each case).

The reversed flow developed subsequently, during the late ST or during the TT.

In these cases, we noticed a rapid unfavourable evolution of UtA Doppler indices.

The first was a pregnancy complicated with early-onset FGR, reversed early diastolic flow in the ST and in the TT, velamentous insertion and very low placental volume.

The case ended in stillbirth.

Although non-specific, some types of histological placental lesions (infarction, syncytial knots, intervillous fibrinoid deposition, villous thrombi) are more often seen in placentas from pregnancies complicated with FGR [7].

It seems that the proportion of these changes is more important than their presence, normal in every term pregnancy.

We describe below the prenatal US features and correlated them with the postnatal aspect (macro-and microscopic data).

The second case was a pregnancy complicated with early-onset FGR and reversed diastolic flow also, and maternal arrhythmia.

It resulted in a preterm prelabour emergency C-section, the live newborn having a favourable short-and long-term evolution.

It seems that women with an arrhythmia have an increased risk for cardiac complications in pregnancy and are significantly more likely to develop FGR than those with other types of cardiac diseases, even in arrhythmias without structural heart lesions.

Maternal physiology during pregnancy favours arrhythmias through the electrophysiological effects of hormones and hemodynamic changes.

We excluded associated structural heart, thyroid and rheumatological diseases, infections and electrolytes imbalance.

In the case presented, the mother had a relatively rapid evolution toward normalization of the heart rate and required no further treatment.

It is less likely that the first-degree atrioventricular block, lasting one week would have an influence on fetal growth.

The third case may be seen as the most intriguing. It presented with isolated plateauing of the growth curve, reversed early diastolic flow in TT, and late occurrence of hypertension, following a complete prenatal follow-up according to current recommendations.

The mother was healthy and young, we identified no risk factors for complications in pregnancy.

The fetus maintained a normal fetal growth curve, despite evolving with moderately high umbilical artery PI for many weeks, and despite the elevated and worsening indices on both uterine arteries.

UmbA ARED occurred abruptly. The case was actively managed and had a favourable outcome for the mother and the neonate.

Case Report No. 1

A 31-year-old non-smoker primigravida was referred to our unit at 24 weeks gestation (WG) for suspected growth abnormality.

The mother had no chronic medication before and during pregnancy and had no identifiable risk factors for a complicated pregnancy.

The combined test for chromosomal abnormalities screening had not been performed.

At presentation, sonography showed normal anatomy in a small fetus (fetal growth corresponding to percentile 7.5% on Hadlock 4 nomogram) and a subjectively small volume of the placenta.

FGR was confirmed based on the Doppler abnormalities.

The patient was admitted, and the couple was counselled about the unfavourable prognosis of the fetus.

Physical examination revealed no associated pathology, hematological and biochemical values were normal, proteinuria was absent and no active or recent infections.

Anticardiolipin antibodies and antinuclear antibody screening were normal.

Antithrombin III, protein C, protein S, and Factor V Leiden were found normal.

Parental karyotype was normal.

Following counselling, cordocentesis was offered and declined by the parents.

The maternal blood pressure at presentation was normal.

We routinely measured it automatically, with a calibrated OMRON M6 Confort device, according to standard procedure [8,9].

The patient did not develop any sign of gestational hypertension or preeclampsia during the prenatal follow-up.

We followed the recommended technique for obtaining the UtA spectral Doppler indices [10].

The pulsatility index (PI) was above the 95th centile in both uterine arteries and mean PI also (Figure 1).

The reversed diastolic flow was noted in the left UtA (Figure 1b).



Figure 1. Case Report No. 1. Results on spectral Doppler interrogation at 24 weeks gestation: right uterine artery waveform: (a) showing early diastolic notch; left uterine artery waveform; (b) showing early diastolic inverted flow (below baseline).

ARED (absent/reversed end-diastolic velocity) in the umbilical artery (UmbA) was present.

Ductus venosus PI and amniotic fluid index were normal.

The small placenta was located in the right horn and velamentous insertion of the umbilical cord was suspected.

The couple was counselled repeatedly about the limited options available in severe, early-onset FGR and about the lack of specific evidence-based therapies [9,11].

We explained in multidisciplinary teams that the baby would have a 50% chance of intact

perinatal survival without major complications if reaching at least 28+0 weeks and at least 700g [12].

Facing the poor prognosis of the neonate, the parents elected fetal abandonment.

Two weeks later (27 weeks), the reversed a-wave in ductus venosus (Figure 2a) and oligohydramnios occurred.

Results in both UtA interrogations remained the same (same range in percentile, inverted diastolic flow in the left UtA).

The growth curve was flattened (see Figure 2b).

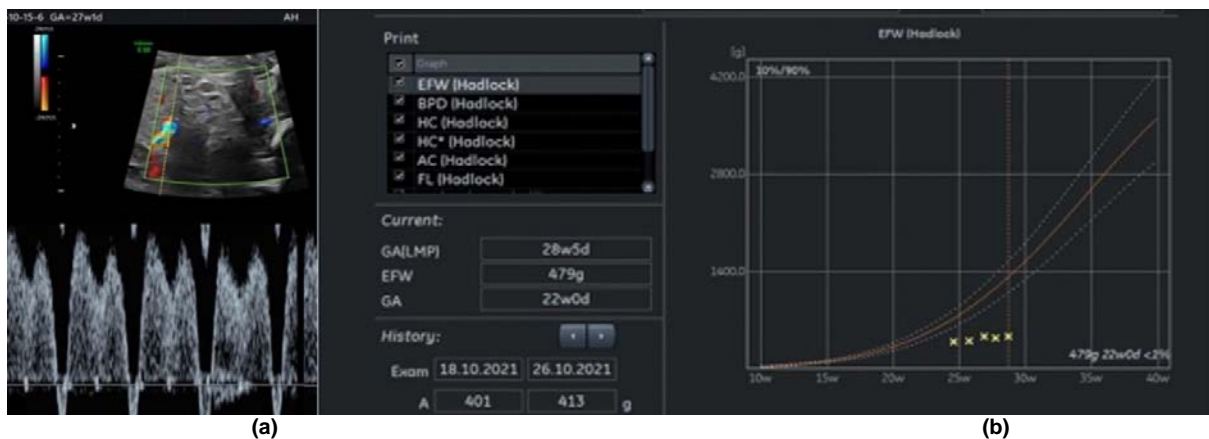


Figure 2. Case Report No. 1. Ultrasound data: (a) Ductus venosus interrogation at 27+1 weeks' (reversed a-wave); (b) growth curve showing severe flattening (estimated fetal weight at 28+5 weeks was estimated 480g, reaching a value below percentile 2).

The stillbirth occurred one day later.

The induction of labour was performed.

The female stillbirth newborn weighed 530g.

Postpartum, the velamentous cord insertion was confirmed (Figure 3a); the placenta weighed 105g.

The microscopic examination described mild villous fibrosis, multiple infarct areas (Figure 3b), intervillous oedema and calcification (Figure 3c).

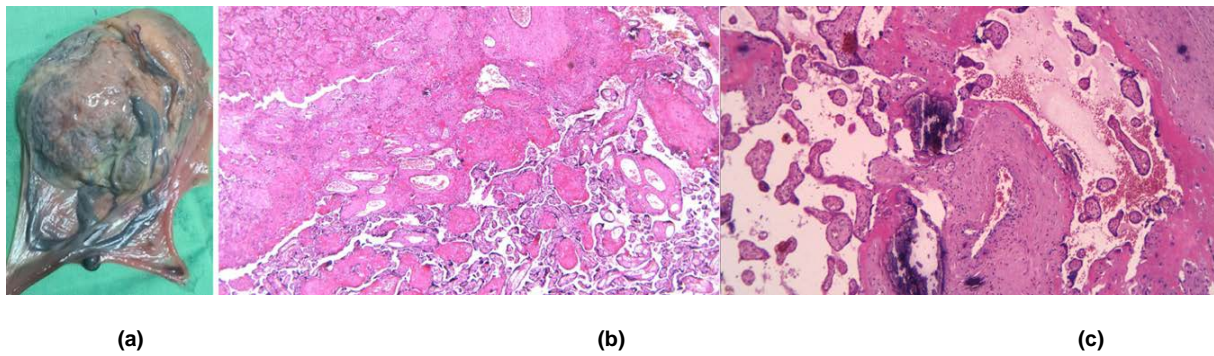


Figure 3. Case Report No. 1. (a) Postpartum data, macroscopic aspect of the placenta: small (reduced maximum diameter) low weight, velamentous umbilical cord insertion. Histological sections: (b) stem villi and placental infarct area Haematoxylin and Eosin (H&E) staining, $\times 40$; (c) stem and mature intermediate villi, with the presence of intervillous oedema and calcification H&E staining, $\times 100$.

Case Report No. 2

A 28-year-old woman in her third pregnancy was referred to our unit for the late FT anomaly scan and combined test for chromosomal anomalies screening.

She had two previous full-term uneventful vaginal deliveries.

We found normal fetal data in the current pregnancy.

Doppler waveforms of UtA showed a high PI and early diastolic notch, yet positive flow during diastole (see Figure 4).

The placenta was posterior and to the right horn.

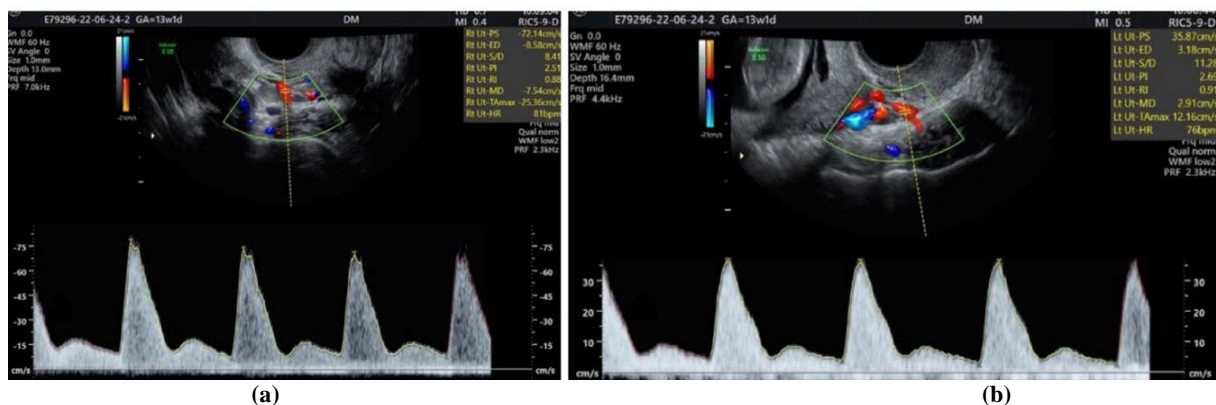


Figure 4. Case Report No. 2. Results on spectral Doppler interrogation at 13+1 weeks' gestation: (a) right uterine artery waveform and (b) left uterine artery waveform; both uterine arteries show velocities indices above the 95th percentile and early diastolic notch.

The second trimester (ST) US anomaly scan was performed at 22 WG.

The fetal ultrasound findings were normal but reversed diastolic flow in the non-placental (left) UtA was noted.

A follow-up scan was scheduled 4 weeks later.

At 26 weeks, the US features suggested FGR the reversed diastolic flow in the left UtA was persistent.

The estimated fetal weight (EFW) was 627g (percentile 15%).

Doppler studies of the umbilical and middle cerebral arteries showed normal figures in velocity indices.

At 28 weeks gestation, the fetus maintained all US well-being criteria (complete biophysical

score), the EFW was roughly 890g (percentile 2.4%), the reversed diastolic flow in the left UtA was persistent and both uterine arteries showed elevated PI.

At 29 weeks the patient was admitted for fetal monitoring.

The same work-up was performed.

A first-degree maternal atrioventricular block was diagnosed and treated.

The cardiac rhythm abnormalities subsided during the next week.

We documented the progressive deterioration of the uterine arteries Doppler indices (both sides) (see Figures 5 and 6).

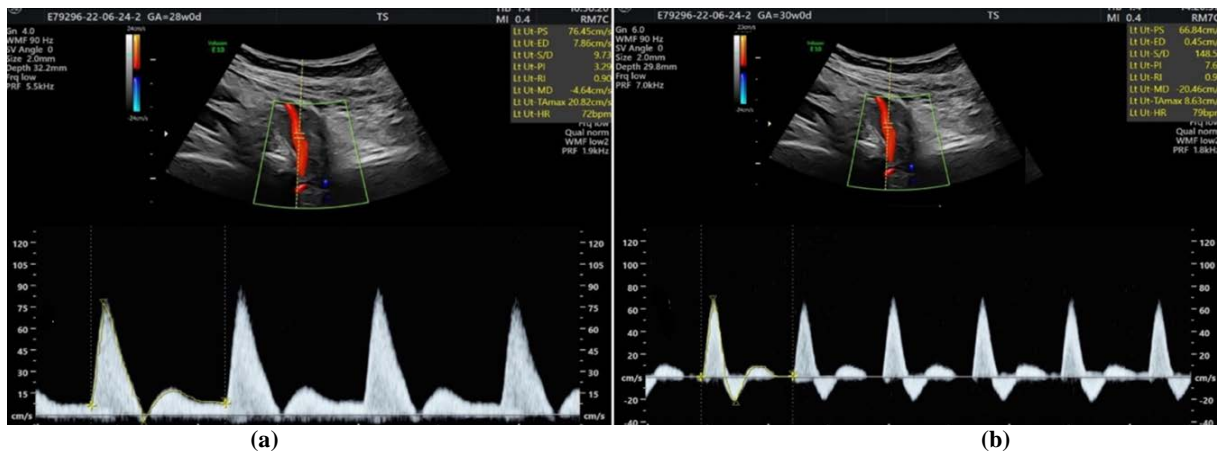


Figure 5. Case Report No. 2. Results on spectral Doppler interrogation (left uterine artery, non-placental) at (a) 28 weeks' gestation and at (b) 30 weeks' gestation. The progressive deterioration is displayed.

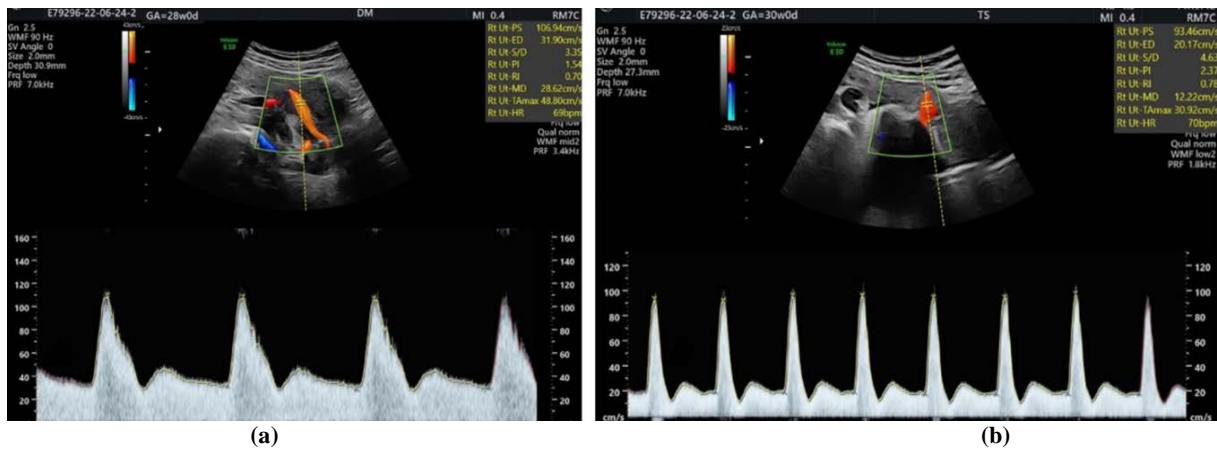


Figure 6. Case Report No. 2. Results on spectral Doppler interrogation (right uterine artery) at (a) 28 weeks' gestation and at (b) 30 weeks' gestation.

Alteration of the cerebroplacental ratio occurred at 30 weeks.

Two times/a day fetal monitoring was initiated.

The amniotic fluid index was normal. EFW was 940g (percentile<1) (Figure 7).

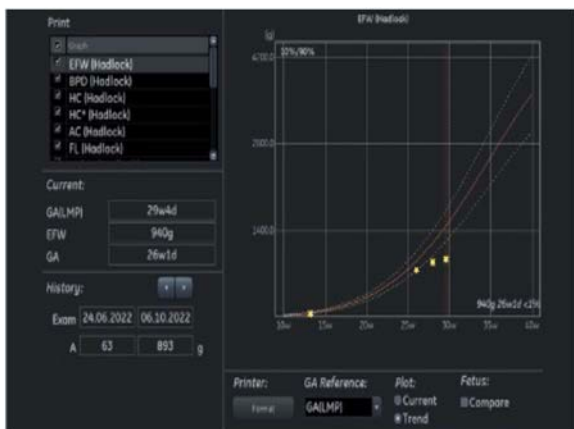


Figure 7. Case Report No. 2. Fetal growth curve showing flattening (estimated fetal weight reaching a value below percentile 1).

One week later, absent end-diastolic flow in the UmbA occurred.

An Emergency lower-segment Cesarean section was performed for persistent fetal bradycardia.

The male neonate weighed 1050g and Apgar scores were 7 at 1 minute and 10 at 5 minutes of life.

The short and long-term follow-up of the baby was uneventful.

The neonate is currently 8 months old and seems to have normal neurodevelopment for age.

Case Report No. 3

The last case we report is a healthy normal weight primigravida, also having no identifiable risk factors for complications in pregnancy.

She was subjected to our unit's protocol for prenatal care: dating, late FT detailed anomaly scan and combined test, and ST assessment of fetal anatomy.

At 12 weeks +4 days, both UtA had similar indices as in Case 2 (full forward flow during diastole, early diastolic notch).

At 20 and 24 weeks, both uterine arteries maintained early diastolic notch.

A closer follow-up was offered.

The patient developed gestational hypertension, diagnosed at 26 weeks: systolic blood pressure was measured at 150mmHg on two occasions (6h apart), the patient having previously documented normal blood pressure.

The values spontaneously decreased, and no treatment was required.

She developed no further clinical or laboratory signs of preeclampsia.

High UmbA-PI (above the 80th centile) was noted, with a positive diastolic flow.

The fetus evolved completely normal until 28 weeks, including a normal fetal growth curve, despite moderately high UmbA-PI, and despite the elevated and worsening indices on both uterine arteries.

At 29 weeks the patient was admitted for monitoring.

She subsequently developed unilateral uterine artery reversed diastolic flow, at 30+5 weeks (Figure 8).

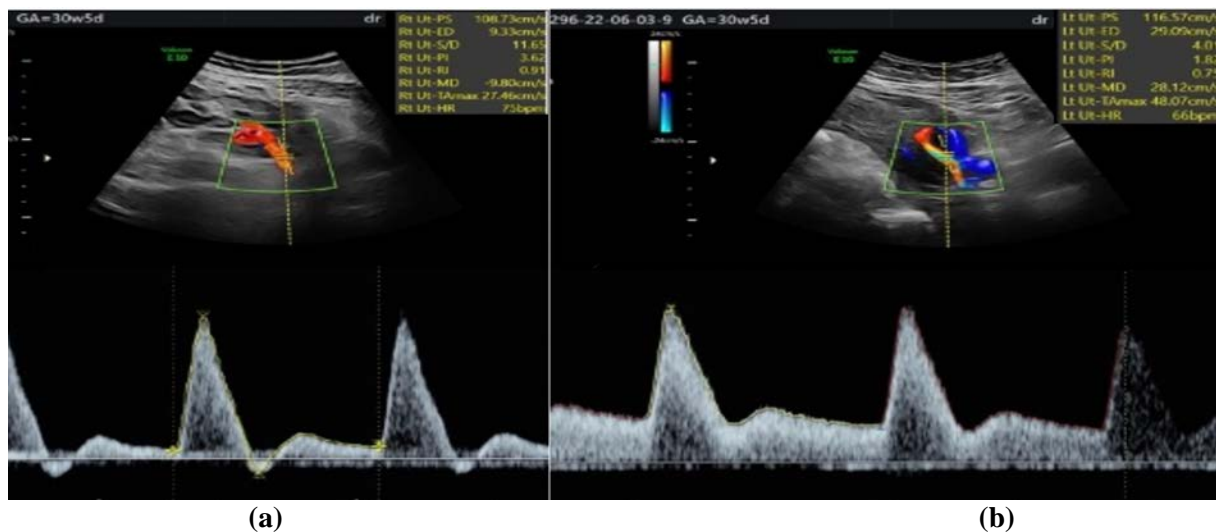


Figure 8. Case Report No. 3. Results on spectral Doppler interrogation on both uterine arteries (a) right uterine artery and (b) left uterine artery at 30+5 weeks' gestation.

Five days later, ARED occurred although the fetal growth was plotted in the 25th percentile using the Hadlock 4 technique.

An elective lower-segment Cesarean section was performed for non-reassuring fetal state (low variability on cardiotocography), at 32 weeks.

The male neonate weighed 1490g and Apgar scores were 7 at 1 minute and 8 at 5 minutes of life.

The short and long-term follow-up of the baby was favourable.

The neonate is currently 8 months old and exhibits normal neurodevelopment for age.

Discussion

Generally, predicting pregnancy complications in advance allows us to stratify cases, increase surveillance, carry out timely interventions, or completely change case management.

The final target is to lower the adverse pregnancy outcome (APO) and-in extremely severe cases, to counsel couples more accurately.

The US method has become essential for the diagnosis and surveillance of fetal well-being and Doppler US has a special place in pregnancy disorders related to poor placentation [13-15].

The trophoblastic invasion has a crucial role in pregnancy: to assure the normal development of the uteroplacental circulation.

It implies two steps in normal cases.

An abnormal trophoblastic invasion of the myometrial layer leads to high uteroplacental resistance, associated with Doppler alterations.

Quantitative parameters (PI, RI, and S/D ratio) and qualitative ones (subjectively diagnosed notching) were proposed to identify abnormal UtA velocities and decreased blood flow [16,17].

The continuous forward flow in the UtA is mandatory for the normal development and growth of the fetus and it is present in almost all cases.

Reversed flow at UtA interrogation has been scarcely reported. Nomograms and reference range for UtA waves were proposed, debated, and formally accepted [10,18-22].

The uterine circulation normally presents a low impedance to flow, and the waves recorded from uterine arteries typically show a biphasic pattern with high diastolic frequencies.

A gradual decrease in mean UtA-PI with advancing GA is considered normal.

Uterine placental vascular impedance declines during angiogenesis and stabilizes after 24 gestational weeks [23].

In a normal pregnancy, there is no significant change in the uterine artery impedance from 24 weeks to the end of pregnancy [24].

Although objective parameters are scientifically preferable, many clinicians use also the rapidly attainable subjective feature of notching.

The diastolic notch was also defined as a quantifiable parameter—a reduction in the maximum diastolic blood flow by at least 50cm/s after 20 GW [25].

The aspect is rather common during the FT and early ST: 46-64% of normal pregnancies [16] and its appearance is considered normal until approximately 24 weeks of gestation.

Its persistence later than 24 GW is a manifestation of abnormal uterine vascular impedance, characteristic of poor placentation [26,27].

Similar to the UtA-PI physiologic decrease during pregnancy, the incidence of notch decreases after 24 weeks.

The common situation is as follows: once the aspect of notching disappears, it doesn't appear again during pregnancy in the specific case.

Many studies have reported UtA Doppler during the FT and the ST [17,20,28-32].

Later than 20 WG, UtA indices higher than the 90th centile are predictive for gestational hypertension and FGR in women with moderate risk [33].

Unilateral and especially bilateral notch, isolated and especially associated with high UtA-PI later than 20 weeks is predictive for APO: PE (especially early-onset form [27]), FGR [34], small for gestational age (SGA), low Apgar score, C-section, spontaneous preterm birth (PTB), HELLP (Hemolysis, Elevated Liver enzymes and Low Platelets), oligohydramnios, placental abruption [35,36].

The combination of UtA-PI, cerebroplacental ratio (CPR) and EFW have an acceptable

sensitivity and a high specificity for stillbirth in the TT [7].

We have information on abnormal UtA Doppler during the TT also [7,9,37-41].

High impedance is related to APO (stillbirth, emergency C-section for fetal distress, low pH of the umbilical blood, PTB, low fetal weight, NICU admission).

Most studies prove the association with PE-mediated complications.

It has been hypothesized that high UtA-PI in term PE patients may be the result of vasoconstriction in uterine placental circulation occurring before the onset of PE symptoms, instead of abnormal placentation in early pregnancy.

Also, the Doppler abnormalities were linked to placental apoptosis, placental dysplasia, and blockage of blood vessels, supposedly underlying some late-onset PE cases [42,43].

Thus, screening patients with late-onset complications seems promising, with high UtA-PI in the TT performing better than that in the FT [44].

It has been proved that late-onset increased UtA-PI is associated with abnormal maternal hemodynamics [45].

Increased UtA-PI and UtA-RI and persistence of UtA notching in the late ST has been associated with a higher risk of PE and FGR, due to the placental insufficiency [7,46].

The predictive value of ST UtA Doppler for APO in a low-risk population is low.

Yet, performing UtA Doppler studies later (23-26 weeks gestation, not before 20 weeks) seems to increase the predictive value for APO [34].

One study measured the UtA blood flow at 24, 28-30, and 34 weeks, respectively [47].

It was found that 49% of patients with abnormal blood flow at 24 weeks returned to normal at 34 weeks.

Although in many centers the UtA spectral Doppler interrogation is targeted in high-risk cases for placental insufficiency (e.g., positive history for PE), the test is recommended and performed routinely in the ST (20-24 WG) in others.

The negative predictive value of normal waves spares unnecessary close follow-up and extensive workup.

It seems that antihypertensive drug usage influences UtA impedance [16].

None of the three patients reported received antihypertensive drugs. Also, UtA impedance is dependent on maternal body mass index (BMI).

All three mothers in our case series were normally weighted.

UtA-PI of the placental side is lower than that of the non-placental side [48].

Our findings are in line with previous results in all three reported cases.

The rare situation consisting of reversed proto-(also end-) diastolic flow (early-and late-diastolic flow) at the Doppler spectral interrogation of uterine arteries in the TT was first flagged decades ago [2].

Unfortunately, the cases ended in intrauterine fetal death at 33 weeks.

Subsequently, we learned that timely extraction of the fetus from the hostile *in-utero* environment may be the only efficient way to manage these cases [49].

Later reports on inverted diastole at the uterine arteries site were occasionally published [1,3].

It has been proved that delayed normalization is associated with a better outcome than persistent abnormal uterine artery Doppler waveforms at 28 to 34 WG [47].

Progressive deterioration of abnormal uterine artery Doppler waveforms (having bilateral protodiastolic notches) during pregnancy was documented [1,50].

Yet, extremely rare toward the extreme feature-the inverted flow in diastole.

It has been hypothesized that reversed diastolic flow in the TT might be the end-result of progressive deterioration due to the underlying vasculopathy of placental insufficiency.

It is supposedly resulting from a secondary insult (placental infarction and/or fibrinoid deposition, added to the primary failure of trophoblastic invasion) [1].

The cases presented are interesting due to three reasons.

Firstly, we provide an accurate demonstration of the abnormal evolution of UtA velocities toward worsening indices, conversely to the three universally accepted patterns: improvement, delayed normalization, and plateau.

We provide proof that the dynamics of this process (dynamics of all US features being accepted during pregnancy) may develop in a reverse direction.

Although presenting early diastolic notch in the late FT, the UtA flow was positive during diastole (both UtA, each case).

Two cases had the nuchal scan performed in our unit.

The reversed flow developed subsequently, during the late ST or the TT.

Secondly, none of our cases were associated with criteria for preeclampsia, including the newly stated ones [8].

The third reason is the scarcity of previously published cases (only four cases showed reversed diastolic flow in UtA in the TT) [8].

In our view, similar cases are underreported, due to the scarce use of UtA Doppler studies in the TT.

All four previously reported cases ended with major complications (IUFD, eclampsia, FGR, and abruptio) and two of them had preeclampsia.

In our case series, no patient had preeclampsia, and two of them had a favourable outcome with active management.

We mention homogeneity in assessing the UtA Doppler indices in our study.

We used in the ST and TT scans the same approach, in all cases: the transabdominal approach.

Using a standard technique is important when assessing apparently normally grown fetuses suspected to be affected by placental insufficiency, as in the last case we presented.

TT routine US in low-risk pregnancies to detect growth abnormalities is gaining popularity and has an increasingly recognized added value in the prenatal care [51].

We align ourselves with recommending routine (repeated) Doppler studies of the UtA each trimester (the ST and TT added to the FT), regardless of the maternal history and previously detected risk factors for APO.

Obstetric history is absent in primigravidae, thus clinically non-relevant (in our case series, two of the three patients had their first TT pregnancy).

Biomarkers of impaired placentation (like UtA-PI) may be used in different informatic models [52,53] to improve the prediction of APO and the perinatal outcome.

Interrogating UtA should become a mandatory test during the ST and the TT in high-risk pregnancies, or if documented abnormal fetal growth.

The additional time is very short (in our experience less than 2 minutes).

The investigation is low-cost, readily available (all currently used US systems incorporate facility and nomograms), acceptable (since feasible transabdominally), reproducible [54] and provides immediate results.

Moreover, it has low false-positive rates, thus avoiding unnecessary parental anxiety.

The added information has the potential to improve management.

Generalizing the UtA Doppler studies throughout the pregnancy would improve understanding of the pathophysiology of severe complications occurring at the end of pregnancy.

Conclusions

Worsening uterine arteries Doppler indices in late pregnancy is possible.

The uterine arteries reversed diastolic flow is an uncommon ultrasound finding during the third trimester of pregnancy.

It is associated with an unfavourable outcome and should prompt a complete work-up for late fetal growth restriction and preeclampsia.

Based on current knowledge, the feature may be considered an ominous sign and should trigger close monitoring of maternal and fetal conditions.

Future studies using the routine investigation of uterine arteries flow late in pregnancy may prove informative.

Spectral Doppler interrogation of uterine arteries in the third trimester is a simple and quick test.

It should be included in the US scan protocol in high-risk pregnancies and in cases with abnormal fetal growth.

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Conflict of interests

None to declare.

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