Fetal cardiac dysfunction in preeclampsia: Combined Doppler ultrasonography and biochemical study.

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ABSTRACT

OBJECTIVE: The purpose of this study was to correlate Doppler ultrasonographic parameters of fetal haemodynamic compromise with neonatal umbilical artery cardiacTroponin T (cTnT) level as a biochemical marker of fetal cardiac dysfunction in pregnancies complicated by preeclampsia (PE)). **PATIENTS AND METHODS:** In this study, 50 pregnant women were included, recruited within two years duration, from the antenatal care clinic and the high-risk pregnancy unit of Alnoor specialist hospital, holy Makkah, KSA. Their gestational ages were ranging between 32-38 weeks and they were divided into: control group (20 women) with normal pregnancies **(GI)** and study group (30 women), out of them 20 with PE without any ultrasonic Doppler detection of transmitted atrial pulsations to the intra-abdominal portion of fetal umbilical vein **(GII)** and 10 women with PE with ultrasonic Doppler detection of transmitted atrial pulsations, to the intra-abdominal portion of fetal umbilical vein **(GIII)**. For all cases routine ultrasound scanning, Doppler velocimetery (S/D ratio) for umbilical artery (UA) and for the intra-abdominal portion of umbilical vein was done. Maternal cubital vein and neonatal UA serum troponin-T levels was measured. **RESULTS:** Cardiac troponin T concentrations showed significant increase (P <0.01) in neonates who had transmitted atrial pulsations in fetal intra-abdominal part of umbilical vein, suggesting fetal myocardial cell damage, with the higher levels in fetuses with severe placental insufficiency showing absent end-diastolic or reversed flow in UA. Maternal troponin T concentrations were within normal levels, even in cases in which neonatal troponin T levels were increased, which demonstrate that the umbilical artery troponin T measured in neonates was not of maternal origin. **CONCLUSION AND RECOMMENDATION:** Doppler detectable transmitted atrial pulsations in the intra-abdominal part of the umbilical vein is an ominous Doppler sign for fetal outcome in cases of PE associated with placental insufficiency, indicating fetal myocardial damage and mandates prompt delivery in hospital with well-equipped neonatal intensive care unit. The optimal timing of delivery in such cases should be before the appearance of this bad prognostic sign, depending on other Doppler parameters of fetal circulation.

Keywords: Doppler ultrasound; Fetal cardiac dysfunction; Preeclampsia

Introduction

Placental insufficiency, preeclampsia and fetal growth restriction are common obstetrical problems, which may have long-term consequences.[1] Noninvasive Doppler ultrasonography enables the examination of placental, fetal central and peripheral hemodynamics.[2,3] Abnormal placental function and intrauterine fetal growth restriction are common findings in pregnancies complicated by preeclampsia. Severe placental insufficiency triggers compensatory mechanisms in the fetus that aim to maintain adequate oxygen and nutritional supply to the most vital fetal organs, the heart and the brain.[4] One of these protective mechanisms of the fetus is redistribution of cardiac output. Right ventricular cardiac output decreases, whereas left ventricular cardiac output usually remains unchanged. Further deterioration in placental function and oxygen supply also result in decreased left ventricular cardiac output, which leads to increased systemic venous pressure.[5]

A rise in placental vascular impedance has been associated with increased perinatal morbidity and

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mortality.[6] The presence of pathologic umbilical artery blood velocity waveforms indicates the need for closer fetal surveillance. In these cases, the timing of the delivery has often been based on pathologic fetal heart rate tracings.[7]

The observation of pulsations in the umbilical vein and an increase in the reverse component of flow from the right atrium into the inferior vena cava with atrial contraction indicates alterations in cardiac function and heart failure in cases of severely increased placental resistance, arrhythmias, and nonimmune hydrops.[8]

It has also been shown that changes in umbilical venous velocities originate in the fetal venous system and are transmitted towards the placenta.[9]

Deteriorating fetal well-being may lead to abnormal blood velocity waveforms in the systemic veins, including an increased atrial contraction wave in the hepatic veins, ductus venosus, and inferior vena cava, and to the detection of atrial pulsations in the portal and umbilical veins, which reflect increased systemic venous pressure in the fetus[5]. The interval between these abnormal venous signals detected by Doppler ultrasonography and an abnormal nonstress test result or fetal death is usually only a few days.[10]

Placental insufficiency was defined as an abnormal umbilical artery blood velocity waveform profile (umbilical artery S/D ratio>3.5).[11]

Placental insufficiency may lead to cardiac dysfunction.[12] Increased pulsatility in the blood velocity waveforms of fetal systemic veins has been associated with biochemical evidence of a rise in fetal systemic venous pressure.[13]

Cardiac troponin T, a thin-filament contractile protein present in high concentrations in the myocardium but usually not in other tissues, is released rapidly after myocardial injury in direct proportion to the extent of injury,[14] and suggests an association with worse prognosis

Subjects and methods

Within 2 years (from 01/ 06/ 2004 to 30/ 06/ 2006), 50 women with singleton pregnancies without fetal chromosomal abnormalities or major malformations were included in this study. They were recruited from the antenatal care clinic, high-risk fetal assessment clinic and Ob/Gyn. emergency room of Al-Noor Specialist Hospital, Holy Makkah, K.S.A.

They were classified into three groups:

Group I (GI): 20 women with normal pregnancies.

Group II (GII): included 20 patients with mild to severe preeclampsia, without any transmitted atrial pulsations, to the intra-abdominal portion of fetal umbilical vein.

Group III (GIII): included 10 patients with severe preeclampsia with evidence of transmitted atrial pulsations to the intra-abdominal portion of fetal umbilical vein.

Diagnostic criteria of maternal hypertensive disorder followed American College of Obstetricians and Gynecologists guidelines (Committee on Technical Bulletins of the American College of Obstetricians and Gynecologists 1996).

In all groups the gestational ages were ranging between 32-38 weeks and they were comparable regarding maternal age and parity.

After routine history taking, general, obstetric examination and routine investigations all patients went through:

Ultrasound scanning for fetal viability, biometry, maturity, placental site and fetal biophysical profile.
Doppler velocimetery (S/D ratio) for umbilical artery (UA) and detection of pulsations in the intra-abdominal portion of umbilical vein (UV).
Non stress test (NST).
Maternal cardiac Troponin-T level.
Neonatal UA cardiac Troponin-T level.
Apgar score.
Cord blood pH.

Ultrasconographic measurements

Image-directed pulsed and color Doppler ultrasonographic equipment (Aloka SSD-5500 color power Doppler machine with 3.5 MHz and 5MHz curvilinear transducers) was used in this study. Doppler parameters (i.e. filter, gate width, gain, flow

and velocity scales) were optimized for detection of blood flow in the umbilical artery and intra-abdominal part of umbilical vein

Placental circulation was assessed by determining the S/D-values of umbilical artery in free loops of the umbilical cord.

The proper plain of abdominal circmference was obtained with 1/3 of umbilical vein seen inside the abdomen and pulsation waves (occurring during atrial contraction) in this intra-abdominal part of umbilical vein were noted

Placental insufficiency was defined as an abnormal umbilical artery blood velocity waveform profile (UA S/D ratio>3.5, absent end-diastolic or reversed flow).[11]

Fetal Non-Stress test

The Fetal Non-Stress test is a simple, non-invasive test performed in pregnancies over 28 weeks gestation. The test is named "non-stress" because no stress is placed on the fetus during the test. The test involves attaching one belt to the mother's abdomen to measure fetal heart rate and another belt to measure contractions. Movement, heart rate and "reactivity" of heart rate to movement is measured for 20-30 minutes.[15]

Cardiac troponin T (cTnT)

During labor or just before elective caesarean section, 2ml of maternal cubital vein blood were drawn then immediately after delivery and after cord clamping, UA blood samples of ≥ 1 ml were drawn and both blood samples were centrifuged and serum stored at -80°C.

Serum cTnT concentrations were measured with commercially available enzyme-linked immunosorbent assay kits (Enzymum-Test Troponin T; Boehringer Diagnostics, Mannheim, Germany) according to manufacturer's instructions

The cut-off level for maternal vein and umbilical artery cTnT was set at 0.10 ng/ml, which has been used as a level of clinically significant myocardial cell damage in adult patients

Results

All women included in this study were delivered in the hospital. Out of them 15 cases were delivered by Caesarian Section, among them two patients belonged to GI group and indication was history of previous two C.S, five cases belonged to GII for abruptio placentae and failed induction after premature rupture of membranes and preeclampsia with refractory hypertension, while eight cases were from GIII for severe antepartum fetal compromise (six of them) and abruptio placentae (remaining two cases).

Out of the nine neonates admitted to NICU, three cases (two from GII and one from GIII) were shifted to intermediate care after couple of days and were discharged after three weeks. In the remaining six cases from GIII, three expired postnatally at day four, two cases developed brain death and one case developed cerebral palsy.

The results of this study were collected and statistically analyzed as decribed in the following tables, and (Fig.1), (Fig. 2) and (Fig. 3a and b).

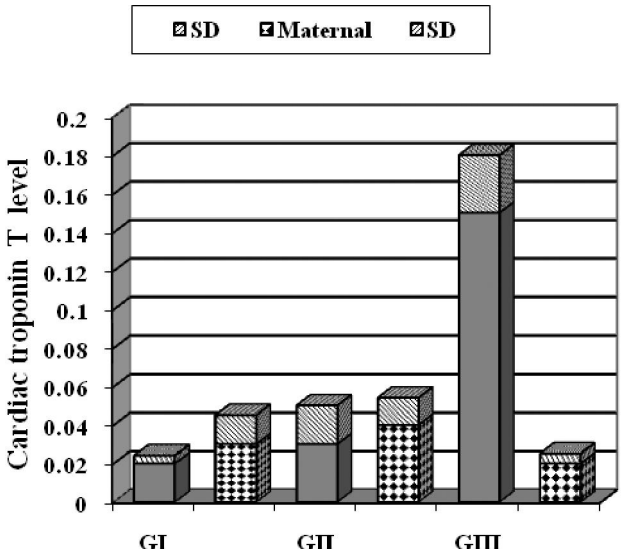


Figure 1: Mean ± SD of maternal and neonatal UA cardiac troponin T level in control and study groups

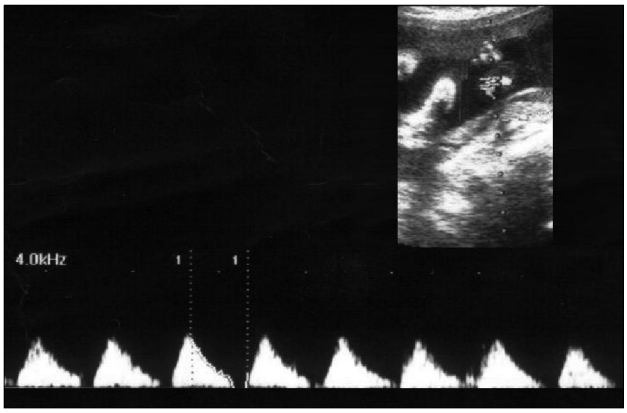
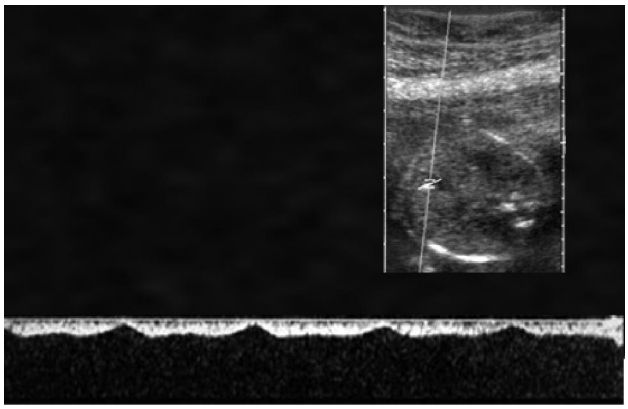
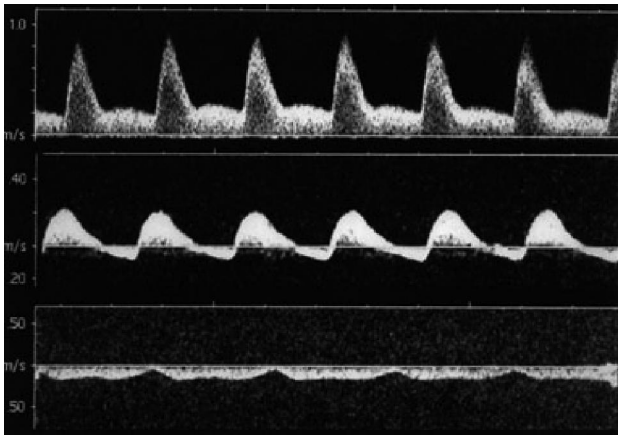


Figure 2: shows absent end -diastolic flow in UA in severe placental insufficiency



3(a)



3(b)

Figure 3(a): shows transmitted atrial pulsations in intra-abdominal portion of fetal umbilical vein. **3(b):** Correlation of transmitted atrial pulsations in intra-abdominal portion in severe fetal compromise.

Table1, shows the demographic data of all groups. They were comparable in maternal ages (M. age) and parity. There were highly significant difference between GI and GIII regarding gestational age (GA) at delivery and birth weight (BWt). The incidence of caesarean section (C.S) was significantly higher in GIII mostly due to fetal compromise. Maternal cardiac troponin T concentrations were normal (less than 0.10 ng/ml) in all groups.

Table 1: Demographic data

	Group I (n=20)	Group II (n=20)	Group III (n=10)
M. age (m±SD)	28.3 ± 2.5	29.4 ± 3.5	27.6 ± 2.8
GA at delivery (wkM±SD)	37.5 ± 2.1	36.1 ± 3.1	34.6 ± 1.8▪
C.S	2(10%)	5 (25%)	8 (80%)▪
BWt (gm) (M±SD)	2950 ± 244	2810 ± 206	1970 ± 320▪
Parity (M±SD)	2.1 ± 1.1	1.9 ± 1.7	2.2 ± 1.4
Maternal cTnT (ng/ml) (M±SD)	0.03 ± 0.015	0.04 ± 0.014	0.02 ± 0.005

▪ Highly significant using t test (P<0.01)

The Non Stress Test (NST) results and the Doppler UA S/D ratio were significantly different between GI and GIII as shown in Table 2.

Table 2: NST and Doppler indices

		GI	GII	GIII
NST	**Reassuring**	19	15	4▪
	Non reassuring	1	5	6▪
UA S/D ratio	**Satisfactory (<3.5)**	18	14	4▪
	Unsatisfactory (>3.5)	2	6	6▪

▪ Highly significant using X^2

In Table 3, the Apgar score after 1 and 5 minutes and cord blood pH were significantly lower in GIII. Neonatal UA troponin T level at delivery showed significant increase in GIII.

Table 3: neonatal outcome

	Group I (n=20)	Group II (n=20)	Group III (n=10)
Apgar score (1min) (M±SD)	8.2 ± 1.1	7.8 ± 1.9	4.6 ± 1.2▪
Apgar score (5min) (M±SD)	8.7 ± 0.5	8.1 ± 1.6	5.3 ± 1.8▪
UA cord blood pH (M±SD)	7.15 ± 0.02	7.1 ± 0.08	6.75 ± 0.09▪
NICU admission	0	2	7▪
Neonatal UA troponin (M±SD)	0.02 ± 0.004	0.03 ± 0.02	0.15 ± 0.03▪

▪ Highly significant using t test P<0.01

Discussion

Fetal cardiac and placental circulation are interconnected through the umbilical arterial and venous vasculature abnormalities of umbilical arterial velocities particularly relative decrease in diastolic velocity compared with systolic velocity has been associated with increase in perinatal morbidity and mortality. However, fetuses with compromise are not consistently identified by means of umbilical arterial velocity examination. Recently it has been discovered that alterations in umbilical venous blood flow velocities are not only present in fetuses with with abnormal umbilical arterial circulation but also in fetuses with cardiac dysfunction like abnormalities of cardiac rate (heart rate more than 180 beats / minute or less than 120 beats /minute), in patients with premature atrial contractions, heart block.[8]

A consistant finding in fetuses with umbilical venous pulsations was an abnormal increase in the velocity of reverse flow of blood into the inferior vena cava with atrial contraction which may be secondary to abnormal umbilical arterial circulation or cardiac dysfunction, but in fetuses with cardiac dysfunction like complete heart

In this study serum troponin T concentrations were increased significantly in neonates (cTnT>0.10 ng/ml) who had transmitted pulsations in fetal intra-abdominal part of umbilical vein, suggesting fetal myocardial cell damage, with the higher levels in fetuses with more severer forms of placental insufficiency, showing absent end-diastolic or reversed flow in UA in GIII (2 cases and one case respectively)

Gestational age at delivery, birth weights, Apgar scores and umbilical artery pH values were significantly lower in fetuses with elevated umbilical artery cTnT levels than in fetuses with normal cTnT values (<0.10 ng/ml).

Maternal troponin T concentrations were within normal levels, even in cases in which neonatal troponin T levels were increased, which demonstrates that the umbilical artery troponin T measured in neonates was not of maternal origin

Mode of the delivery and GA did not affect cTnT concentrations in neonates born for GI and GII. Neonatal intensive care unit (NICU) admission was significantly higher in GIII.

We noticed the pulsating pattern in fetal intra-abdominal part of umbilical vein in 6 cases of severe placental insufficiency as shown by bad non-stress test and abnormal Doppler of UA. The outcome was poor in these cases. These results are in agreement with one study which concluded that pulsating venous pattern, extended to the intra-abdominal part of the umbilical vein, is an ominous finding in high-risk pregnancy and is associated with poor perinatal outcome.[17] Velocimetric modifications in the fetal venous compartment constitute a relevant prognostic sign in the prediction of perinatal mortality and neonatal resuscitation. The further the vessels compromised are from the heart, the higher is the relative risk for perinatal mortality, that may reach up to 95% when pulsations are obtained on the umbilical vein.[18] Umbilical venous pulsations were suggesting adverse outcome of severely compromised fetuses.[19]

The last two studies are matched with the results obtained in this study.

Changes in diastolic venous blood velocity and pulsation in the umbilical vein were closely related to perinatal mortality.[20] These findings are similar to our findings where all the fetuses with pulsations in the intra-abdominal part of umbilical vein were admitted immediately to the NICU where they were ventilated on high ventilator parameters.

In normal pregnancies with uncomplicated deliveries, neonatal troponin T concentrations were not significantly increased (<0.10 ng/ml).

Maternal hypertensive disorders and preeclampsia, with or without signs of placental insufficiency and with normal umbilical venous return, were not related to clinically significant elevations of neonatal troponin T concentrations. On the other hand, when these pregnancy complications were associated with abnormal fetal umbilical venous return, neonatal troponin T concentrations were clinically significantly increased.[5] These findings are in agreement with the results of this study

Conclusion and recommendation

Severe deterioration of placental function, leads to decrease in both right and left ventricular cardiac output (congestive heart failure), and increased fetal systemic venous pressure.

The presence of pulsations in the intra-abdominal part of the umbilical vein is an ominous Doppler sign for fetal outcome in cases of preeclampsia with placental insufficiency as it is usually associated with bio-chemically detectable fetal myocardial damage and mandates prompt delivery in hospital with well-equipped neonatal intensive care unit.

This study recommends that the optimal timing of delivery in cases of preeclampsia with placental insufficiency should be before the appearance of transmitted atrial pulsations in the intra-abdominal portion of the umbilical vein and should depend on other Doppler parameters in the fetal circulation that could precede the development of this bad prognostic sign.

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References

1. Eriksson JG, Forsen T, Tuomilehto J, Osmond C & Barker DJP. Early growth and coronary heart disease in later life: longitudinal study. BMJ 2001; **322:**949–53

2. Wladimiroff JW, Tonge HM & Stewart PA. Doppler ultrasound assessment of cerebral blood flow in the human fetus. Br J Obstet Gynaecol 1986; **93(5):** 471–5

3. Moise KJ, Jr., Huhta JC, Sharif DS, Ou CN, Kirshon B, Wasserstrum N & Cano L. Indomethacin in the treatment of premature labor. Effects on the fetal ductus arteriosus. N Engl J Med 1988; **319(6):** 327–31

4. Rizzo G, Arduini D. Fetal cardiac function in intrauterine growth retardation. Am J Obstet Gynecol 1991; **165:** 876-82

5. Makikallio K, Vuolteenaho O, Jouppila P, et al. Association of severe placental insufficiency and systemic venous pressure rise in the fetus with increased neonatal cardiac troponin T levels. Am J Obstet Gynecol. 2000; **183:** 726–31

6. Rochelson B, Schulman H, Farmakides G, Bracero L, Ducey J, Fleischer A, Penny B & Winter D. The significance of absent end-diastolic velocity in umbilical artery velocity waveforms. Am J Obstet Gynecol 1987; **156(5):** 1213–8

7. Arduini D, Rizzo G, Soliani A & Romanini C. Doppler velocimetry versus nonstress test in the antepartum monitoring of low-risk pregnancies. J Ultrasound Med 1991; **10(6):** 331–5.

8. Indik JH, Chen V, Reed KL. Association of umbilical venous with inferior vena cava blood flow velocities. Obstet Gynecol. 1991; **77(4):**551-7

9. Reed KL & Anderson CF. Changes in umbilical venous velocities with physiologic perturbations. Am J Obstet Gynecol 2000; **182(4):** 835–8

10. Hecher K, Campbell S, Doyle P, Harrington K, Nicolaides K. Assessment of fetal compromise by Doppler ultrasound investigation of the fetal circulation: arterial, intracardiac, and venous blood flow velocity studies. Circulation 1995; **91:**129-38.

11. Forouzan I, Cohen AW & Arger P. Measurement of systolic-diastolic ratio in the umbilical artery by continuous-wave and pulsed-wave Doppler ultrasound: comparison at different sites. Obstet Gynecol 1991; **77(2):** 209–12

12. Rasanen J, Kirkinen P & Jouppila P. Right ventricular dysfunction in human fetal compromise. Am J Obstet Gynecol 1989; **161(1):** 136–40.

13. Capponi A, Rizzo G, De Angelis C, Arduini D & Romanini C. Atrial natriuretic peptide levels in fetal blood in relation to inferior vena cava velocity waveforms. Obstet Gynecol 1997; **89(2):** 242–7.

14. Gerhardt W, Katus H, Ravkilde J, Hamm C, Jorgensen PJ, Peheim E, et al. S-troponin T in suspected ischemic myocardial injury compared with mass and catalytic concentrations of S-creatine kinase isoenzyme MB. Clin Chem 1991; **37:** 1405-11.

15. Gonzalez JM, Stamilio DM, Ural S, et al. Relationship between abnormal fetal testing and adverse perinatal outcomes in intrauterine growth restriction. Am J Obstet Gynecol 2007 May, **196(5):**48-51.

16. Reed K L, Appleton C P, Anderson C F, et al. Doppler studies of vena cava flows in human fetuses. Circulation 1990;**81:**498-505.

17. Hofstaetter C, Dubiel M, Gudmundsson S. Two types of umbilical venous pulsations and outcome of high-risk pregnancy. Early Hum Dev. 2001 Mar; **61(2):** 111-7.

18. Gramellini D, Piantelli G, Verrotti C, Fieni S, Chiaie LD, Kaihura C. Doppler velocimetry and non stress test in severe fetal growth restriction Clin Exp Obstet Gynecol. 2001; **28(1):** 33-9.

19. Dubiel M, Breborowicz GH, Gudmundsson S. Evaluation of fetal circulation redistribution in pregnancies with absent or reversed diastolic flows in the umbilical artery. Early Hum Dev. 2003 Apr; **71(2):** 149-56.

20. Hofstaetter C, Gudmundsson S, Hansmann M. Venous Doppler velocimetry in the surveillance of severely compromised fetuses. Ultrasound Obstet Gynecol. 2003 Jan; **21(1):** 98-9; author reply 99.