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Umbilical artery doppler flow patterns in high-risk pregnancy and foetal outcome in Mulago hospital

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ABSTRACT

Objective: To demonstrate the flow patterns and factors associated with adverse foetal outcome in high-risk pregnancy at Mulago Hospital using Doppler ultrasound of the foetal umbilical artery. Design: Cross-sectional descriptive study. Setting: Mulago National Referral Hospital, Kampala Uganda. Study Subjects: One hundred and ninety-two patients in a 4-month period (December 2008-April 2009). Results: Maternal age was 16 to 41 years. Twenty-one foetuses had abnormal flow patterns (12 had reduced end-diastolic flow, 8 had AEDF and 1 had RF). Prematurity was associated with abnormal flow patterns. 11 out of 12 foetuses with reduced end-diastolic flow survived. Of the foetuses with AEDF, 3 survived but were admitted to the neonatal special care unit while 5 died. One foetus had RF and was a stillbirth. Eighteen foetuses were delivered after an obstetric intervention. Conclusions: 1) The prevalence of abnormal flow patterns is 10.9%. 2) Abnormal flow patterns, low biophysical profile score, premature delivery, low birth weight and low Apgar score are related to adverse foetal outcome. 3) A low biophysical profile score is related to AEDF/RF. 4) Foetuses of low parity mothers are more likely to have abnormal flow patterns. Recommendation: Umbilical artery Doppler Biophysical profile scores should be done in high-risk pregnancy.

Keywords: Doppler; Umbilical Artery

1. INTRODUCTION

High-risk pregnancy constitutes conditions that predispose to placental insufficiency. These cause foetal compromise and are detected early by combined antepartum surveillance methods saving infant lives as well as reducing foetal disabilities [1].

High-risk pregnancy is a situation in which the mother has a condition likely to cause an adverse effect on the foetus. High-risk groups include women with: a previous complicated pregnancy, insulin dependent diabetes connective tissue diseases, phenylketonuria, age over 35 years, alcohol and drug dependence, maternal infections such as rubella, cytomegalovirus and toxoplasmosis [2]. According to the Uganda Clinical Guidelines (2003), a high-risk pregnancy is one with a risk of an adverse outcome for the mother or baby [3]. The criteria for high-risk pregnancy are extremes of reproductive age (below 18 or greater than 35 years), young primigravida, high parity or short birth interval, large infants of 4 kilograms or more, prematurity, low birth weight of less than 2.5 kilograms, obstructed and difficult labours, poor obstetric history, history of reproductive tract surgery, genetic or familial diseases, medical conditions such as diabetes, cardiac or renal disease, hypertension, rhesus incompatibility, maternal disabilities, those with obstetric risks such as multiple pregnancy, malpresentations and others, antepartum haemorrhage, postpartum haemorrhage, deep vein thrombosis, intrauterine growth retardation, premature rupture of membranes, post dates and cephalopelvic disproportion [4].

Hypertension may cause abnormal flow patterns in the umbilical artery and other foetal vessels. Diabetes predisposes pregnant mothers to preeclampsia and eclamp-

sia. Abnormal flow velocities may be seen in the umbilical and uterine arteries in foetal growth retardation [5].

Doppler ultrasound besides other obstetric tests can detect impeding foetal hypoxia [5]. Reversal of flow or absent end-diastolic flow in the umbilical artery shows foetal compromise [1]. Doppler ultrasound in high-risk pregnancies improves a number of obstetric care outcomes and appears promising in helping to reduce perinatal deaths [6]. The intrapartum stillbirths are 14 times more in developing than developed countries [7].

The perinatal mortality rate in Uganda is 53 per 1000 live births, infant mortality 88 per 1000 live births and neonatal mortality is 41% of all infant deaths [8,9]. In Mulago Hospital, there are about 15 neonatal deaths per 1000 births [9] and the still birth rate is 23 per 1000 births [10]. High-risk pregnancy is associated with a high rate of obstetric intervention in a bid to save the mother's and/or baby's life.

Doppler ultrasound is available in Mulago Hospital, therefore, it can be done in high-risk pregnancies to detect foetal compromise and intervention, if necessarily instituted to save infant lives. This study was aimed to demonstrate the Doppler foetal umbilical artery flow patterns and their relationship with the foetal outcome at Mulago Hospital.

2. MATERIALS AND METHODS

The study was carried out in Mulago National Referral Hospital.

Informed consent was obtained from all the study participants. The sample size was calculated using Kish and Leslie's formula [42] for cross-sectional studies and it came to 202 participants. 192 (94%) patients were, however, recruited due to limited resources.

2.1. Inclusion Criteria

All high-risk pregnancy mothers of 28 weeks gestational age and above who attended antenatal clinic or were admitted in the obstetric wards from December 2008 to April 2009.

2.2. Exclusion

Multiple pregnancy mothers and those in labour.

Real time ultrasound with a curvilinear 3.5 MHz probe and Doppler was used. The umbilical arteries were identified by colour-flow mapping and one artery sampled at random. With the Doppler power settings set as low as possible, using a minimal wall filter, the Doppler measurements were done away from the cord insertion of the umbilical artery where the audible signal was highest (*i.e.* where flow was maximum) [43,44]. The Doppler recordings were made with the angle of insonation between the Doppler beam and direction of flow less than 30 degrees [45]. The mothers were told to hold their breaths when recording the Doppler spectra [1]. The resistance indices were calculated using the formula: systolic-diastolic flow/systolic flow. The biophysical profile was done for each pregnancy.

3. RESULTS

One hundred and ninety-two patients were recruited. Their age range was 16 to 41 years of age. Thirty-four percent of the patients were in the 21 - 25 year age range. The mean age of the patients was 23, the median age was 28.5 and the mode was 23 years.

One hundred and seventy-four (90%) of the mothers had hypertension in pregnancy, 14 (7%) had IUGR without hypertension while 8 had IUGR with hypertension and 4 (2%) had Diabetes Mellitus.

All the mothers were residing in the central region around the city of Kampala.

3.1. Prevalence of Abnormal Umbilical Artery Doppler Flow Patterns

The prevalence of abnormal flow patterns in Mulago Hospital according to this study was 10.95% and these included: reduced end-diastolic flow (6.25%), AEDF (4.2%) and RF (0.5%).

All the foetuses with AEDF/RF were delivered prematurely, 8 by obstetric intervention *i.e.* 4 by caesarian section and 4 after induction of labour. This is statistically significant. P = 0.0004 OR 17.54 (1.98 - 155.4).

The majority of foetuses with AEDF and RF had low birth weights (less than 2.5 kg); 5 of them weighed less than 1.5 kg. Most were admitted to the neonatal special care unit. This was a high rate of still/births among foetuses with AEDF/RF. P =< 0.0001 OR 38.7 (6.61 - 226).

Of the twelve foetuses with reduced end diastolic flow, 8 (66.7%) were born prematurely but the most survived. Nine of them (75%) had a good Biophysical profile score and 8 (66.7%) had an Apgar score of 8 - 10.

Ten of the foetuses (83%) were delivered by obstetric intervention, 6 by caesarian section and 4 by induction of labour. The birth weights of the foetuses were $\leq$2.5 kg for 7 of the foetuses and of these 2 were below 1.5 kg.

The foetuses with AEDF/RF were more at risk of having an adverse outcome than the ones with normal flow patterns. There were only 9 foetuses (5%) with adverse outcomes among those with normal flow patterns.

Five of the 9 foetuses with AEDF/RF had a low biophysical profile score.

Nine of the 12 foetuses with reduced end-diastolic flow (75%) had a good biophysical profile score of 8 to 10.

A sub-analysis of the resistance indices of 150 patients

was done. The resistance indices ranged from 0.21 to 0.88. Thirty-two of the 34 (94%) foetuses with high umbilical artery resistance indices were of hypertensive mothers.

Foetuses delivered at 28 - 36 weeks were 3 times more likely than those delivered at 37 - 42 weeks to have had a high umbilical artery resistance index. OR 3.17 (CI 1.40 - 7.17) P = 0.00. This is statistically significant. A big proportion of the foetuses with high umbilical artery resistance indices (88%) had an obstetric intervention and of these 18 (53%) were delivered by caesarian section.

High resistance indices were not associated with poor foetal outcome.

High umbilical artery resistance indices were not associated with a low biophysical profile score (8 - 10).

4. DISCUSSION

A cross-sectional descriptive study on the umbilical artery Doppler flow patterns in high-risk pregnancy and foetal outcome in Mulago Hospital which is in the city of Kampala, Uganda was done.

Most of the study patients were in the age range of 21 - 25 years. This is because it is when most women have their children in Uganda. It is just after the age of consent (18 years). Many women leave school early so they tend to start having children at an early age.

Eighty-four percent of the mothers were multiparous. Pregnancy-induced hypertension, which most of the mothers had has been reported to be common among nulliparous women by some studies [45,46]. It is also reported that PIH occurs in multiparous women because of increased incidence of chronic hypertension with increasing maternal age [4]. The fertility rate in Uganda is one of the highest in the world (6.5 in 2007) [47] and there is no government limit on how many children a couple can have. The infant mortality rate is high and most mothers want many children because of the belief that if some children die, they can retain some. Since Mulago Hospital is a national referral hospital, many multiparous mothers also come because they are referred from the peripheral units.

The prevalence of abnormal flow patterns in Mulago Hospital according to this study was 10.95% with reduced end-diastolic flow (**Figure 1**) being 6.25%, AEDF (**Figure 2**) 4.2% and RF (**Figure 3**) 0.5%. This is almost the same as reported in literature *i.e.* is 5% - 8% for AEDF and 0.5% for RF [1] although it was a little bit lower. This could be that some of the mothers whose foetuses had abnormal flow patterns were missed since some of them deliver from home or the smaller health units with no Doppler ultrasound machines. A total of 21 foetuses had abnormal flow patterns (12 with reduced end-diastolic f1ow, 1 with RF and 8 with AEDF). These were seen among foetuses with IUGR and those whose

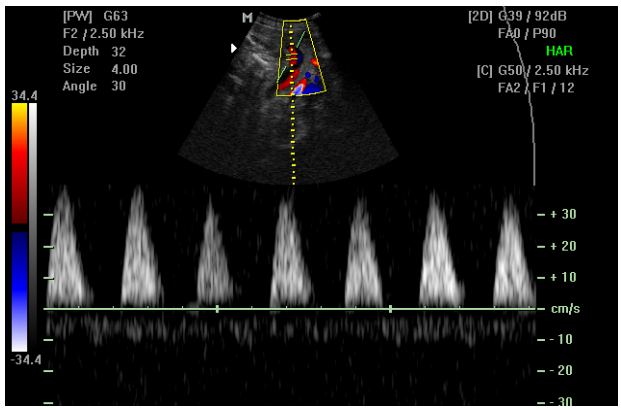

Figure 1. An example of reduced end-diastolic flow in Mulago Hospital.

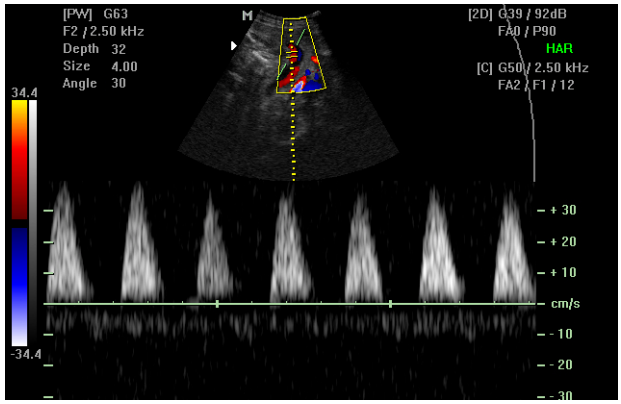

Figure 2. AEDF in the foetal umbilical artery. The mother was 26 years old and had pregnancy-induced hypertension. The foetus was delivered prematurely by Caesarian section, admitted to neonatal special care unit and died within 24 hours of delivery. It was less than 2.5 kg. A similar flow pattern was seen in 7 other foetuses, 4 of whom died (2 in utero and 2 after delivery) and 3 survived.

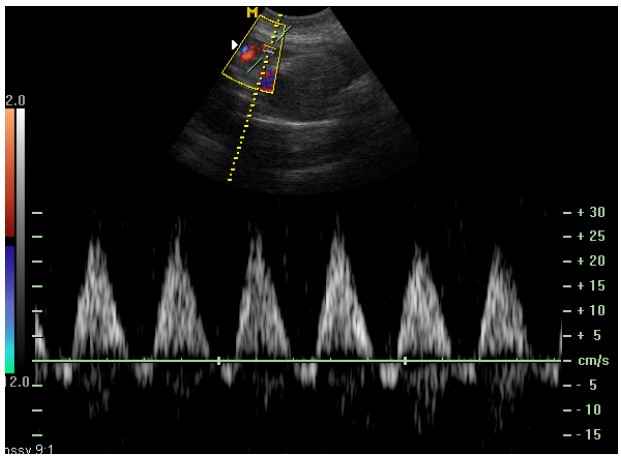

Figure 3. RF at umbilical artery Doppler. The mother was 18 years old and had pregnancy-induced hypertension. The foetus was born prematurely at 30 weeks and was a stillbirth after induction of labour. The foetal weight at delivery was less than 1.5 kg.

mothers were hypertensive. This is in agreement with studies which have shown that pregnancy induced hypertension; along with intrauterine foetal growth restriction (IUGR) have a significantly high association with reversal of flow (RF) or absent end-diastolic flow (AEDF) in the foetal umbilical artery [1,23,24,25].

None of the diabetic patients had foetuses with abnormal flow patterns. This is because they were very few (only 4) those who could have had abnormal flow patterns were not recruited.

AEDF/RF was associated with stillbirths or foetal death within 24 hours of delivery. P =< 0.0001 OR 38.7 (6.61 - 226). This is reflected in **Table 1**. Only one of the 12 foetuses with reduced end-diastolic flow died within 24 hours of delivery. Diabetes mellitus, hypertension and IUGR are all associated with placental insufficiency which causes increased impedance of blood flow. This in turn leads to AEDF or even RF and thus increases mortality [32,33].

Four of the foetuses with AEDF survived but after being admitted to the special care unit (**Table 1**). The reason why some of them survived and others died cannot be explained by this study.

Premature delivery was common among foetuses with abnormal flow patterns (**Table 1**). AEDF/RF was also associated with low birth weight according to **Table 1**. Hypertension and Diabetes in pregnancy are associated with placental insufficiency which can lead to intrauterine foetal growth restriction. This explains the majority of foetuses being of a low birth weight [1]. Literature also shows that abnormal flow patterns are associated with premature deliveries because of early obstetric intervention (Caesarian section and induction of labour) [22].

The majority of foetuses with abnormal flow patterns were born after an obstetric intervention (caesarian section or induction of labour) as seen in **Table 1**.

Induction of labour is also one of the obstetric interventions used in Mulago Hospital and elsewhere besides Caesarian section [48,49]. Most of the mothers who were recruited had an intervention and the commonest intervention was Caesarian section (52.60%). The main rea-

Table 1. AEDF/RF and foetal outcomes.

Variable	Total	AEDF/RF (%)	OR (CI)	P Value
Weight at delivery (kg)				
≥2.5	131	0 (0)		
<2.5	59	9 (15.3)		
Apgar score				
0 - 2	12	4 (33.3)		
5 - 7	27	4 (14.81)	0.35 (0.66 - 1.83)	0.192
8 - 10	153	1 (0.65)	0.01 (0.001 - 0.19)	0.000
Primary Outcomes				
Term	126	1 (0.79)		
Premature	65	8 (12.39)	17.54 (1.98 - 155.4)	0.0004
Secondary outcomes				
Good	177	3 (1.69)		
Stillbirth/ Death within 24 hours	15	6 (40)	38.7 (6.61 - 226)	<0.0001
Gestational age at delivery (weeks)				
37 - 42	122	0 (0)		
28 - 36	70	9 (12.86)		
Obstetric Intervention				
Yes	154	8 (5.19)		
No	36	1 (2.78)	0.52 (0.06 - 4.34)	0.54
Type of Intervention				
Caesarian section	81	4 (4.94)		
Induction	73	4 (5.48)	1.12 (0.27 - 4.65)	0.88
Admission to Neonatal special care unit				
No	177	4 (2.3)		
Yes	15	5 (50)	21.6 (5.2 - 42.1)	0.00

son for the caesarian section was to save the mother and baby's lives in high-risk pregnancy whether the umbilical artery Doppler flow pattern is normal or abnormal. The other intervention was induction of labour. Caesarian section is done for those mothers whose foetuses are in a poor condition because it is the quickest method of delivery. The Caesarian section rate in Mulago Hospital is 27% [9] compared to 15% recommended by WHO [50]. The reason for this is because Mulago is the national referral hospital where most of the peripheral units refer complicated cases many of which need to be managed by Caesarian section. Induction of labour is done for those mothers in a better condition and whose foetuses are not in distress. Of the foetuses with abnormal flow patterns, 88.9% had an obstetric intervention and half of these were Caesarian sections (**Table 1**). This study is in agreement with other studies which have shown that there is an increased Caesarian section rate in abnormal umbilical artery Doppler findings [25,51].

Several studies have also shown that abnormal umbilical artery Doppler flow patterns are associated with increased admission to the neonatal intensive care unit, perinatal morbidity and mortality [25,48,51,52]. This is similar to what was found out in this study: There was a better outcome among foetuses with reduced end-diastolic flow although many were born by Caesarian section. This is because when there is reduced end-diastolic flow, the foetus is not yet severely compromised and can be saved by obstetric intervention.

The good outcome realized with the foetuses with high resistance indices (**Table 2**) shows that in spite of this finding, the foetus can survive if delivered early. It is reported that if the resistance index is high and there is diastolic flow, it may not be significant [17] so probably some of the foetuses were not compromised.

According to the multivariate logistics model (**Table 3**), the foetuses with AEDF or RF were more at risk of having an adverse outcome than the ones without. Those born prematurely (28 - 36 weeks of gestation) were also more likely to have an adverse foetal outcome than those born at term. This is because of the increased mortality that has been reported in premature babies [4]. Most of the foetuses with adverse outcomes (14 out of 15) had a birth weight of less than 2.5 kg (**Table 2**). It is well known that a low birth weight is associated with a poor foetal outcome [4,54]. Only one of those with an adverse outcome had a weight of more than 2.5 kg. Fourteen of the 15 foetuses with an adverse outcome had an Apgar score of 0 to 7 while only one had an Apgar score of 8 to 10 (**Table 3**). Low 5 minute Apgar scores are predictive of neonatal death in preterm infants [4].

Therefore apart from abnormal flow patterns, premature delivery, low birth weight and low Apgar score are associated with adverse foetal outcome.

In this study, AEDF and RF were associated with a low Biophysical profile score (**Table 4**).

Table 2. High resistance indices and foetal outcome.

Gestational age at delivery	Total	High RI	OR (CI)	P-value
37 - 42	94	14 (14.89)		
28 - 36	56	20 (35.71)	3.17 (1.40 - 7.17)	0.00
Obstetric Intervention				
Yes	123	30 (24.39)		
No	26	4 (15.38)	0.56 (0.18 - 1.78)	0.32
Type of intervention				
C/S	65	18 (27.69)		
Induction	58	12 (20.69)	0.68 (0.29 - 1.58)	0.37
Primary Outcome				
Term	96	16 (16.67)		
Premature	53	18 (33.96)	2.57 (1.5 - 5.7)	0.02
Secondary Outcome				
Good	141	32 (22.70)		
Stillbirth	3	1 (33.33)	1.70 (0.15 - 19.59	0.85
Death within 24 hours	6	1 (16.67)	0.68 (0.76 - 6.09)	0.85
Apgar Score				
0 - 2	7	1 (14.29)		
5 - 7	21	4 (19.05)	1.41 (0.12 - 16)	0.77
8 - 10	122	29 (23.77)	1.87 (0.21 - 16.36)	0.48

Table 3. Multivariate logistic model results.

Variable	Total	Adverse outcome (%)	AOR (95%CI)	P value
AEDF/RF				
No	183	9 (4.9)		
Yes	9	6 (66.7)	9.3 (2.2 - 92..47)	0.005
Gestational age at delivery (weeks)				
28 - 36	70	11 (15.7)		
37 - 42	122	4 (3.3)	0.014 (0.001 - 0.02)	<0.001
Birth weight*				
<2.5 kg	59	10 (17.0)		
≥2.5 kg	131	4 (3.1)	9.58e−08	
Apgar score*				
8 - 10	153	1 (0.7)		
0 - 7	39	14 (35.9)	4.06e+15	

Table 4. AEDF/RF and the biophysical profile score.

Variable	Total	AEDF/RF (%)	COR (95% CI)	P Value
Biophysical profile score				
8 - 10	146	4 (2.74)		
0 - 6	46	5 (10.87)	4.32 (1.1 - 17.2)	0.023

Table 5. High resistance indices and the biophysical profile score.

Biophysical profile	Total	High RI (%)	OR (CI)	P Value
0 - 6	38	9 (23.7)		
8 - 10	112	25 (22.32)	1.4 (0.44 - 4.61)	0.39

Foetuses with abnormal flow patterns usually have a poor outcome (**Table 3**). A low biophysical profile score is also associated with a poor foetal outcome because there is a high probability of foetal asphyxia with a score of 4 - 6, and it is almost certain with a score of 0 or 2 [1].

Most of the foetuses with reduced end-diastolic flow and those with high resistance indices had a Biophysical profile score of 8 - 10 because they were not yet severely compromised (**Table 5**). This is in agreement with a study in Kenya which showed that Doppler ultrasound is more sensitive than the biophysical profile score in detecting foetal compromise [12] since the Doppler findings were abnormal before the Biophysical profile.

According to the American College of Obstetricians and Gynecologists (1999) there is no 'best test' to evaluate foetal well-being. Therefore the Biophysical profile should be used together with umbilical artery Doppler Ultrasound to assess foetal well-being [55].

In conclusion, Doppler ultrasound of the foetal umbilical artery is important in predicting foetal outcome and reducing on perinatal mortality. Therefore there is need to avail ultrasound machines with Doppler application to hospitals with maternity units and to train more health personnel in using them.

5. CONCLUSIONS

- The prevalence of abnormal umbilical artery flow patterns in high-risk pregnancy at Mulago Hospital is 10.95% (Reduced end-diastolic flow = 6.25%, AEDF = 4.2% and RF = 0.5%) from this study.
- AEDF and RF are related to poor foetal outcome.
- Foetuses delivered before reduced end-diastolic flow converting to AEDF or RF have better outcomes.
- High resistance indices may not predict a poor foetal outcome.
- There is a relationship between a low biophysical profile score and AEDF/RF.

Recommendations

- Umbilical artery Doppler ultrasound and Biophysical profile should be done routinely for all high-risk pregnancies above 28 weeks.
- Radiologists and Obstetricians should be trained in the use of Umbilical artery Doppler ultrasound because it aids in reducing perinatal mortality and predicting foetal outcome.
- Ultrasound machines with Doppler application should be available in all hospitals where high-risk pregnancies are managed.
- Studies including malaria and multiple pregnancies, with longer follow-up periods should be done to find out the trend in these conditions and any other long term complications in foetuses with abnormal flow patterns.

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