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COMPARISON OR DOPPLER STUDIES IN OBSTERICS WITH FOETAL OUTCOME
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COMPARISON OF DOPPLER STUDIES IN OBSTETRICS WITH FOETAL OUTCOME

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ABSTRACT

***Objective*: To compare umbilical and middle cerebral artery doppler ultrarasound values in high and low risk pregnancies with fetal outcome.**
***Design*: Descriptive prospective study.**
***Setting*: Aga Khan University Hospital, Nairobi between the months of February and November 2007.**
***Subjects*: One hundread and twenty one consecutive female subjects, between 24 and 443 years of age, at or over 28 weeks gestation, referred to the Radiology Department of Aga Khan University Hospital for obstetric doppler ultrasonography.**
***Main outcome measures*: Foetal outcome was defined as poor by using either APCAR score (below eight out of ten at five minutes), weight, head circumference and length below tenth percentile for gestation at delivery or by mortality.**
***Results*: Outcome was available for 100 of the 121 patients. twenty six percent of pregnancies had poor outcome. Of these 73% (19) and 27% (7) were classified as high risk and low risk respectively. Accuracy for umbilical artery doppler in predicting foetal outcome was 80.8 and 82.9% for high and low risk pregnancies respectively. Accuracy for middle cerebral artery doppler was 71.2% and 97.6% for high and low risk pregnancies respectively. Overall, accuracy for umbilical artery and middle cerebral artery doppler in predicting foetal outcome was 76 and 82% respectively. Umbilical artery alone or in combination with middle cerebral artery doppler was shown to have 100% specificity for predicting foetal outcome. However, sensitivities and negative predictive values were poor, ranging from 8-21 % and 17-35% respectively. Middle cerebral artery specificities were lower at 80 and 85% for high and low risk pregnancies respectively.**
***Conclusion*: Umbilical and middle cerebral artery doppler values in pregnancy are fair predictors of foetal outcome. However, these doppler indices are useful in pregnancy to exclude foetal compromise.**

INTRODUCTION

Doppler studies of the umbilical arteries have been the first step in learning more about the true nature of foetal smallness, with an abnormal umbilical artery (UA) index helping to isolate the small sick foetus from the small healthy fetus. In high-risk pregnancies complicated by maternal hypertension, intrauterine growth restriction or multiple gestations, evidence supports the use of UA doppler studies as part of antenatal assessment (1,2).

Soregarol *et al* confirmed the existence of a strict correlation between umbilical doppler velocimetry and an increased incidence of perinatal complications in intra-uterine growth restricted (lUGR) foetuses. This was in a retrospective analysis of 578 singleton pregnancies with a diagnosis of lUGR (3).

In Kenya, a study by Nguku, *et al*, showed that UA doppler is more sensitive than biophysical prol1le in the evaluation of patients with pregnancy induced hypertension (2). UA indices are especially predictive of placental abnormalities, especially lesions of maternal underperfusion and foetal vascular obstruction (2,4).

U A doppler ultrasound has ell so been utilised in normal pregnancy. Five trials involving 14,338 women were done to assess the usefulness of UA doppler ultrasound as a screening test in low risk pregnancies. These concluded that routine doppler ultrasound in pregnancy did not confer clinical benefit except for placental calcification grading (4)

The UA doppler measurements do not provide Information on how the foetus is coping with a compromised supply and therefore will not identify all the compromised foetuses in a population. For this reason, study of systemic vessels such as the middle cerebral artery (MCA) is also carried out.

An association between abnormal doppler indices of the MCA and intrauterine growth restriction, pre-eclampsia and foetal hypoxia has detmonstrated. When the foetus is hypoxic, the cerebral arteries tend to become dilated in order to preserve the blood flow to the brain. In the MCA, the systolic to diastolic ratio will decrease due to this increase in diastolic flow in the presence of chronic hypoxic insult to the foetus. The increase can be evidenced by doppler ultrasound of the MCA and has been referred to as the 'brain sparing effect'. It manifests as an increase as in foetal cerebral arterial doppler end-diastolic velocity resulting in a decreased resistance index (5-7).

Many indices have been devised but three are in regular clinical use. These are the resistance index (RI), the pulsatility index (PI) and the systolic- diastolic (S/D) ratio. Resistance index was used in this study. It is calculated using the following formula:

Resistance index (RI) =(Peak systolic velocity -End diastolic velocity peak)÷systolilic velocity.

As shown above, the use of foetal doppler studies has largely been limited to the study of high risk pregnancies. Also commonly used in practice is comparison of indices with gestation specific reference ranges.

In the Radiology Department of Aga Khan University Hospital, Nairobi (AKUHN), both high and low risk pregnancies are studied using RI of 0.71 as the cutoff point for both umbilical and middle cerebral arteries, at or above 28 weeks gestation. The cutoff of 0.71 for doppler resistance indices has been used in AKUHN radiology department for many years and is derived from the reference values published by Kurmanavicius *et al* (23). In this paper, the 50th percentile umbilical artery resistance index at 25 weeks gestation is 0.717 and this falls with advancing gestation. Resistance indices above this level is what, in our practice, would warrant closer monitoring of the pregnancy.

In the case of middle cerebral artery, resistance indices also decrease with advancing pregnancy. Zero point seven one is the middle cerebral 50^{th} percentile at 42 weeks of gestation and was chosen to err on the safe side. However, in the MCA, values less than 0.71 would warrant closer monitoring of the pregnancy.

The rationale for this study was to assess the effectiveness of the doppler ultrasound protocol utilised in this institution (as described in the methodology section) in predicting foetal outcome in high and low risk pregnancies.

MATERIALS AND METHODS

This study was carried out from February 2007 to November 2007, a period of ten months, at the Aga Khan University Hospital, Nairobi.

Using Stata version 9 (StataCorp, College Station, Texas, USA) α of 0.05 and power of 90%, the sample size was determined to be ninety seven.

Consecutive patients, aged between 24 and 43 years, at or over 28 weeks gestation, during this period, referred to the Radiology Department, Aga Khan University Hospital, Nairobi for Doppler ultrasonography were recruited into the study.

Excluded from the analysis were those for whom follow-up, in terms of foetal outcome, was not available. This was due to various reasons such as incomplete information in patient records or lack of access to information due to delivery at another institution. Scanning was carried out at Aga Khan University Hospital, Nairobi's Radiology Department by a radiologist, radiology resident or qualified ultrasonographer.

Scanning was carried out on HDI 5000 Philips or Logiq 9 GE ultrasound machines, using a 3-5 MHz curvilinear probe. The Ultrasonologist Ultrasonographer was required to follow a strict departmental protocol, detailed later in this paper, when scanning patients. Following the scan, the person who carried out the scan filled in a questionnaire which included the gestational age, UA and MCA resistance indices.

Patients were classified as high risk or low risk depending on the clinical information provided on the requisition card. High risk conditions included intrauterine growth retardation, maternal hypertension and decreased foetal movements. Low risk pregnancies were those which had no known risk factors or complications at the time of scanning.

Poor outcome was defined by foetal mortality or appearance, pulse rate, grimace, activity, respiration (APGAR) score less than eight at five minutes or weight less than 10^{th} percentile for gestation 20 or head circumference and length below 10^{th} percentile for gestation (21).

This information was acquired from patient records. Machine derived resistance indices of umbilical and middle cerebral arteries measured on pulsed doppler were recorded.

The umbilical cord was traced to determine whether it was around the foetal neck and doppler flows measured in a free floating loop in amniotic fluid. The middle cerebral artery closer to the maternal anterior abdominal wall was used to take the doppler readings. Measurements of the middle cerebral artery were taken from its middle section while maintaining the angle of insonation as close to zero degrees as possible. In the event of an abnormal value being obtained, at least two more values were taken for confirmation using the same technique, the most abnormal being used in analysis.

Normal values were taken as over 0.71(RI) for middle cerebral artery; less than 0.7 1 (RI) for umbilical artery. Sensitivity, specificity, positive and negative predictive values as well as accuracy of UA and MCA resistance indices of high and low risk pregnancies in predicting foetal outcome were calculated.

Analysis was carried out using Stata Version 9 (Stata Corp, College Station, Texas, USA). Due to the fact that doppler measurements were a routine, non-invasive and safe part of the antenatal sonographic assessment and management of the patients, no specific consent was sought. In the final data analysis, the identity of patient was concaeled

RESULTS

One hundred and twenty one patients were recruited of which outcome was not available for 21 patients. This included a foetus that was delivered at 30 weeks due to severe pre- eclampsia and IUGR, for whom head circumference and length was not measured at birth and was therefore excluded from analysis. However, weight below 3rd percentile and APGAR score of six at five minutes as well as eventual mortality after 42 days could be taken JS an adverse outcome. In this particular case, UA resistance index was increased (0.77) in an examination carried out two days prior to delivery.

In subjects who had multiple examinations, the last was taken far analysis. Accuracy for UA doppler in predicting foetal outcome was 80.0 and 82.9% for high and low risk pregnancies respectively. Accuracy for MCA doppler was 71.2 and 97.6% for high and low risk pregnancies, respectively. Overall accuracy for UA and MCA doppler in predicting foetal outcome was 76 and 82% respectively.

MCA specificities were 80 and 85% for high and low risk pregnancies respectively. MCA positive predictive values were 44% in high risk category and 83% in low risk category. There was no significant difference between specificities in the high and low risk categories for each of the parameters.

Initial classification into high risk and low risk pregnancy had been determined by the clinical information given on the requisition form. Using this method, there were 59 patients with high risk pregnancies and 41 with low risk pregnancies, giving a total of 100 patients.

Evaluation after the indications for doppler examinations showed that pregnancies referred with a diagnosis of intrauterine growth restriction had the highest percentage of abnormal outcomes (Table 6).

Table 1

Dopler values against foetal outcome in high risk Pregnancies

		Foetal outcome Cross tabulation		
		Abnormal	Normal	Total
UA doppler	Abnormal	2	0	2
	Normal	17	40	57
	Total	19	40	59
MCA doppler	abnormal	10	8	18
	Normal	9	32	41
	Total	19	40	59

Table 2

Doppler values against foetal outcome in low risk pregnancies

		Fetal outcome	Cross tabulation	
		Abnormal	Normal	Total
UA doppler	abnormal	0	0	0
	Normal	7	34	41
	Total	7	34	41
MCAdoppler	Abnormal	1	5	6
	Normal	6	29	35
	Total	7	34	41

Table 3
Sub-analysis of high and low risk groups

	Sensitivity (%)	Specificity (%)	Positive Predictive Value(%)	Negative Predictive Value(%)	Accuracy (%)
MCA High risk	53	80	44	22	71.2
MCA Low risk	14	85	83	17	97.6
UA High risk	11	100	0	30	80.8
UA Low	0	100	0	17	82.9

Table 4
Analysis of combination of UA and MCA

	Sensitivity (%)	Specificity (%)	Positive Predictive Value %	Negative Predictive Value %
Both UA and MCA-high Risk	21	83	60	35
Both UA and MCA-low risk	18	86	71	22

Table 5
Overall analysis (without stratification into high and low risk groups)

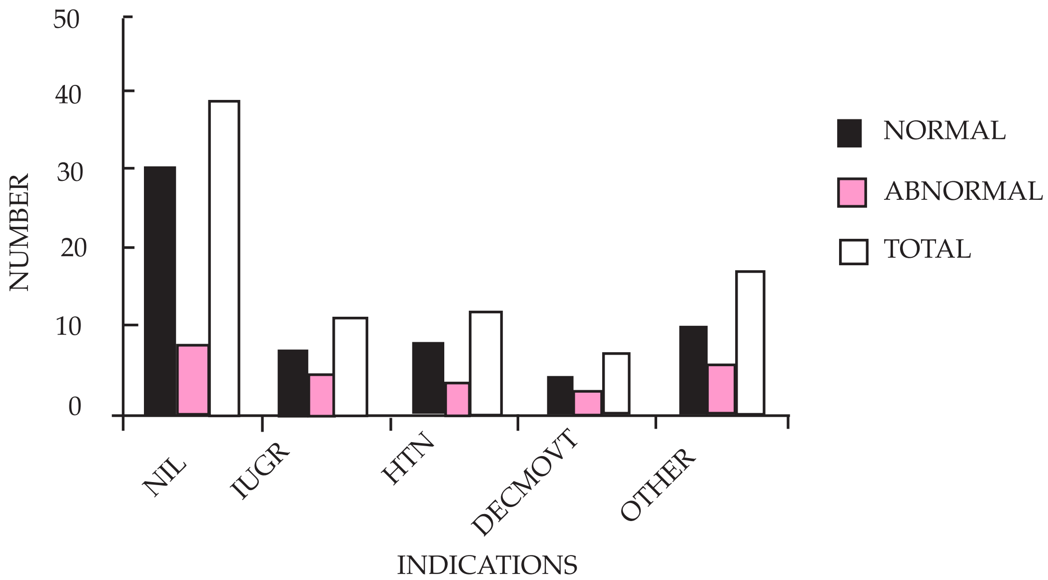
	Sensitivity (%)	Specificity (%)	Positive Predictive Value(%)	Negative Predictive Value(%)
UA	8	100	0	26
MCA	23	68	76	33
UA &MCA	9	100	45	26
UA or MCA	20	84	64	30

Table 6
Frequency of specific outcome measures

Adverse outcome	Number
Birth weight below 10th percentile for Gestation	21
Head circumfrenceat birth below 10th Percentile for gestation	2
Length at birth below 10th percentile for Gestation	6
Apgar score at or less than seven at five minutes	10

Frequency of specific outcomes showing 'low birth weight' being the most common (21) and 'small head circumference' as the least common (2).

Figure 1
Indications for doppler ultrasonography



DISCUSSION

The primary aim of foetal surveillance is timely recognition of foetal compromise to enable appropriate intervention and prevent further serious complications (8). Because of the low sensitivities registered in the results of this study; single abnormal doppler results are probably not useful for liming delivery. However, they are helpful in distinguishing between the foetuses that require closer surveillance from those that are uncompromised. Vergani, *et al* have argued that growth restricted foetuses approaching term (>32 weeks) are at very low risk for perinatal mortality or for life threatening morbidities and therefore the goal of optimal obstetric management at this gestation is aimed at minimising the occurrence of morbidity. Because of this, a higher false positive rate may be allowed. It should be noted that high false positive rates are reported for tests used commonly in monitoring growth restriction such as non stress test and amniotic fluid index.

However, in this study, despite good specificities, poor negative predictive values were calculated from the UA doppler values, (0%) in both high risk and low risk pregnancies.

In a prospective longitudinal study of 130 singleton pregnancies (total of 513 observations) to determine reference ranges of UA doppler indices, resistance indices were estimated to decrease by 0.005 per week although this was to some extent modified by placental weight (10).

Therefore, it is possible that the predictive value of this test was weakened by using a single cut off figure (0.71) as opposed to comparison against gestation specific values. However it should be noted that a decrease of 0.005 per week in UA resistance index in absolute terms gives a maximum difference of 0.07 between 28 and 42 weeks.

It should be mentioned that there was a weakness in the initial stratification of pregnancies into high and low risk categories. In this study, stratification was based on clinician information on the requisition card which could not be substantiated. A more accurate and robust way of recruiting high risk pregnancies due to growth restriction would have been based on an ultrasound exam before or at 20 weeks gestation showing ultrasound estimated abdominal circumference below 10^{th} percentile for gestational age (2, 11). It would also be important during this initial examination to exclude foetal anomalies which would interfere with the foetal outcome (12).

Other factors that were considered in classifying pregnancy as high risk in this study such as maternal hypertension, pre-eclampsia or eclampsia or reduced foetal movement would have been more objectively assessed at recruitment utilising parameters such as blood pressure, biochemical measurements and foetal kick chart recordings.

To our knowledge, these factors have not been considered in previous studies when recruiting patients for foetal doppler assessment. However they are considered important indications by obstetricians.

Another issue to be considered was the mode of determining outcome end points. For this study, these were foetal mortality, APGAR score (score of 8/10 at five minutes being taken as the cut off), head circumference, weight and length below 10th percentile for gestation at delivery.

The American College of Obstetricians and Gynecologists has chosen to define intrauterine growth restriction as a foetus with an estimated weight below the 10th percentile for gestational age because perinatal mortality and morbidity increase when the birth weight is below that percentile (9, 13, 14). Two previous studies have used Apgar score of seven at five minutes as opposed to eight which was used in this study. However, no rationale was given for the choice of this cut off.

A better parameter for determining outcome would have been foetal cord pH (8,9). Umbilical cord blood acid-base analysis provides a more objective method of evaluating newborn's conditions especially in relation to hypoxia and acidemia (15). A mathematical model prepared by Chauhan *et a1* that allows for the calculation of the umbilical artery pH up to 60 hours after delivery permits the estimation of foetal pH at birth (16). Umbilical artery pH of less than 7.0 would be considered a poor outcome (17). This would be an appropriate cut off as according to a study that included data from more than 19,000 deliveries, the lower limits of normal pH in neonatal umbilical arteries were found to range from 7.04 to 7.10 (18). However, during the period of our study, foetal cord pH was not routinely measured in institution.

An obvious problem with the APGAR scoring system is that several of the components are subjective. Moreover, factors such as maternal anaesthesia and medications, congenital malformations and infections affect the score. A factor to considered justifying the use of multiple outcomes is that relatively small numbers of adverse perinatal outcomes were encountered. This was also the case in the study by Odibo *et al* which also prompted the use of composite of adverse perinatal outcomes in analysis (19).

In this study, inter-observer variability was not measured. It was hoped that the competence of ultrasonographer / ultrasonologist performing the exam and adherence to the strictly set protocol in carrying out Doppler exams would help minimise this variability.

It was interesting to observe that in this study, the middle cerebral artery doppler was abnormal in 17 cases whereas the umbilical artery doppler was normal. However, it has been reported in the literature that vascular redistribution (which can be detected by middle cerebral, renal, adrenal doppler) can occur in the presence of a normal umbilical doppler. In fact it has been asserted that in the case of a small foetus in late gestation, MCA doppler is superior to UA doppler in detecting foetal compromise (22).

The cross sectional design of this study meant that progression of doppler ultrasound values during pregnancy could not be assessed. A further study to assess the predictive value of gestation specific doppler of UA and MCA in foetal outcome including umbilical cord pH as a parameter and longitudinal evaluation of the doppler value changes in high risk pregnancy and how it influences intervention would be worthwhile.

In conclusion, this study has shown that umbilical and middle cerebral artery doppler values in pregnancy are fair predictors of foetal outcome. Although UA and MCA doppler specificities are useful in excluding foetal compromise, sensitivities and negative predictive values are poor. The main implication from these findings is that doppler values as per current protocol should not be used in isolation to guide management of the compromised foetus

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