Original Research Paper

Neonatology

PREDICTION OF FETAL ACIDOSIS BY DOPPLER SONOGRAPHIC EXAMINATION OF UMBILICAL AND MIDDLE CEREBRAL ARTERIAL BLOOD FLOW AT 36 WEEKS OF GESTATION

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ABSTRACT   **Objective:** To predict fetal acidosis in high risk pregnancies who show abnormal blood flow in umbilical artery and middle cerebral artery by Doppler indices Method: After a brief history Doppler ultrasound was carried out at 36 weeks of gestation to assess the Doppler parameters of PI, SD ratio and CPR of umbilical and middle cerebral artery. Perinatal outcome was studied in terms of APGAR score, cord blood PH, and NICU admission. Results: Umbilical Artery SD ratio revealed sensitivity, specificity, PPV and NPV of 93.33%, 83.33%, 90.32% and 88.23% respectively in predicting the adverse perinatal outcome, while MCA SD ratio revealed sensitivity, specificity, PPV and NPV of 90%, 83.33%, 90% and 83.33% respectively in predicting the adverse perinatal outcome. Conclusion: Doppler indices like PI, SD ratio, and CPR of Umbilical and middle cerebral artery as depicted in our study, could serve as reliable diagnostic methods of detecting compromised fetuses.

INTRODUCTION

Hypertension peculiar to pregnancy (Pre eclampsia and gestational hypertension) is a pregnancy specific syndrome characterized by reduced organ perfusion secondary to vasospasm and endothelial pathology.[1] Pre-eclampsia is a disorder in pregnancy characterized by the onset of hypertension and proteinuria after 20 weeks of gestation. It affects 2-8% of all pregnancies [2]. Intrauterine growth retardation (IUGR)/fetal growth restriction is defined as a birth weight below the 10th percentile for a given gestational age[3]. Some people do not use size criteria alone and incorporate abnormal umbilical artery doppler waveform in the diagnosis of IUGR.[4,5]. Up to 3-5% of pregnancies result in a neonate that is SGA.[6] Intra uterine growth retardation is associated with an increased risk of perinatal mortality, morbidity and impaired neurodevelopment. The correct detection of the compromised IUGR fetus to allow for timely intervention is one of the main objective of antenatal care[7]. The most common methods for evaluating health in fetuses identified as SGA are the Biophysical profile (BPP) and the non-stress test (NST) [10]. Unfortunately, neither of these tests is particularly sensitive for predicting poor outcome in IUGR pregnancies. The fetoplacental perfusion can be studied non-invasively by means of Doppler Ultrasound [10]. Doppler ultrasound velocimetry provides a non-invasive method of measuring changes in blood flow in the uteroplacental circulation and fetoplacental circulation, thus assessing fetal wellbeing.[11]. Nowadays, Doppler ultrasound velocitometry of utero-placental, umbilical and fetal vessels have become established method of antenatal monitoring. Fetal umbilical artery is the mainstay of risk assessment in small fetuses and those who are at risk of compromise.[12] The vascular changes in PIH can be reflected in Doppler studies well in advance compared to conventional antenatal tests of fetal well being. The brain sparing effect is maximum 2-3weeks before the occurance of late decelerations on cardiotocogram, suggesting that patient with high risk for unfavourable pregnancy outcome may have alteration in blood flow in MCA, 2-3 weeks prior to delivery.[13,14].

Perinatal Doppler velocimetery can identify those IUGR fetuses before with worst perinatal outcome, But a meta analysis of nine randomized trial showed that length of stay & perinatal mortality were significantly reduced when UA Doppler velocimetery was used as an adjuvant to FHR monitoring , as by the time FHR tracing become abnormal , up to 77% of fetuses are already hypoxic &academic[15,16]. Fetal cardiovascular responses to hypoxia,is redistribution of the cardiac output towards vital organs, and most important being redistribution of blood flow towards the fetal brain known as the 'brain-sparing effect'. Because theMCA/UA ratio incorporates data not only on placental status but also on fetal response, it is potentially more advantageous in predicting perinatal outcome. Doppler data combining both umbilical and cerebral velocimetery provide additional information on fetal consequences of the placental abnormality [17]. Abnormal MCA/UA PI Doppler ratio is strongly correlated with worse fetal prognosis. In normal pregnancies the diastolic component in the cerebral arteries is lower than in the umbilical arteries at any gestational age. Therefore, the cerebrovascular resistance remains higher than the placental resistance and the MCA/UA PI is greater than 1. The index becomes less than 1 if the flow distribution is in favor of the brain in pathological pregnancies. [18]

MATERIALAND METHODS:

Study Design: We performed a prospective observational study in the department of gynaecology and obstetrics at SKIMS Medical College and hospital Srinagar. This is an urban tertiary care center in Srinagar, over a period of 3 years from 1st,June,2014, through 31st,May,2016 after taking clearance from the institutional ethical committee(IEC). Informed written consent from parents of the infants was obtained.

Participants, Case definitions: All high risk (with PIH and IUGR) pregnant ladies admitted or referred to our hospital by or before 36 weeks of gestation were included in study and all pregnancies complicated by chromosomal anomalies, congenital malformations, maternal diabetes mellitus, and multiple pregnancies were excluded from study.

Data Collection and Laboratory Tests Measurement: Brief history was taken from each patient according to proforma. Main emphasis was done on history of PIH/Gestational hypertension, any past history

of still birth , iud, abruption or IUGR. Gestational age was calculated from LMP and first trimester scan .General physical examination and obstetric examination was done as per proforma.

Doppler Ultrasound study was carried out at 36 weeks of gestation to assess the parameters in the form PI, RI, SD Ratio of Umbilical Artery and MCA .The Doppler sonographic examination was carried with a pulsed duplex Doppler machine Siemens Acuson X300 with curvilinear probes with transducer frequency of 3-5MHz. The pulsality index was calculated from the maximum frequency envelope. Uniform flow velocity waveforms were recorded from umblical artery and middle cerebral artery with the fetus in steady state(excluding breathing movements) and with a heart rate between 120 -160 beats/min.The sample volume was positioned over MCA near to a point where internal carotid artery separates into anterior and middle cerebral artery. The high pass filter was set at 75 Hz. Gain was set at around 21.Perinatal outcome was studied in terms of APGAR score,cord blood pH,NICU admission.Apgar score was assessed at 5 minutes after birth, and fetal cord blood sampling to determine blood pH was done immediately after delivery. Apgar score ≤ 6 at 5 minutes, neonatal acidemia(pH≤ 7.2), and/or neonatal admission to neonatal intensive care unit (NICU)   indicated neonatal morbidity.

Statistical analysis;Accuracy of Doppler ultrasonography was checked in terms of sensitivity,specifity, PPV, NPV.Statistical analysis was done by using SSPS16.

RESULTS AND OBSERVATIONS:
The study was conducted at the SKIMS MC Bemina Srinagar, Kashmir (India), in the department of Gynaecology and Obstetrics. This was a prospective observational study, from June 2014 to May 2016 and included 50 cases of high risk pregnancies (Gestational hypertension/PIH and IUGR).In the present study following results and observations were obtained:

The mean age of presentation seen was 28.48 years, with maximum and minimum age recorded as 38 years and 24 years respectively. Among the 50 cases, 24(48.0%) were primigravida, followed by gravida 2nd n=13(26%), gravida 3rd n=10(20%), gravida 4th n=2 (4%) and gravida 5th n=1 (2%) as shown in **table no. 1. And fig. No. 1.**

CLINICAL PRESENTATION: Most of the patients presented in the 36th week of gestation,n=45(90%), followed by 35 weeks and 4 days,n=3(6%) and 36weeks 3days,n=2(4%).All the 50 (100%) cases were known cases of PIH/gestational hypertension.IUGR was found in 10 (20%) cases. Urine for proteins (Dip stick method) was found in 30(60%) patients as traces, in 7(14%) as 1+ , in 5(10%) as 2+ and 3+ in 8(16%) patients.

Doppler Findings:
1. Umbilical Artery Pi Value And Sd (systolic –diastolic Ratio) Ratio:
Umbilical artery PI value was found abnormal (above 95th percentile) in 31 (62%) cases and normal in 17 cases (34%).Umbilical artery SD ratio was abnormal (>3) in 31 (62%) cases and normal in 17 (34%) cases and 2 cases (4%) had reversal of diastolic flow in umbilical artery. Umbilical artery PI value revealed sensitivity, specificity, PPV and NPV of 96.66%, 88.88%, 93.54% and 94.11% respectively in predicting the adverse perinatal outcome(Fisher's exact test:0.152) . Umbilical Artery SD ratio revealed sensitivity, specificity, PPV and NPV of   93.33%, 83.33%, 90.32% and 88.23%   respectively in predicting the adverse perinatal outcome.

2. Mca Pi Value And Sd Ratio:
MCA PI was abnormal (<5th percentile) in 32 (64%) cases and normal in 16 (32%) of the patients. MCA SD was found abnormal (<4) in 30 (60%) cases and normal in 18 (39%) patients.MCA PI value revealed sensitivity, specificity, PPV and NPV of 90.0%, 72.22%, 84.37%% and 81.25% respectively in predicting the adverse perinatal outcome. MCA SD ratio revealed sensitivity, specificity, PPV and NPV of 90%, 83.33%, 90% and 83.33%   respectively in predicting the adverse perinatal outcome.

5.3 .CPR (cerebro placental Ratio) Findings:
CPR was abnormal (<1.08) in 32 (64%) patients and normal in 18 (36%) cases revealing sensitivity, specificity, PPV and NPV of 90.32%, 78.94%, 87.50% and 83.33% respectively in predicting the adverse perinatal outcome.

Mode Of Delivery:
34 (68%) cases delivered vaginally, out of which 27(79.41%) were hypertensive and 7 (20.58%) with hypertension and IUGR. 16 (32%) got terminated by LSCS which included 13(81.25%) cases of hypertension and 3 (18.75%) cases with hypertension and IUGR as shown in **table no. 2.**

10 (62.50%) were done on emergency basis and 6 (37.50%) were done electively Patients with abnormal Doppler indices were terminated at 36 completed weeks of gestation and rest were   carried to term (38weeks).

Perinatal Outcome:
Perinatal outcome was determined in terms of APGAR Score (≤ 6 abnormal) at five minutes and Cord Blood pH (≤ 7.2 = acidosis). APGAR score at 5 minutes was abnormal in 32 (64%) neonates and acidosis was present in 30 (60%) neonates.2 (4%) were IUD. 1 neonate was having APGAR score <4 and died immediately after birth. All the neonates with abnormal APGAR score and acidosis were admitted in NICU for more than 24 hours as shown in **table no. 3 and fig. No. 2**

Table no. 1 Gravidity

GRAVIDITY	Number of patients(n)	Percent (%)
1	24	48.0
2	13	26.0
3	10	20.0
4	2	4.0
5	1	2.0
Total	50	100.0

Table no. 2 Mode of delivery.

Mode of delivery	Hypertension	IUGR + Hypertension	Total
NVD	27	7	34(68%)
LSCS	13	3	16(32%)
Total	40	10	50

Table 3. Perinatal Outcome

Perinatal outcome	Abnormal	Normal	Total
APGAR score	32(64%)	16(32%)	48
Cord blood pH	30(60%)	18(36%)	48

Table no. 4 showing comparision of present study with Dandolo Gramellini et al and Kumbar et al in diagnosing perinatal outcome.

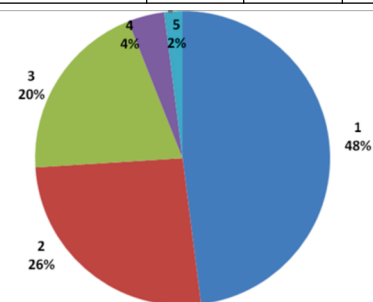| Doppler Index		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
UA PI	Present Study	99.66	88.88	93.54	94.11
	DandoloGramellini et al	64.0	90.7	72.7	86.7
	Kumbar et al	89.0	85.7	85.0	90.0
MCA PI	Present Study	90.0	72.22	84.37	81.25
	DandoloGramellini et al	24.0	100	100	73.3
	Kumbar et al	78.9	68.4	65.3	76.4
CPR	Present Study	90.32	78.94	87.50	83.33
	Gramellini et al	68.0	98.4	94.4	88.0
	Kumbar et al	94.7	90.4	90.0	95.0

Fig.1. GRAVIDITY
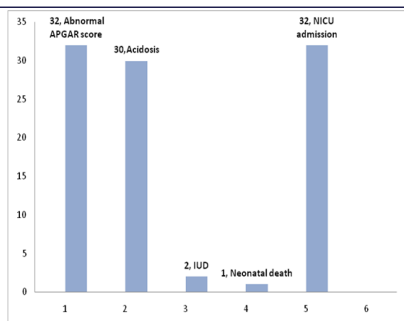
Figure 2

DISCUSSION AND CONCLUSION:

Traditionally common methods for detection of compromised foetus have been Biophysical profile (BPP) and the non-stress test (NST). Unfortunately as pointed out by Ismail Syed et-al neither of these tests is particularly sensitive for predicting poor outcome in IUGR pregnancies [10]. So in this study, we focused our analysis on whether there is any role of Umbilical and Middle cerebral artery Doppler indices in high risk pregnant women in predicting adverse foetal outcome, and to allow for timely intervention of the compromised foetus. The present study included 50 cases of high risk pregnancy (gestational hypertension and IUGR) in the age group of 24 to 38years with mean age of presentation being 28.48 years. Maximum number of cases .i.e 24(48.0%) were primigravida, followed by gravida 2nd n=13(26%), gravida 3rd n=10(20%), gravida 4th n=2 (4%) and gravida 5th n=1 (2%). Thus, PIH was reported common in young adults and primigravida. Our results were consistent with the study conducted by BN Lakhar et al[7], Mishra et al [12], M.Khalid et al [19], AthitaChanthasenanont et al[21] and PrashanthAdiga et al.[1]

Doppler indices of our study:

In our study, Doppler USG was done at 36 weeks of gestation. Various similar studies have conducted Doppler at different gestational ages e.g Vishwanathan G Kumbar et al [9] at 35.8weeks +/- 3.46 weeks; PrashanthAdiga et al [1] at 33.82 +/- 3.47 weeks; B N Lakhar et al [7] and Mishra D et al [12] did it beyond 30 weeks of gestation; Hinal Bhagat et al [8] did at 20 to 40 weeks; and Smitha K et al [22] at 28 to 40 weeks. In our study Umbilical artery PI value was found abnormal (above 95th percentile) in 31 (62%) cases and normal in 17 cases (34%) revealing sensitivity, specificity, PPV and NPV of 96.66%, 88.88%, 93.54% and 94.11% respectively in predicting the adverse perinatal outcome. Umbilical artery SD ratio was abnormal (>3) in 31 (62%) cases and normal in 17 (34%) cases and 2 cases (4%) had reversal of diastolic flow in umbilical artery revealing sensitivity, specificity, PPV and NPV of 93.33%, 83.33%, 90.32% and 88.23% respectively in predicting the adverse perinatal outcome. MCA PI was abnormal ($<5^{th}$ percentile) in 32 (64%) cases and normal in 16 (32%) of the patients, revealing sensitivity, specificity, PPV and NPV of 90.0%, 72.22%, 84.37%% and 81.25% respectively in predicting the adverse perinatal outcome. MCA SD was found abnormal (<4) in 30 (60%) cases and normal in 18 (39%) patients revealing sensitivity, specificity, PPV and NPV of 90%, 83.33%, 90% and 83.33% respectively in predicting the adverse perinatal outcome. CPR was abnormal (<1.08) in 32 (64%) patients and normal in 18 (36%) cases revealing sensitivity, specificity, PPV and NPV of 90.32%, 78.94%, 87.50% and 83.33% respectively in predicting the adverse perinatal outcome. In current study, Umbilical artery PI value revealed the highest sensitivity, specificity, PPV and NPV in predicting the adverse perinatal outcome among the Doppler indices taken. Our results were comparable with Dandolo Gramellini et al [23] and Kumbar et al [9] as shown in **table no. 4**.

Perinatal outcome: In our study, perinatal outcome was determined in terms of APGAR Score (≤6 abnormal) at five minutes and Cord Blood pH (≤7.2 = acidosis). APGAR score at 5 minutes was abnormal in 32 (64%) neonates and acidosis was present in 30 (60%) neonates. 2(4%) cases were IUD. 1 neonate was having APGAR score 4 , cord blood pH of 6.8 with grade III HIE and died immediately after birth. All the neonates with abnormal APGAR score and acidosis were admitted in NICU for variable period of time. Our results were consistent with the studies conducted by Vishwanathan G Kumbar et al [9], G V Prasad et al[20] and Lakhar et al [7].

Considering the high mortality and morbidity of compromised foetus in high risk pregnancy it would be extremely valuable to find a cost-effective, reliable, and readily available diagnostic tests with high diagnostic efficiency to pick up compromised fetuses' at their earliest. Knowing traditional common methods of Biophysical profile (BPP) and the non-stress test (NST) not being particularly sensitive for predicting poor outcome in IUGR pregnancies, Doppler indices like PI, SD ratio, and CPR of Umbilical and middle cerebral artery with good test characteristics of sensitivity, specificity, negative predictive values and positive predictive values as depicted in our study, could serve as reliable diagnostic methods of detecting compromised foetuses. Being a rapid, readily available and bedside investigation, early referral to a hospital where facilities for neonatal resuscitation and Neonatal intensive care are available, could be made, which may significantly decrease the morbidity and mortality among compromised foetuses.

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