

A Study on Color Doppler and Non Stress Test as Predictor of Perinatal Outcome in Pregnancy Induced Hypertension and Intrauterine Growth Restriction in a Tertiary Care Hospital in Eastern India

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Abstract

Introduction: Antepartum surveillance to evaluate fetal health have been the focus of intense interest for more than decades. The timely detection of morbid changes in fetal status followed by adequate interventions to avoid death or disabilities, is of paramount importance.

Objective: To compare the effectiveness of non-stress test and color doppler studies in the prediction of perinatal outcome in terms of mode of delivery, gestational age at delivery, birth weight, admission in neonatal intensive care unit (NICU), fetal morbidity and mortality.

Material & Methods: A prospective observational study was conducted among (n=100) antenatal patients admitted in the obstetric indoor of a hospital in Kolkata, West Bengal complicated by pre eclampsia and intra uterine growth retardation (IUGR) beyond 34 weeks of gestation after matching with inclusion and exclusion criteria. Recruited participants were then divided into four groups: group A having both tests normal, group B with normal NST and abnormal doppler, group C with normal doppler and abnormal NST and group D with both abnormal tests respectively. The patients were followed by serial fetal doppler assessment and non-stress test (NST). The results of the last doppler and NST within one week of delivery were considered in the subsequent correlation with perinatal outcome. The time interval in days between the first abnormal doppler and the development of abnormal NST was used to calculate the lead time. The perinatal outcome parameters studied were mode of delivery, gestational age at delivery, birth weight, neonatal morbidity in terms of Apgar score < 7 at 5 minutes, NICU stay, and perinatal mortality. The major adverse perinatal outcomes, if any was observed amongst the four study groups.

Results: 40% percent of multigravidas had a history of preeclampsia in their previous pregnancy. 18% of the study population had a combination of preeclampsia and IUGR. 38 women had both NST and doppler study normal (Group A) while both tests were abnormal in 31 patients (Group D). There were 54 women with abnormal doppler findings and 39 with abnormal NST. Brain sparing effect (BSE) was seen in 38 women. Group A had majority of cases (65.78%; 25 out of 38) with only IUGR and had the least morbidity and best perinatal outcome. Group D had the maximum number of cases having combined preeclampsia with IUGR (70.96%; 22 out of 31) and had the worst perinatal outcome associated with prematurity and low birth weight; there were only 15.78% NICU admission in the group A; in contrast 77.4% fetuses required NICU admission in group D. Only 39.4% had operative delivery for fetal distress in group A in contrast to 70.96% women in group D. There were 4 intra uterine and 13 neonatal deaths. Majority of fetuses showed abnormal doppler changes prior to NST. The lead time varied between 0-9 days with a mean of 4.11 days. **Conclusion:** Though both test results were effective in predicting abnormal perinatal outcome, a significant advantage of doppler over NST was it showed abnormal changes earlier than NST giving a significant lead time of up to 9 days which is important in the management of preterm high-risk pregnancies. An abnormal NST following an abnormal doppler is associated with the worst perinatal outcome. Both the tests are complimentary to one another in fetal surveillance of high-risk pregnancies.

KEYWORDS: Antepartum fetal surveillance, color doppler studies, non-stress test, preeclampsia, intra uterine growth restriction.

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Introduction

Every new-born has the right to born healthy mentally as well as

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physically. The realization of this goal plays a crucial role in materno-fetal medicine, whose exclusive objective is that every pregnancy should lead up to into a healthy baby and mother. The incidence of intrauterine growth retardation (IUGR) in a population where mother is healthy and well-nourished is about 3-5%. [1] In a population where mother is suffering from hypertension or previously growth restricted fetus the incidence is higher 10- 20%. [1] National neonatal perinatal

database of India reported the incidence of IUGR 9.65% among hospital born live fetus, and with very low birth weight infant is 43% [2]. Almost 18.7% neonatal death occurs due to birth asphyxia resulting from IUGR or pregnancy induced hypertension (PIH) [3]. Ante partum fetal surveillance is the basis of preventive obstetric management focused at lessening maternal and perinatal mortality and morbidity. With the development of the electronic fetal monitoring, the world of the fetus which was earlier hidden from scientific probe was instantly obtainable to newer technology. Apart from various other non-invasive tests like non stress test (NST) which provide information after the clinical features have set in, umbilical artery doppler studies give us vital information regarding the fetus in utero [1]. Doppler sonography too offers a unique tool for the non-invasive evaluation of physiological hemodynamic fetoplacental blood flow information. There are specific abnormalities in doppler parameters in intrauterine growth retardation. Umbilical arterial (UA) doppler velocimetry is the most rigorously evaluated tests of fetal well-being [4]. Doppler ultrasound researches of the human fetal circulation have shown that in those with IUGR there is a significant decrease in middle cerebral arterial (MCA) pulsatility index when juxtaposed with those in normal fetuses [5]. Our study focuses on establishing the role of umbilical artery and middle cerebral artery Doppler ultrasound as well as non-stress test in predicting adverse perinatal outcome in high-risk pregnancies like IUGR, PIH and the role of these tests in clinical management of such pregnancies. Although plenty of literature is available in international journals, there are few Indian studies in this matter especially there are hardly any studies available in Eastern part of India. It is our endeavor to find out the comparative usefulness of doppler and NST in management of IUGR and severe pre-eclampsia, thus reducing fetal morbidities and admission in NICU. This endeavor was under taken with the primary objective to evaluate and compare the performance of ultrasound scanning with Doppler study and NST with biophysical profile to predict and initiate timely interventions. The secondary objectives were to detect any abnormalities in fetoplacental unit and fetal circulation in fetus of hypertensive mother and clinically intrauterine growth restricted, to identify the hypoxic fetus (if any) & attempt for timely delivery so as to prevent academia and to correlate the occurrence of adverse perinatal outcome with degree of abnormality in the doppler indices.

Materials & Methods

This single centered, institution based, prospective observational study has been conducted at the Department of Obstetrics and Gynecology in Nilratan Sircar Medical College and Hospital, Kolkata after approved by the institutional ethical committee over a year (01.03.19 to 29.02.20). The study population has been comprised of (n=100) pregnant mothers with gestational age above 34 weeks either suffering from pregnancy induced hypertension or chronic placental insufficiency or intrauterine growth retardation or chronic hypertension. Those with low risk of pregnancy, gestational age below 34 weeks, having intrauterine death, high risk patients who are in labor at the time of admission, maternal heart disease, Rh-iso immunisation, gestational diabetes mellitus, anemia with hemoglobin less than 8 gm % and oligohydramnios were excluded from the study. Detailed obstetric history including the history of pregnancy induced hypertension; chronic hypertension history of smoking alcoholism, previous pregnancies including birth weight of previous babies, perinatal deaths, and mode of delivery was documented. The fetal growth and maternal conditions were assessed by NST and Color Doppler study by a single radiologist. Recruited participants were then divided into four groups: Group A having both tests normal, Group B with normal NST and abnormal doppler, Group C with normal doppler and abnormal NST and Group D with both abnormal tests respectively. Impaired uterine artery blood flow is identified by doppler when persistent abnormal indices e.g.(resistance index) RI and (pulsatility index)PI >95th centile, High PI (>1.45), high RI (>

0.58 after 24weeks), persistent early diastolic notch beyond 26 weeks gestation, S/D ratio>2.6 and significant differences in the indices between right and left uterine artery S/D ratio >1.0 [6]. Changes in the umbilical artery include elevated indices as well as changes in the flow direction [7].

The NST is an evaluating tool used from 32 weeks of pregnancy up to term in estimating fetal health through the use of electric fetal monitors that constantly record the fetal heart rate (FHR). A normal test result, as defined by the American College of Obstetrics and Gynecologist (ACOG) [8], is one in which two or more accelerations peak at 15 bpm or more above baseline, each lasting 15 seconds or more, and all happening within 20 minutes of initiation of the test. It is important to note that an abnormal stress test is not always threatening and can occur with a sleeping fetus. If a test is non-reactive, FHR monitoring for at least 40 minutes is done to account for the fetus sleep cycle, and vibro-acoustic stimulation used to stimulate fetal movement. Continuous non-reactive NST can indicate central nervous system depression, but further evaluation is necessary, usually in the form of a biophysical profile or contraction stress test.

The perinatal outcome parameters studied were mode of delivery, gestational age at delivery, birth weight, perinatal mortality, neonatal morbidity in terms of Apgar score < 7 at 5 min, neonatal intensive care unit (NICU) stay, and complications that developed.

The comparison of major adverse perinatal outcome amongst the four study groups was done by chi square test. A p value less than 0.05 was considered significant. Odds ratio (OR) and 95% CI were calculated. The sensitivity, specificity and Positive predictive value, Negative Predictive Value then calculated. Finally, after collecting all the data it has been analyzed using SPSS and MEDCALC software [Version - 20.023]

Results

Among the total (n =100) mothers their ages ranged from 17 years to 31 years. Majority of the mothers (80%) belonged to 20-30 years age group. The average age of the patients was 24.5 years. Among the PIH parturient, there were 36 primigravida and 14 multigravida. In the IUGR group, there were 21 multigravida mothers and 29 primigravida. Among the (n=100) mothers, 30 had PIH, 8 had chronic hypertension, 1 had pre-existing disease causing chronic placental insufficiency like chronic renal disease and 2 of systemic lupus erythematosus (SLE), 34 had growth restricted fetuses whereas 25 were suffering from both PIH and IUGR respectively.

In our study population, Uterine Artery Doppler study showed 53 mothers (53%) had an elevated uterine artery RI and 47 patients (47%) had normal findings. Among all the women, 52 antenatal mothers (52%) had a persistent early diastolic notch in the uterine artery whereas 48 patients (48%) had normal uterine artery flow waveform. Doppler study showing Umbilical artery PI revealed that it was elevated in 51 patients (51%) and was normal in 49 (49%) patients. Eighteen of the fetuses (18 %) showed absent umbilical artery end diastolic flow pattern and 6 fetuses (6%) had reversal of end diastolic umbilical artery flow with the total of 24 fetuses (24%) were having abnormal waveforms whereas 76 fetuses (76%) showed normal positive end diastolic flow. In Middle Cerebral Artery Doppler study, we found 34% of the fetuses had decreased pulsatility index and 66% were normal. Out of all the fetuses, 38% had evidence of redistribution of blood to the brain as evidenced from the value of the ratio of PI in the MCA and umbilical arteries showing values less than 1.08 while 62% had values more than or equal to 1.08. Non Stress Test done among 100 patients showing 61 of them had normal CTG tracing (61%), 12 patients had abnormal tracing (12%) and 27 patients had pathological tracing (27%).

Rate of vaginal delivery was more in group A- 60.5%, whereas, percentage of operative delivery increased when NST and Doppler findings were abnormal. The distribution of the mode of delivery among the study population is depicted in Table: 1.

Table 1: Distribution of mode of Delivery in the study population

Perinatal Outcome	Group A (n=38)	Group-B (n=23)	Group-C (n=8)	Group-D (n=31)
Survival	37(97.36%)	20(86.95%)	7(87.5%)	19(61.29%)
Intra Uterine Death	0	1	0	3
Neonatal Death	1	2	1	9
Perinatal Death	1(2.63%)	3(13.04%)	1(12.5%)	12(38.7%)

In this study, 83(83%) women delivered live baby whereas 4% pregnancies led to intrauterine death and 13% led to early neonatal death (Table-2). Assessing the perinatal outcome among all the women, 46% women gave to preterm birth, 38% women gave birth to low birth weight baby. Among all the babies, 16% had Apgar score < 7 at 5 minute of birth. Out of all babies, 42% had to admit in NICU among which 33% had perinatal complications like hypothermia, hypoglycemia, pulmonary hemorrhage, septicemia, and respiratory distress syndrome, shock and 17% led to perinatal death (including 4 intra uterine deaths).(Table -3)

Table 2: Distribution of pregnancy outcome in the study population

Mode of Delivery	Group-A (n=38)	Group-B (n=23)	Group-C (n=8)	Group-D (n=31)
Vaginal	23(60.5%)	6(26%)	2(25%)	10(32.25%)
Caesarean	15(39.4%)	17(73.91%)	6(75%)	21(67.74%)

Table 3: Distribution among groups on the basis of perinatal outcome

Perinatal Outcome	Group-A (n=38)	Group-B (n=23)	Group-C (n=8)	Group-D (n=31)
Gestational Age at Delivery (years)	38.3	37.0	36.1	35
Preterm Birth	3(7.89%)	13(56.5%)	5(62.5%)	25(80.6%)
Average Birth Weight (grams)	2439.4	2112.2	1934	1634.5
Low APGAR Score <7 at 5minutes	1(2.63%)	2(8.69%)	2(25%)	11(35.4%)
Admission in NICU	6(15.78%)	9(39.1%)	3(37.5%)	24(77.4%)
Perinatal Complication	3(9.6%)	4(17.39%)	3(37.5%)	23(74.19%)

In (Table 4) perinatal outcome between Gr D and Gr. A & B were compared and the findings were quite significant as depicted in the table. When NST and color doppler were compared then the former was found to be more specific whereas color doppler was more sensitive device (Table 5)

Table 4: Comparison of perinatal outcome in between study groups

Perinatal outcome parameters	Group A vs Group D			Group B vs Group D		
	p value	OR	CI	p value	OR	CI
Caesarean Delivery	0.0213	3.2200	1.1904 - 8.7101	0.0062	0.7412	0.2239- 2.4540
Perinatal Death	0.0035	23.3684	2.8227- 193.4639	0.0461	4.2105	1.0255- 17.2880
Preterm Baby	<0.0001	48.6111	11.0888- 213.1006	0.0113	3.2051	0.9520- 10.7905
APGAR<7 at 5 min	0.0053	20.3500	2.4471- 169.2326	0.0346	5.7750	1.1356- 29.3678
Admission in NICU	<0.0001	18.2857	5.4413- 61.4497	0.0057	5.3333	1.6266- 17.4870

Perinatal complication	<0.0001	33.5417	8.0476-139.7990	0.0001	13.6563	3.5569-52.4306
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OR-Odd's Ratio

CI-Class Interval

Table 5: Comparison between NST and COLOR DOPPLER results in prediction of poor perinatal outcome

Parameter	Non Stress Test		Color Doppler	
	Value	95%CI	Value	95%CI
Sensitivity	49.30%	37.22%-61.44%	66.20%	53.99%-77.00%
Specificity	86.21%	68.34%-96.11%	75.86%	56.46%-89.70%
Positive Predictive Value	89.74%	77.37%-95.73%	87.04%	77.52%-92.89%
Negative Predictive Value	40.98	49.72%-69.67%	47.83%	38.42%-57.39

Discussion

Ante partum detection of fetus at risk of death or compromise in utero remains the major challenge in modern obstetrics. Specific and accurate methods for detection of fetus at risk can result in early appropriate intervention and hence reduce fetal loss. The diagnosis and careful monitoring of high-risk pregnancy has now become possible in our practice. Apart from various other non-invasive tests like NST which provide information after the clinical features have set in, umbilical artery doppler studies give us vital information regarding the fetus in utero. Doppler measurement of the pulsatile blood flow velocity in umbilical artery gives direct information on fetoplacental circulation and hence identifies placental circulatory failure.

Although a number of methods have been used to identify fetuses with IUGR such as the maternal weight gain, fundal height less than the normal for corresponding gestational age, ultrasound with doppler seems to be the most accurate and sensitive method of identifying IUGR fetuses. The utero-placental blood flow is the most important determinant of fetal growth. Restricted blood flow through the placental vascular bed has been shown to be associated with IUGR.

In our study, we found that majority of the patients were in the age group of 21-25 years. Among all the patients, 40% percent of multigravidas had a history of preeclampsia in their previous pregnancy. 18% of the study population had a combination of preeclampsia and IUGR. There were 38 women where both NST and doppler were normal (Group A) while both tests were abnormal in 31 patients (Group D). However Group C with normal doppler and abnormal NST comprised of only 8 mothers and thus not considered for statistical analysis. Group B with normal NST and abnormal doppler had 23 cases. There were 54 women with abnormal doppler findings and 39 with abnormal NST. Brain sparing effect (BSE) was seen in 38 women. In 6 mothers of Group D there was loss of BSE, followed by abnormal NST. Group A where both test results were normal had majority of cases (65.78%; 25/38) with only IUGR and had the least morbidity and best perinatal outcome. Group D which had the maximum number of cases having combined preeclampsia with IUGR (70.96%; 22/31), had both the test results abnormal, and had the worst perinatal outcome associated with prematurity and low birth weight – (mean birth weight about 700g less when compared to that in Group A). There were only 15.78% NICU admission in the group with reassuring NST and normal blood flow pattern in color Doppler. In contrast 77.4% fetuses required neonatal admission when both NST was non-reassuring and color Doppler showed hypoxia.

The statistical significance for perinatal outcome in Group A vs D and Group B vs D are shown in Table 16. Presence of preeclampsia with IUGR significantly increased perinatal mortality (P=0.0035), prematurity (P<0.0001) and NICU admissions (P<0.0001) in Group D when compared to those in Group A. The number in Group C was too small for statistical comparison. Fetuses in Group B (normal NST, abnormal Doppler) were more advanced in gestation and had better neonatal outcome compared to those in Group D. Only 39.4% had operative delivery for fetal distress when NST was reassuring and color doppler showed normal blood flow pattern. In contrast 70.96% women underwent operative delivery for fetal distress when NST was non-reassuring or color doppler showed fetal hypoxia. Hence cesarean section rate was higher in group D (67.74%). Though, in Group D there were some cases where cesarean section was deferred when neonatal survival prospects were poor. Perinatal deaths (P=0.046) prematurity (P=0.011), and neonatal complications (P=0.001) were significantly more in Group D compared to those in Group B. Actually 4 of our IUGR cases in Group B had shown abnormal doppler findings early in gestation (prior to 34 weeks) but the findings did not deteriorate on serial doppler studies and pregnancy could be continued further till the babies attained a little more weight and lung maturity. There were seven cases of placental abruption, one in Groups A, one in group B and five in Group D. Fortunately all these babies survived because of timely intervention as the mothers were hospitalized for severe preeclampsia. There were four intrauterine deaths and thirteen neonatal deaths in the study population. The neonatal death in Group A was from pulmonary hemorrhage due to IUGR on 7th neonatal day. Major causes of neonatal death were pulmonary hemorrhage, septicemia, and respiratory distress syndrome, shock. Highest number of perinatal mortality and neonatal morbidity were observed in Group D where both tests were found to be abnormal. Majority of fetus showed abnormal doppler changes prior to NST. This time interval is the Lead time. Only in 4 cases of severe preeclampsia in Group D, showed both doppler and NST abnormalities on admission and hence it was not possible to know which preceded the other.

Here in this study, we have conducted doppler ultrasound and NST in a group of women with high risk pregnancy comprising of IUGR and/or preeclampsia. It is evident that when both NST and Doppler are abnormal the baby weight and gestational age at birth are low while perinatal mortality and neonatal morbidity are high. Though both test results were effective in predicting abnormal outcome, the significant advantage of doppler over NST observed in our study in

Group D was that Doppler showed changes earlier than NST giving a significant lead time of up to 9 days with an average of 4.11 days. This lead time is very important as babies can be delivered in this period or can be followed up in this interim period to gain a little more pulmonary maturity, which may be crucial for a preterm fetus. Steroid prophylaxis can be administered during this period in preterm fetuses. The significant lower birth weight of fetuses when both doppler and NST are abnormal (Group D) indicates that these fetuses suffer from a more severe degree of placental insufficiency. Though doppler was abnormal in both B and D groups, perinatal outcome was better in Group B. When neonatal survival prospects are good it is better to deliver the compromised fetus than to monitor till the development of abnormal NST as was evident from the perinatal outcome in Group B. These babies were less compromised and were relatively more advanced in gestation. So early intervention was possible. The Growth Restriction Intervention Trial (GRIT)[9], which was designed to time delivery in compromised preterm fetuses, showed that delaying delivery to increase maturity in severe hypoxemia increased stillbirths to nearly fivefold while deaths before discharge fell by one third. The hemodynamic changes picked up by doppler occur in the compensatory phase of growth restriction. Fetal heart rate abnormalities occur much later in the decompensation phase, which is a late sign of fetal compromise. We have already seen that the lead-time is shorter in presence of preeclampsia through this study. Arduini et al [10] in their study of 37 fetuses had a lead time ranging from 1 to 26 days. They observed that it is shorter in the presence of preterminal doppler changes like pulsatile umbilical vein and in preeclampsia. One interesting observation they made was that gestational age influenced this interval which was not found here. In the early part of gestation longer time interval between abnormal doppler and NST was observed in few cases of idiopathic IUGR. This is because smaller fetuses have lowered nutritional and oxygen requirements allowing them to develop longer metabolic adaptations reflected by an abnormal doppler. The time sequence of deterioration therefore depends on gestational age and concomitant maternal disease. There is quick deterioration of placental function in the presence of preeclampsia resulting in shorter lead time. Verma U et al [11] conducted a study on 100 antenatal patients of >34 weeks gestation. They categorized the patients into 4 sub-groups according to NST and Doppler findings. They concluded that doppler is useful in recognizing foetal compromise earlier than NST. It gives a lead time which is important in management of preterm high risk pregnancies. Doppler reproduce chronic hypoxic changes while NST can detect acute episodes in presence or absence of chronic hypoxia. An abnormal NST following an abnormal Doppler is associated with worst perinatal aftermath. Yelikar et al [12] studied 189 patients concluded that a group had best perinatal outcome with mean gestation of delivery of 37.3 weeks, NICU admission in 7.3% babies with mean birth weight of 2288 grams and no perinatal deaths whereas Group D patients were delivered at mean gestation of 34.6 weeks with 100% NICU admissions and perinatal deaths in 33.3% of the babies. Ott et al [13] studied the single doppler parameter MCA/UA S/D ratio in comparison with NST to predict the neonatal compromise in a larger group of 447 cases and concluded that combination of NST and MCA/UA PI ratio was excellent predictor of perinatal outcome. This was explained by the fact that loss of brain sparing effect in sick fetuses may have caused MCA/UA doppler to be normal. So, it is important to view the entire clinical scenario rather than act only on the basis of test results. Doppler can detect fetal adaptations like BSE occurring early in the decompensation cascade. A nadir in the value of PI in MCA and/or cerebroplacental ratio <1.08 reflects it. In the study by Weiner et al [14] 6 fetuses showed loss of BSE (brain sparing effect) followed by development of abnormal fetal rate pattern. They compared fetal doppler with computerized fetal heart rate monitoring. They opined that a loss of autonomic reactivity occurs first in the brain followed by similar response in the heart manifested by abnormalities in fetal heart patterns. Computerized analysis of fetal heart rate provides an objective assessment of the cardiocography with emphasis on short

term variation and seems to be superior to traditional NST. We observed loss of BSE followed by development of abnormal NST in six cases resulting in five perinatal deaths. This loss of BSE can be attributed to the development of cerebral edema in a terminally hypoxic fetus. Fetal Doppler has the power to discriminate between sick and healthy fetuses and with serial measurements it is possible to monitor any deterioration in the fetus. In chronic hypoxia Doppler changes occur first while abnormal fetal heart tracings represent late signs of fetal deterioration.

Therefore, combined fetal testing modalities such as doppler, NST and biophysical profile provide a wealth of information regarding fetal health. Integrated fetal testing would be ideal for individualized care of the preterm compromised fetus for timed intervention. Disadvantages of doppler technique are the requirement of sophisticated equipment and a degree of operator skill and expertise. They may not be available in all centers. And the advantage is it can detect the compromised hypoxic fetus much more before than NST, thus gives us time to make decision regarding delivery of the baby. Advantages of NST include ease of use and interpretation, low cost, and minimal time required. Therefore, it may remain the workhorse in detection of a compromised fetus in many hospitals.

Conclusion

Thus, it can be concluded that doppler is useful in recognizing fetal compromise earlier than non-stress test giving a lead time which is important in the management of preterm high- risk pregnancies. This lead-time is very important as babies can be delivered in this period or can be followed up in this interim period to gain a little more pulmonary maturity, which may be crucial for a preterm fetus. An abnormal NST following an abnormal doppler is associated with the worst perinatal outcome. In cases with abnormal doppler if the prospects for neonatal survival are good, it is better to deliver the fetus before NST becomes abnormal. NST still holds its importance in fetal monitoring because of its ease of performance and cost effectiveness. But both the tests are complimentary to one another in fetal surveillance of high- risk pregnancies. The clinical scenario however dictates the choice of the appropriate test.

Limitations

In spite of every sincere effort this study has some lacunae as it has been done in a single centre in a small sample of mothers. The outcome of the study cannot be generalized though it paved the path for conduct of more such studies in future.

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