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Acceptance and Utility of Combined Screening for Aneuploidies in First Trimester of General Population of North India

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ABSTRACT

Introduction: Nuchal translucency (NT) measurement is the most powerful marker for general population screening of Down's syndrome, done by specially trained sonologist using standardized technique. With the advent of better ultrasound machines and expertise of doctor, assessment of fetal anatomy at 11 to 13^{+6} weeks scan has improved a lot. Combined screening by maternal age, NT, FHR, biochemical markers, allows calculation of risk for trisomies 21,18 and 13. It also allows early detection of fetal structural defects which cannot be detected by cell free fetal DNA.
Objective: To find out the acceptability of combined screening and to detect aneuploidies as well as early fetal structural defects so that first trimester MTP can be offered.
Materials & Methods: It was a prospective study from Feb.2016 to Aug. 2019. Only 531 antenatal women between 11 to 13^{+6} weeks gave consent to undergo NT scan and double marker test. All values of NT scan, double marker, maternal age, MAP and other parameters were entered in software issued by FMF U.K. and risk was calculated.
Results: 13 patients fell in high risk group out of which 9 patients underwent CVS and 1 showed T21. 4 patients refused for karyotyping and underwent level 2 USG out of which 1 showed multiple soft markers and amniocentesis showed T18.
Conclusion: Acceptability for combined screening was found to be 84.1%. If aneuploidies are detected earlier in first trimester, then patient can be offered first trimester MTP which saves family from challenges of bringing up.

Keywords: first trimester, combined screening, nuchal translucency, aneuploides

INTRODUCTION

The early fetal ultrasound assessment at 11 to 13^{+6} weeks of pregnancy has become an important part of antenatal care for earliest detection of fetal chromosomal and structural abnormalities. NT measurement is the most powerful marker for general population screening of Down's syndrome, done by specially trained sonologist using standardized technique.[1] Nicolaides et al reported the significance of NT measurement[2], subsequent studies have confirmed the significance of this first trimester sonographic marker. With the advent of better ultrasound machines and expertise of doctors, the assessment of fetal anatomy in first trimester has improved a lot. Similarly, combined screening by incorporating together the maternal age, NT, fetal heart rate, biochemical markers (free βhCG and PAPP-A) allows calculation of risk for trisomies 21, 18 and 13.[3] It also allows detection of fetal structural defects which cannot be detected by cell free fetal DNA (NIPT). The abnormal fetuses can be easily terminated by first trimester MTP

after confirmation by karyoptyping by chorionic villus sampling (CVS) and saves family from burden of bringing up. NT is the only auditable parameter in first trimester and also indicates about risk of fetal cardiac abnormalities and structural defects.[4] Newer USG markers like nasal bone (NB), ductus venosus flow (DV) and tricuspid flow help to increase the detection rate and reduce false positive rate. These new markers can be used in all or intermediate risk group cases. An added advantage of screening in this period can be pre eclampsia (PE) screening.[5,6]

Aims & Objectives

The study was aimed to study the acceptability of combined screening in first trimester amongst patients attending the antenatal OPD. Second objective was early detection of aneuploidies as well as fetal structural defects so that first trimester MTP could be offered.

MATERIALS AND METHODS

It was a prospective study over 3.5 years, from Feb.2016 to Aug. 2019. Out of 3896 antenatal patients, 617 patients with singleton pregnancy were between 11 to 13^{+6} weeks of pregnancy, who were counseled about benefits of combined screening. Only 531 gave consent to undergo the combined screening and be a part of the study. The ultrasounds were conducted by trained doctor, certified with FMF (fetal medicine foundation, U.K.) on WIPRO GE V-1.0.7 (model no. 5772556) machine. On confirming the viability of pregnancy by transvaginal ultrasound, the patients were counseled about the importance of screening for chromosomal anomalies in first trimester by an NT-NB scan and double marker test, explaining the incidence of chromosomal anomalies and its implications besides early detection of other structural abnormalities. Patients were advised to follow up between 11^{+6} to 13^{+6} weeks of pregnancy for NT scan. On USG we measured the NT, NB, FHR, DV for 'a' wave, BPD, abdominal wall for insertion of umbilical cord, abdomen for presence of stomach bubble and urinary bladder.

For measurement of NT, the CRL (crown rump length) should be between 45 and 84mm with magnification of image such that the thorax and fetal head can occupy the whole screen. With mid-sagittal view of face, fetus in neutral position (head in line with the fetal spine) the calipers are placed to measure the maximum lucency from edge to edge of thin nuchal lines. Following this report, they were advised to undergo double marker test (β hCG and PAPP-A) along with other routine antenatal tests. A note was made for age, parity, duration of pregnancy, history of chromosomal anomalies in previous pregnancies, history of hypertension, pre eclampsia or diabetes in previous pregnancy, antiphospholipid disease, smoking or alcohol intake. Risk of development of PE and FGR can be calculated by taking mean PI (pulsatality index) of uterine arteries. Cervix was also assessed. The common reasons for refusal of participation in study were cost of USG, number of USGs in pregnancy and ignorance about chromosomal anomalies.

RESULTS

Of 531 study cases, five had missed abortion. MTP was conducted in two cases (1 acrania and 1exomphalos). DV was abnormal in six patients. NB was found abnormal in two cases. NT ranged from 1 mm to 2.5 mm. uterine artery mean PI was raised in six patients, who were put on low dose aspirin (150mg) to prevent development of PE. Cervical length was found less than 2.5 cm in two patients who were put on vaginal progesterone pessary to prevent preterm delivery. All the values obtained were entered in software issued by FMF U.K. and risks were calculated for chromosomal anomalies, for development of PE and FGR. Those who fell in high risk group, were referred to fetal medicine specialist for further management (e.g., CVS, amniotic fluid sampling or NIPT) and to confirm or rule out chromosomal defects.

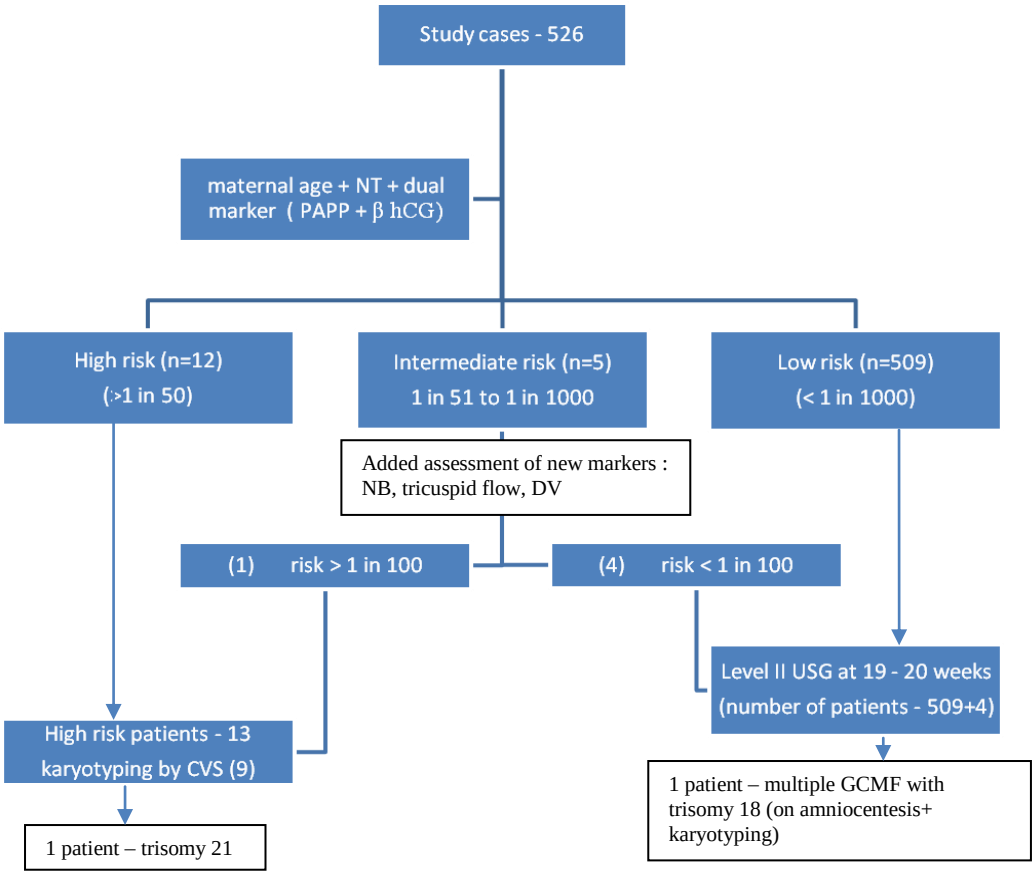
Table 1 : Demography

Characteristic	Mean ± S.D.
Age (years)	25.42 ± 3.70
Mean arterial pressure (mmHg)	88.96 ± 4.98
Parity	
Primipara	284
Multipara	242
Patients with pre existing medical disorders	18 (3.4%)
BMI (KG/m^2)	22.15± 1.96

Table 2 : Parameters studied in study population with their values

Parameter	Normal	Abnormal
NT measurement	523	3 (>95th percentile)
NB	524	2 (absent)
D.V. 'a' wave	524	2 (negative)
D.V. PI	522	4 (increased)
Uterine A PI	520	6 (raised)
TR(tricuspid regurgitation)	523	3 (present)
FHR	522	4 (abnormal)
Cervical length	524	2 (reduced)
Serum PAPP-A	522	4 (<0.5 MOM)
Serum free βhCG	523	3

Flowchart: Detection of aneuploidies



Out of thirteen high risk cases, four refused for karyotyping and NIPT. Nine patients underwent CVS but only one came out positive for trisomy 21, and rest 11 had normal karyotype. Rest four (refused CVS) went for level II scan at 18 weeks besides 509 low risk patients, out of which only one was found to have multiple congenital anomalies, underwent amniocentesis and came positive for trisomy 18. Incidence of Down's syndrome in studied population was 0.18% and for Edward's syndrome was 0.18%.

DISCUSSION

Tests involving two markers in combination with maternal age, are significantly better than those involving single markers with or without age. Combined screening at 11 – 14 weeks is not commonly done in low resource country like ours, where majority of antenatal care is concentrated around second and third

trimester. Early anomaly scan have their own limitations including need for expertise including quality of machine, cost concerns in low resource countries, single versus multiple anomalies. In our country majority patients get anomaly scan done between 18 – 22 weeks, which present in form of second trimester MTP challenge. However, with proper counseling, if combined screening can be offered in first trimester itself, it can save the family from challenges of bringing up.

At 11 to 13^{+6} weeks of pregnancy, the FMF U.K. society gives incidence of trisomy 21 (1in 200), trisomy 18 (1 in 450) and trisomy 13 (1 in 1400). We could achieve a good detection rate for anomalies which is quiet comparable to published literature. Incidence of Down's syndrome in our studied population was 1 in 180 and for Edward's syndrome was 1 in 180. No data are available on what proportion of our population has access to first trimester aneuploidy screening. Our study showed an acceptability of 84.1% for first trimester screening which is higher than the study conducted by Mulvey and Wallace in 2000 (74%).[7]

CONCLUSION

Public awareness and larger support is required from government in form of cost reduction of combined screening for its wide implementation in public health sector especially in low resource countries like ours. With good counseling at primary level public health centers, a good proportion of fetal abnormalities can be picked up at the earliest while providing reassurance for women at high risk.

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