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Original Research Article

A comparison of detection of chromosomal abnormalities by Amniocentesis in patients screened by dual marker test vs those screened by ultrasonography for nuchal translucency and nasal bone in first trimester

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ABSTRACT

Background: It becomes important to detect chromosomal abnormalities prenatally and early in the pregnancy. The present thesis is aimed to assess the performance of prenatal screening tests for chromosomal abnormalities detection i.e., dual marker test, first trimester ultrasound which measures the nuchal translucency and presence or absence of nasal bone, and their correlation with diagnostic test which is the karyotyping after amniocentesis.
Materials and Methods: It is a prospective & observational clinical study conducted in Obstetrics and gynaecology department of a tertiary care hospital. Two hundred pregnant females above 18 years of age attending ANC OPD (Antenatal Check-up Out-patient department) were considered for this study.
Results: In this study we found the presence of chromosomal abnormalities in 10% of participants. Combined sensitivity of NT and Dual marker test was found to be 83.75% in detecting chromosomal abnormalities.
Conclusions: It can be concluded at the end of the study that; prenatal diagnosis with ultrasonography for nuchal translucency either alone or in combination with dual marker test offered good detection rate for these chromosomal abnormalities.

1. Introduction

One of the most common complications of pregnancy associated with emotional distress is recurrent abortions. Recurrent abortions can result from various causes like endocrine dysfunctions, autoimmune disorders, genetic abnormalities, advanced maternal age, infections, environmental toxins and congenital and structural uterine abnormalities.[1]

It has also been observed that about 15-20% of all pregnancies result in spontaneous miscarriages and the contribution of chromosomal abnormalities among these cases is as high as 70%. It has been observed that majority of these miscarriages are caused due to balanced chromosomal rearrangement detected in one of the partner couples. This eventually leads to either chromosomal duplication or deletion in the foetus. The consequences of such imbalances are usually fatal and result in spontaneous abortions or birth of a malformed child.

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Prenatal diagnosis requires either amniocentesis from 16 weeks of gestation or chorionic villous sampling from 11 weeks of gestation. Randomized studies have demonstrated that the procedure-related risk of miscarriage is the same (approximately 1%). Consequently, invasive testing is carried out only in pregnancies that are considered to be at high risk for chromosomal abnormalities. The traditional method of screening is maternal age, with which invasive testing in 5% of the population identifies approximately 30% of the fetuses with trisomy 21. There is now extensive evidence that ultrasound examination, combined with maternal serum biochemical testing at 11 to 13 weeks of gestation, can identify 95% of the fetuses with major chromosomal abnormalities.

Thus, it becomes important to detect such chromosomal abnormalities prenatally and early in the pregnancy so that the couple can be saved from the emotional distress and be counselled about the same.

Various methods of detection are available these days for detection of chromosomal abnormalities and usually a combination of two or three of them is uses simultaneously to arrive at a diagnosis. After the screening's tests are positive confirmatory tests are done so that the pregnancy can be terminated at an earlier period.

Among the tests available the most used ones are:

1. First trimester ultrasound at 11-13th week of gestation for measuring Nuchal Translucency.
2. First trimester screening with dual marker test.
3. Amniocentesis for karyotyping.

It should be emphasized that first trimester screening overestimate detection rate of chromosomal abnormalities. Since these fetuses have an increase loss rate during pregnancy.[2]

The present thesis is aimed to assess the performance of prenatal screening tests i.e. dual marker test which measures beta-hCG and PAPP-A, in terms of test positivity and negativity, first trimester ultrasound which measures the nuchal translucency and presence or absence of nasal bone, and their correlation with diagnostic test which is the karyotyping after amniocentesis.

The assessment of screening tests is done on the basis of detection rate (proportion of affected individuals yielding a positive result), positive predictive value and the negative predictive value.

2. Materials and Methods

A prospective observational clinical study was carried out in Obstetrics and gynaecology department of a tertiary care hospital from December 2018 to December 2019 after getting approval from the ethical committee. A total of 200 pregnant females above 18 years of age attending ANC OPD (Antenatal Check-up Out-patient department) and as per inclusion criteria were included in the study.

2.1. Inclusion criteria

1. All pregnant females above 18 years of age attending ANC OPD (Antenatal Check-up Out-patient department).
2. All patients with singleton viable pregnancy.
3. All patients coming for early ANC (Antenatal Check-up) registration.
4. All patients referred for Amniocentesis from other hospitals.
5. All primigravida and all multigravida females.

2.2. Exclusion criteria

1. Multiple gestations.
2. Patients who refuse to participate.

Nuchal Translucency & Nasal Bone scan followed by Dual Marker Test (DMT) was done in every woman registered at 1st trimester on regular basis. Routine USG scan (Transabdominally 5 MHz and Transvaginally 8 MHz) at 11-13+6 weeks for Nuchal Translucency & Nasal Bone was done by Doctors registered under PC PNDT Act (Pre-Conception and Pre-Natal Diagnostic Techniques Act, 1994). Dual Marker Test was done by standard laboratory. Woman with Nuchal Translucency > 3 mm and/or hypoplastic or absent nasal bone or dual marker test showing increased risk for trisomy 21, trisomy 18, trisomy 13 were the candidates for amniocentesis which was done by senior doctors of a tertiary care hospital. Karyotyping report was be noted and results of all the tests where be compared. Patients followed up to Antenatal period only outcome of MTP (Medical Termination of Pregnancy), abortion or delivery were not considered.

3. Results

A total of 200 pregnant female participants with age 18 years and above were considered in this study. Majority of the study participants were above the age of 30 (53.5%). 10% (20) of the study participants had abnormal karyotype result while 90% (180) had normal karyotype result. The mean age in those having abnormal karyotype was found to be 29.05+/-6.6 years and in those with normal karyotype it was found to be 30.9+/-7.9 years. Incidence of chromosomal abnormalities among those aged 35 and above was 5.2% and among those aged less than 35 was 12%, it is also observed that among those who had chromosomal abnormalities 85% were less than 35 years. (Table 1)

It was observed that 10% (20) of the participants had abnormal karyotype while 90% (180) had normal result. Those who had abnormal karyotype majority i.e., 75% (15) had trisomy 21 followed by 20% (4) having trisomy 18 while 5% (1) had trisomy 13. So, among the various chromosomal abnormalities encountered, Down's syndrome (trisomy 21) was the most common (75%). (Table 2)

Table 1: Distribution of abnormality and age group among study participants. (N=200)

			Abnormality present or absent		Total
			Abnormality present	Abnormality absent	
Age wise grouping	Less than 35	Count	17	125	142
		% within age wise grouping	12.0%	88.0%	100.0%
		% within abnormality present or absent	85.0%	69.4%	71.0%
	above 35	Count	3	55	58
		% within age wise grouping	5.2%	94.8%	100.0%
		% within abnormality present or absent	15.0%	30.6%	29.0%
Total		Count	20	180	200
		% within age wise grouping	10.0%	90.0%	100.0%
		% within abnormality present or absent	100.0%	100.0%	100.0%

Table 2: Distribution of detected abnormalities on basis of karyotype. (N=20)

Abnormality	Frequency	Percentage
Trisomy 21	15	75
Trisomy 18	4	20
Trisomy 13	1	5
Total	20	100

It was observed that the mean NT in those with chromosomal abnormality was 3.09+/-0.9mm and in those with normal karyotype was 2.49+/-0.7mm. The difference was statistically significant with p-value 0.002. Out of 200, it was observed that 39.5% (79) of the study participants had Nuchal translucency of 3mm and above while 60.5% (121) had values less than 3mm. Among those with abnormal karyotype the NT value was 3mm and above in 75% of cases (15). It was observed from the above table that the NT cut-off value of 3mm and above was able to detect 73.3% cases of trisomy 21, 75% cases of trisomy 18 and 100% cases of trisomy 13. (Table 3)

It was observed that nasal bone was absent in 16.5% (33) of the foetuses while it was present in the rest 83.5% (167). Out of 20 abnormal cases nasal bone was absent in 30% cases (6) with abnormal karyotype. It was observed that nasal bone was absent in 33.5% cases with trisomy 21, 25% cases with trisomy 18 and 15% cases with normal karyotype. (Table 4)

Out of 200 it was observed that dual marker test was positive in 58.5% (117) study participants while it was negative in 41.5% (83) participants. Out of 20 cases with chromosomal abnormality detected by karyotyping dual marker test was positive in 35% (7) of the cases while it was negative in the remaining 65% (13). It was observed that among those with trisomy 21 DMT was positive in 26.7% (4) cases and in those with trisomy 18 it was positive in 75% (3) cases. (Table 5)

4. Discussion

In our study majority of the study participants (29%) were aged above 35 followed by those between 31-35years (24%). Daniela Neagos et al in their study to assess the importance of screening and prenatal diagnosis in identification of numerical chromosomal abnormalities observed that 0.43% of the participants were 20yrs and younger 4.57% were aged 21-25, 22.95% were aged 26-30, 34.5% were between 31-35years and 37.5% were 35 and above, the findings in the present study are closer to those observed by Neagos et al where in the majority of the participants were aged 35and above followed by those ages 31-35 and least proportion was aged less than 20years.[3]

It was observed in our study that 10% (20) of the study participants had abnormal karyotype result while 90% (180) had normal karyotype result. The mean age in those having abnormal karyotype was found to be 29.05+/-6.6years and in those with normal karyotype it was found to be 30.9+/-7.9 years. Comas et al in their study observed that mean age in those with chromosomal abnormality was 34+/-4.9years. The findings of the present study are different from those observed by Comas et al.[4]

In our study we observed that the incidence of chromosomal abnormalities among those aged 35 and above was 5.2% and among those aged less than 35 was 12%, it is also observed that among those who had chromosomal abnormalities 85% were less than 35 years. J Szabo et al in their study observed that incidence of chromosomal abnormalities was 2.9% and 0.43% in women aged 35 and above and those aged less than 35. The findings of the

Table 3: Detection of various chromosomal abnormalities with respect to NT. (N=20)

NT value	Karyotype finding		
	Trisomy 21	Trisomy 18	Trisomy 13
3 and above	11(73.3%)	3(75%)	1(100%)
less than 3	4(26.7%)	1(25%)	0
total	15(100%)	4(100%)	1(100%)

Table 4: Detection of various chromosomal abnormalities on karyotyping and their correlation with nasal bone status. (N=20)

Nasal bone status	Karyotype finding			
	Trisomy 21	Trisomy 18	Trisomy 13	Normal
Absent	5(33.5%)	1(25%)	0	27(15%)
Present	10(66.7%)	3(75%)	1(100%)	153(85%)
Total	15(100%)	4(100%)	1(100%)	180(100%)

Table 5: Dual marker test and correlation with various karyotyping findings. (N=20)

Dual marker test result	K aryotype finding			
	Trisomy 21	Trisomy 18	Trisomy 13	Normal
Positive	4(26.7%)	3(75%)	0	110(61.1%)
Negative	11(73.3%)	1(25%)	1(100%)	70(38.9%)
Total	15(100%)	4(100%)	1(100%)	180(100%)

present study are more than those encountered by Szabo et al.[5]

We found that 10% of the participants had abnormal karyotype while 90% had normal result. Snijders et al in their study to assess maternal age specific risks for trisomies at 9014weeks found the incidence of fetal chromosomal abnormalities to be 2.8%, the findings of the present study are more than those reported by Snijders et al.[6]

We observed from our study that among those who had abnormal karyotype majority i.e. 75% (15) had trisomy 21 followed by 20% (4) having trisomy 18 while 5% (1) had trisomy 13. Baverley Hewitt in her study to assess nuchal translucency in the first trimester observed that trisomy 21 was present in 41.6% cases. The findings of the present study are not consistent with those reported by Beverly Hewitt.[7]

In our study we observed that the mean NT in those with chromosomal abnormality was 3.09+/-0.9mm and in those with normal karyotype was 2.49±0.7mm. The difference was statistically significant with p-value 0.002. D. Loncar et al in their study also observed a statistically significant difference between the values of NT between chromosomally normal and abnormal children with p-value less than 0.05, the mean MT in abnormal group was 2.49± 0.37mm and in normal group was 1.92± 0.39. The findings of present study are also similar in the sense that statistically significant difference is observed between NT values in normal and abnormal group but the mean BT observed in both is different from those observed by Loncar et al.[8]

In our study we observed that nasal bone was absent in 33.5% cases with trisomy 21, 25% cases with trisomy 18 and 15% cases with normal karyotype. C. Larose et al in their study observed that among foetuses with Down's syndrome nasal bone was absent in 52.4% cases. The findings of present study are lower than those observed by Larose et al.[9]

In our study we observed that among those with trisomy 21 DMT was positive in 26.7% (4) cases and in those with trisomy 18 it was positive in 75% (3) cases. K. Nicolaides et al in their study to assess nuchal translucency and other first trimester sonographic markers of chromosomal abnormalities observed that the detection rate with dual markers was around 59.8% for trisomy 21. The findings in the present study are less than those reported by Nicolaides et al.[10]

In our study it was observed that when NT cut-off of 3mm and dual marker positivity are used in parallel the sensitivity in identifying abnormal karyotype is raised to 83.75%. H.S.Cuckle et al in their study observed that routine ultrasound nuchal translucency with addition of dual markers will increase the detection rate to 86.4%, the findings of present study are consistent with those reported by Cuckle et al.[11]

5. Conclusions and Recommendations

Chromosomal abnormalities are one of the important conditions found among ANC mothers and need to be detected at the earliest. Prenatal diagnosis with ultrasonography for nuchal translucency either alone or in combination offers good detection rate for these chromosomal abnormalities. Down's syndrome is the commonest chromosomal abnormality encountered.

Based on the findings of the study it can be recommended that Prenatal diagnosis for detection of chromosomal abnormalities must form an integral part of antenatal care. Nuchal translucency by ultrasonography either alone or in combination with dual marker test offers effective detection of chromosomal abnormalities and must be offered to all pregnant women at 10-13 weeks of pregnancy.

6. Source of Funding

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7. Conflict of Interest

None.

References

1. Rao L, Murthy K, Babu A, Venkata P, Deenadayal M, Singh L. Chromosome inversions and a novel chromosome insertion associated with recurrent miscarriages in South India. *Arch Gynecol Obstet*. 2005;272(4):273–7.
2. Cuckle HS, Wald NJ, Thompson SG. Estimating a woman's risk of having a pregnancy associated with Down's syndrome using her age and serum alpha-fetoprotein level. *Br J Obstet Gynaecol*. 1987;94(5):387–402.
3. Neagos D, Cretu R, Sfetea RC, Bohiltea LC. The importance of screening and prenatal diagnosis in the identification of the numerical chromosomal abnormalities. Maedica (Buchar). *Maedica (Bucur)*. 2011;6(3):179–84.
4. Comas C, Torrents M, Muñoz A, Antolín E, Figueras F, Echevarría M. Measurement of nuchal translucency as a single strategy in trisomy 21 screening: should we use any other marker? *Obstet Gynecol*. 2002;100(4):648–54.
5. Szabó J, Gelén J, Szemere G. First-trimester ultrasound screening for fetal aneuploidies in women over 35 and under 35 years of age. *Ultrasound Obstet Gynecol*. 1995;5(3):161–3.
6. Snijders RJM, Holzgreve W, Cuckle H, Nicolaides KH. Maternal age-specific risks for trisomies at 9-14 weeks' gestation. *Prenat Diagn*. 1994;14(7):543–52.
7. Hewitt B. Nuchal Translucency in the First Trimester. *Aust New Zeal J Obstet Gynaecol*. 1993;33(4):389–91.
8. Lončar D. Credibility of the combined test in prenatal diagnostics. *Genetika*. 2011;43(2):285–96.
9. Larose C, Massoc P, Hillion Y, Bernard JP, Ville Y. Comparison of fetal nasal bone assessment by ultrasound at 11-14 weeks and by postmortem X-ray in trisomy 21: a prospective observational study. *Ultrasound Obstet Gynecol*. 2003;22(1):27–30.
10. Nicolaides KH. Nuchal translucency and other first-trimester sonographic markers of chromosomal abnormalities. *Am J Obstet Gynecol*. 2004;191(1):45–67.
11. Cuckle HS, Lith J. Appropriate biochemical parameters in first-trimester screening for Down syndrome. *Prenat Diagn*. 1999;19(6):505–12.

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