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Screening for trisomy 21by maternal age, maternal serum biochemistry and nuchal translucency at 11-14 weeks of pregnancy: A South Indian study

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Abstract
Background: To determine the relation between chromosomal abnormality trisomy 21 and trisomy 18 in the pregnancy with respect to maternal age.
Materials and Methods: This was a screening study for trisomy 21 and 18 by a combination of maternal age, maternal serum biochemistry and foetal Nuchal Translucency (NT) and crown- rump length (CRL), conducted at one of the south Indian private medical college, Kerala. We screened 88 pregnant women during their 11-14 weeks of pregnancy from 10th February 2019 to 10th August 2020.
Results: The study included 86 singleton pregnancies and 2 twin pregnancies, mean age 26.53(SD±5.2), 74% were between 21-30 years of age and majority of them from 12 weeks of their pregnancy. In this study the mean CRL was 58.3(SD±10) and 5.7% (n=5) were chromosomally abnormal among this two were positive for Downs syndrome 60% (n=3), one was trisomy-18 20% (n=2), Nuchal translucency (NT) and age (P= 0.00: R^2 =0.477), crown- rump length and age (P= 0.041: R^2 =-0.219) have an association. The study shows an association with chromosomal abnormality with age (P= 0.00: R^2 =0.00), NT (P= 0.00: R^2 =0.00) and it has a correlation with CRL (R^2=0.00), free β-hCG (R^2=0.00).

Keywords: Chromosomal abnormality, crown-rump length, nuchal translucency, downs syndrome, biochemistry, screening, trisomy 21

Introduction
Worldwide 7.9 million infants were born with serious birth defects [1]. It was estimated that every year about one in every 33 babies in United States live with birth defects [2, 3]. In India 7% of neonatal mortality is, and 3.3 million under-five deaths are associated with birth defects its prevalence varies from 61- 69.9/1000 live births[4]. Over 50% of birth defects are unknown. The birth defects mainly associated with chromosomal abnormalities like trisomy-21 (Downs syndrome) that was about 1 in 1000 and trisomy-18 (Edward syndrome) about 1 in 5000 births [5, 6]. The Economical and psychological consequences of abnormal deliveries can be prevented by early detection of Chromosomal abnormalities trough maternal biochemical values like free β-hCG and PAAP-A values and foetal measurements like NT and CRL [7-10]. There for early detection of chromosomal abnormalities are very essential in India like country trough maternal biochemical values and foetal measurements Nuchal Translucency and crown- rump length (CRL) can be calculated through sonography in the 11-14 weeks.

Materials and Methods
Study settings
The study conducted in a Sree Utradam Thirunal Medical College, Thiruvanthapuram, and Kerala. The screening included 88 pregnant women at their first trimester pregnancy from 10th February 2019 to 10th August 2020.

Inclusion criteria
- 11-14 weeks of pregnancy who took an appointment in Obstetrics & Gynaecology OPD.

Exclusion criteria
- Late pregnancy
- Above 15 weeks

- Not willing to sign in informed consent from

Procedure

This was a screening study for trisomy-21 and 18 by a combination of maternal age, maternal serum biochemistry and fetal Nuchal Translucency (NT) and crown-rump length (CRL). All the participants had given consent for their results to be used anonymously for research purposes. We maintained each person's data in one excel sheet and kept it very confidentially in Primary investigator's PC. The measurements of crown-rump length and nuchal translucency were calculated according to the Foetal Medicine Foundation guidelines (11-13 weeks of screening). We used Mindray DC-7 ultrasound machine for sonography and maternal serum biochemistry was studied with Roche COBAS e601 immunoassay analyser that uses electrochemiluminescence technology. Then the values were entered into the ROSH software SSDW and which was approved by Foetal Medicine Foundation. The data collected included demographic details like maternal age, weight, history of smoking, insulin dependency and history of IVF of the mother and foetal NT, foetal crown- rump length (CRL), maternal serum free β-hCG and PAPP-A, combined estimated risk for trisomy 21 and 18 at the 11-14 weeks of live pregnancy.

Statistical analysis

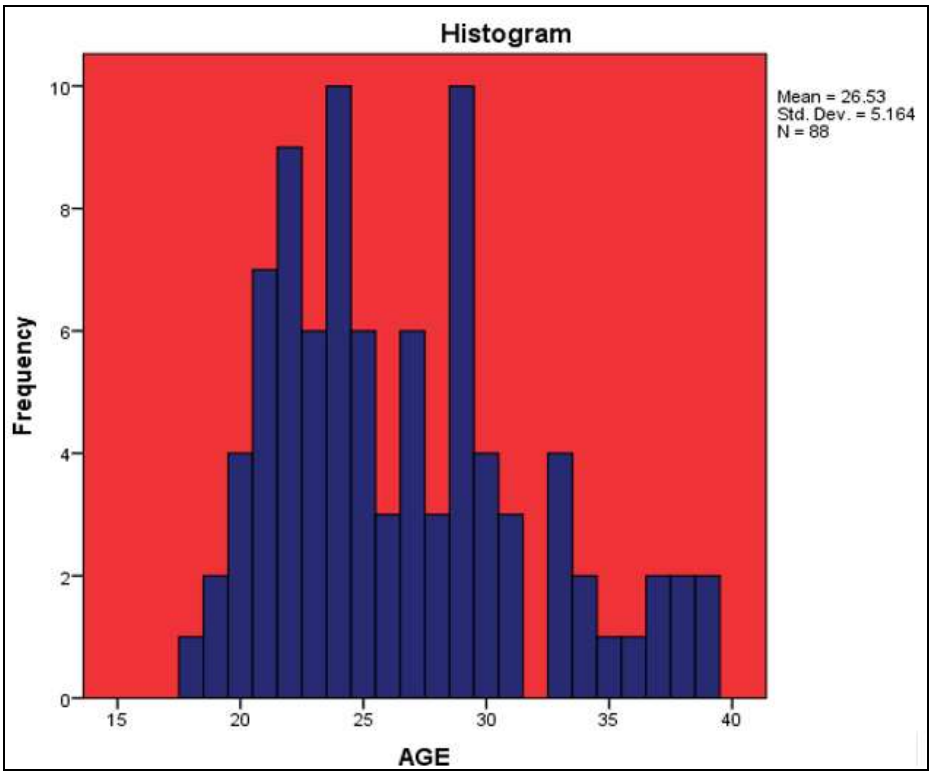
The data was expressed in number, percentage, mean and standard deviation. Statistical Package for Social Sciences (SPSS 16.0) version used for analysis. P value less than 0.05 considered statistically significant at 95% confidence interval.

Results

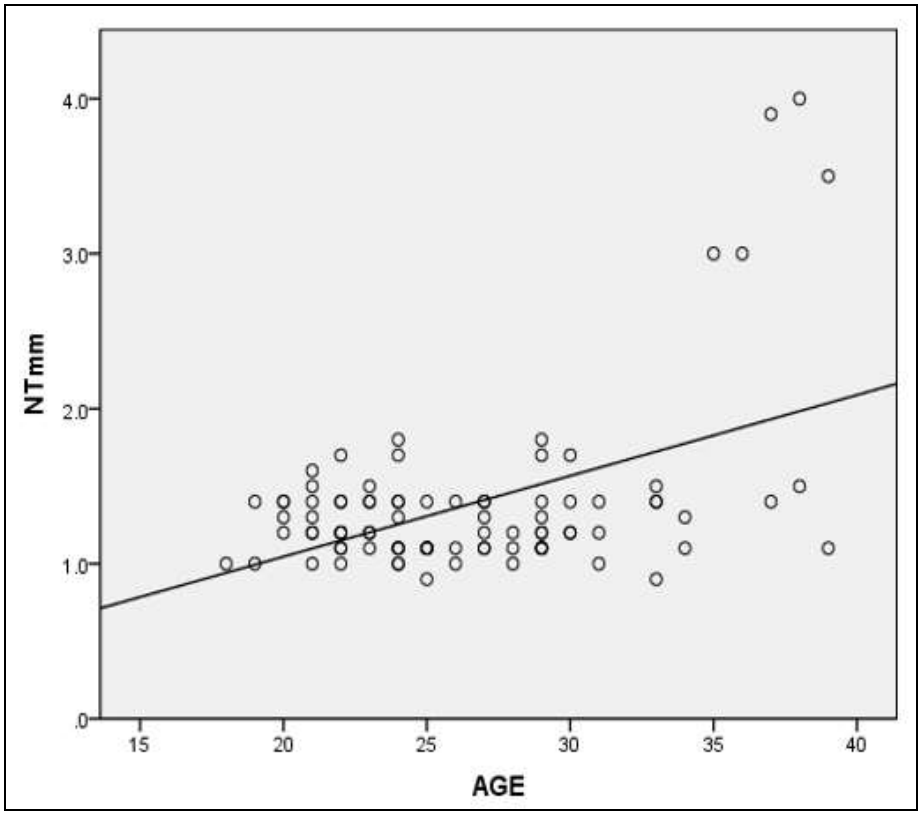
During the study period a total of 86 singleton pregnancies and two twin pregnancies were subjected to the screening for trisomy-21 and trisomy-18 along with foetal NT and maternal serum free β-hCG and PAPP-A. The mean maternal age was 26.53 (SD ±5.2) ranges from 18 -39 years and about 74% (Fig.1) most of the participants were from the age group of 21-30years (n=65) and majority of the participants were screened at 12 weeks (range 11-14 weeks) of pregnancy. In this study the mean CRL was 58.3(SD±10). In the total study subjects Abnormal foetal NT was above the 95th centile of the reference range, supplied by the Foetal Medicine Foundation London, in this 5.7% (n=5) were chromosomally abnormal. Among this two were positive for Downs syndrome 60% (n=3), one was trisomy -18 20% (n=2), probably poor prognosis. It has been found that the Nuchal translucency was increased with age (Fig.2), this relationship was highly significant because p-value was0.00 and the crown– rump length decreased with age (Fig.3). The MOM values of free β-HCG and PAPP-A were highly significant and was positively correlated (Fig.4) (Table. 1). The bi-variate analysis shows that maternal factors like age and foetal factor like Nuchal Translucency value shows high significance with the outcome chromosomal abnormality (Table. 2).

Discussion

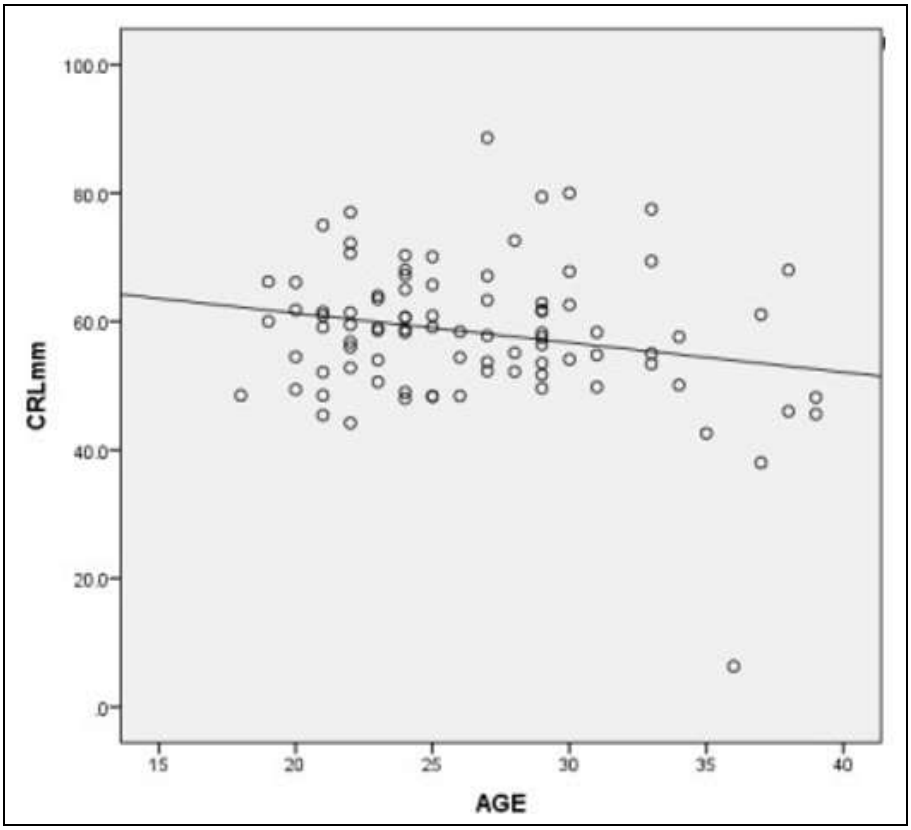
Over the last decade trisomy study occurs at 11-14 weeks of pregnancy of a pregnant woman by using the combination of maternal blood biochemical markers like free β-hCG and PAAP-A values and foetal Nuchal translucency [8, 11-13]. The screening helps the doctor for early detection of the chromosomal abnormalities and its types [9, 14, 15]. The increasing maternal age increases the risk of getting chromosomal abnormalities in the foetus [16] and maternal biochemical marker abnormal values like free β-hCG and PAAP-A and the foetal factors like increased NT value and decreased CRL values also influences the foetal outcomes like Downs syndrome [10, 12, 17], Trisomy- 18 [18, 19].



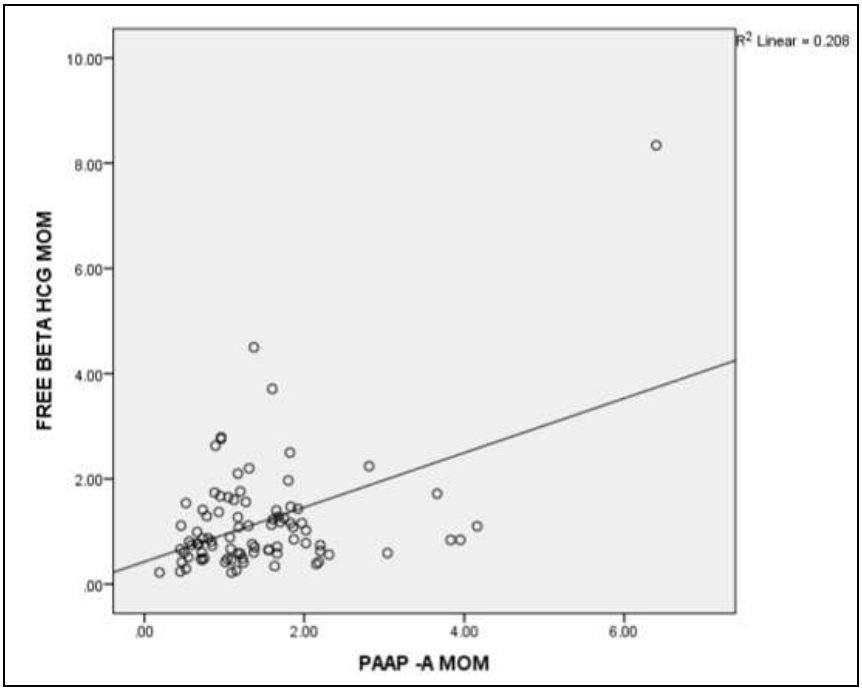
Graph 1: Distribution of patients based on the age



Graph 2: Correlation between Nuchal translucencies with age



Graph 3: Correlation between crown rump length with age



Graph 4: Correlation between MOM values of free beta-hCG and PAAPA

Table 1: Association of between maternal and foetal values

Observation	AGE	
Variable	**Correlation coefficient**	**p value**
Nuchal translucency	0.477**	0.00***
Crown-rump length	-0.219*	0.041**
Free β-hCG	0.045	0.677
PAPP-A	-0.25	0.056
Correlation between MOM values of free β-hCG		
PAPP-A	0.456**	0.00

Table 2: Correlation of chromosomal abnormalities with maternal and foetal factors

Chromosomal abnormality (Outcome) / Variable	Correlation	p value
Age	0.00	0.00
CRL (mm)	0.253	0.00
NT (mm)	0.00	0.00
Free beta-hCG (MOM)	0.248	0.00
PAAP-A (MOM)	0.842	0.065

Conclusion

Increased Age of the mother and maternal biochemical values like free β-hCG and PAAP-A values and foetal measurements like NT and CRL helps to early detection of the chromosomal abnormalities of the foetus. The parents in the developed nations exhibit an increased interest on early determination of chromosomal abnormality and this early anomaly detection helps them to take an appropriate decision and it prevents from the adverse outcomes in the future.

Conflict of interest: Nil

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