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ORIGINAL RESEARCH

Study on early detection of chromosomal anomalies, maternal outcome by performing biochemical and sonological tests between 11-14 wk of gestational age

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ABSTRACT

Introduction: Chromosomal disorders are caused by changes occurring in either chromosome number or structure usually during the formation of gametes or soon after fertilisation. These changes can affect the autosomes, with chromosomal disorders divided into the two corresponding groups.

Aims: To screen for chromosomal abnormalities namely trisomy 21, 18 & 13, during the first trimester of pregnancy using biochemical tests like freeβ-hCG, PAPP-A and ultra sound measurements of nuchal translucency, nasal bone and ductus venosus flow.

Materials and methods:The Prospective study on early detection of chromosomal anomalies by performing a combination of biochemical and sonological tests between 11-14 wk of gestation. To the existing first trimester screening tests of double marker (free β- hCG and PAPP-A) Combined with NT,two more sonological markers were added is NB,DVF to improve the diagnostic sensitivity.

Results: Mean age at presentation was 28yrs.Prevalence of high risk after the combined test is 7%, none of them had chromosomal anomalies. However low PAPP-A (<0.52 MoM) was significantly associated with increased preeclampsia, preterm delivery and miscarriage.Absent NT can also be an independent marker for identifying high risk cases.

Conclusion: The analysis of the individual & combination of various markers have revealed interesting findings of maternal outcome, some of them having statistically significant.

Keywords:Nuchal Translucensy(NT), Pregnancy Associated Plasma Protein A(PAPP-A), Ductus venosus flow(DVF).

INTRODUCTION

Every woman has a risk that her fetus/baby has a chromosomal defect. In order to calculate the individual risk, it is necessary to take into account the background risk (which depends on maternal age, gestation and previous history of chromosomal defects) and multiply this by a series of factors, which depend on a series of screening tests carried out during the course of the pregnancy. Every time a test is carried out the background risk is multiplied by the test factor to calculate a new risk, which then becomes the background risk for the next test. This process is called sequential screening. With the introduction of OSCAR (one-stop clinics for assessment of risk), this can all be achieved in one session at about 12 weeks of pregnancy[8].

Prenatal diagnosis by various screening methods is performed during different gestational weeks to assess the individual's risk for chromosomal anomalies of the fetus. The risk of birth defects for all patients is 2-3%. Chromosome abnormalities account for approximately 10% of birth defects. Trisomy 21, commonly known as Down syndrome is one of the commonest chromosomal anomalies occurring in approximately 1 in 500 live births[1]. Worldwide, more than 2 lakh children are born with Down syndrome every year.

In India the overall prevalence of Down syndrome is 1.17/1000 live births[2]. The risk of genetic burden in India according to a multi centre study by ICMR is 14% (Bangalore 12.6%, Mumbai 23%) [3]. The emphasis shifted to the first trimester when it was realized that the great majority of fetuses with major aneuploidies can be identified by a combination of maternal age, maternal serum free β-human chorionic gonadotropin (β-hCG) and pregnancy-associated plasma protein-A (PAPP-A) and fetal nuchal translucency (NT) thickness. In the last 10 years, several additional first trimester sonographic markers have been described which improve the detection rate of aneuploidy and reduce the false-positive rate[4].We aim to estimate the incidence of chromosomal anomalies in our hospital and study the maternal and fetal outcome of these pregnancies.

MATERIALS AND METHODS

It is a Prospective study in hospital outpatient clinic all pregnant women who are attending the department of DDH are registered. Those women who are in their first trimester are recruited for the study after obtaining informed consent a total of 100 pregnant women both primi& multi gravida in their first trimester are selected and properly designed proformas are filled with relevant information.

INCLUSION CRITERIA

Primi and multi gravidae, Period of gestation (11-13+6 weeks).

EXCLUSION CRITERIA

Gestation age > 14 weeks and<11 weeks.

Patients attending the Out Patient Department of DDH&RC were registered and a detailed history was obtained from 100 pregnant women. Pregnant women between 11– 13+6 weeks were selected for the study purpose. A specially designed proforma was filled up after obtaining written consent from the patient.

Peripheral venous blood sample was drawn for the bio-chemical markers (β -hCG& PAPP-A) in addition to the routine antenatal profile followed in our hospital as per protocol.

First Trimester Serum Screen test Includes Serum free β-hCG (hCG), pregnancy associated plasma protein A (PAPP-A) combined with patient supplied maternal age .Relevant patient history (eg, previous Down syndrome pregnancy) was also noted.Complete information is necessary to interpret the test. Patient information was provided to the laboratory using the Maternal Prenatal Screening test request form.

The data was analysed with statistical methods of mean, standard deviation, chisquare and P value for variable analysis of data. We have taken the support of SPSS software.

RESULTS

In the present study the data collected from 100 pregnant women between 11-14 wk of gestational age has been analysed. Biochemical analysis was performed on maternal blood samples for serum markers (free β-hCG, PAPP-A) & ultrasonography was performed at the same time to check for 3 sonographic markers namely-nuchal translucency thickness(NT) ,nasal bone(NB) and ductus venosus flow (DVF). Parameters that have been analysed are age, education, husband's age, parity, gestational age at screening test and consanguinity.

The mean age of pregnant women in the present study is 28yrs. Maximum number of pregnant women in the study were in the age group of 26-30yrs. 54% of pregnant women had degree qualification. The average age of the husbands in present study is 32.52yrs.Maximum numbers of spouses are in the age range of 26-35yrs. Majority of pregnant women in present study are primigravid, 64% and 36% are multigravidas. The test was accepted by pregnant women more in 11-13 wks and only 8 were in 14 wks gestation age. The analysis shows 14% had a consanguinous marriage, 86% had a non consanguinous marriage. The average maternal weight was 58.58kg. Maximum weight was 74kg, minimum weight was 42kgs.

Table-1: The estimated ranges of variable in present study.

free β- hCG	No of women	Percentages
0.1-1.0	63	63
1.01-2.0	28	28
2.01-3.0	6	6
3.01-4.0	3	3
PAPP-A(MoM)		
0.1-1.0	60	60
1.01-2.0	30	30
2.01-3.0	6	6
3.01-4.0	4	4
NT(mm)		
0.5-1.0	40	40
1.01-1.5	44	44
1.51-2.0	14	14
2.01-2.5	1	1
2.51-3.0	1	1

This is estimated as multiples of median(MoM) in the ranges of 0.1-4 MoM. PAPP-A has been estimated as multiples of median(MoM) in the ranges of 0.1-4 MoM.. The Nuchal thickness has beenranging between 0.5-3.0 mm.

Table-2: Absent Nasal Bone(4/100) in patients of present study

History	Free β-hcG(MoM)	PAPP-A(MoM)	NT mm	NB	DVF	Others
Primi,12wks	3.05	0.18	1.2	-	N	High risk,spont. Abortion, Normal karyotype.
Primi,14wks	3.14	0.24	0.94	-	N	PE,PTL(36wks)NV,High risk
Primi,11wks	3.12	0.2	0.92	-	N	PE,NVD,High risk
Multi,CM,13wks	2.54	0.53	1.1	-	**AbN**	Abortionat14wks(hydrops)

Colourdoppler shows 4% pregnant women having abnormal DVF. Among these, 1% women developed preeclampsia, 1% pregnant women developed gestational hypertension. 1% pregnant women underwent MTP at 14wks in view of hydrops. 1% of women had uneventful pregnancies

Table-3:Abnormal DVF(4/100) in patients of present study

History	BetahcG (MoM)	PAPP-A(MoM)	NT mm	NB	DVF	others
Primi,12wks	2.56	1.25	3	+	**AbN**	High risk,PE,NVD
Primi,11wks	2.42	0.45	0.95	+	**AbN**	High risk, Gest HTN, NVD
Primi,11wks	2.32	0.89	1.3	+	**AbN**	NVD
Multi,CM,13wks	2.54	0.53	1.1	**Absent**	**AbN**	MTP at 14 wks(hydrops)

Table-4: Free β-hCG and PAPP-A in association with maternal outcome

Free β-hCG Vs Gest.HTN			**Gest.HTN**		**Total**
			no	**yes**	
Free β- hCG	<0.539	Count	27	1	28
		% within free β- hCG	96.4%	3.6%	100.0%
	>=0.54	Count	63	9	72
		% within free β- hCG	87.5%	12.5%	100.0%
Total		Count	90	10	100
		% within free β- hCG	90.0%	10.0%	100.0%
Free β-hCG Vs Preeclampsia			no	yes	
Free β- hCG	<0.539	Count	25	3	28
		% within free β- hCG	89.3%	10.7%	100.0%
	>=0.54	Count	64	8	72
		% within free β- hCG	88.9%	11.1%	100.0%
Total		Count	89	11	100
		% within free β- hCG	89.0%	11.0%	100.0%
Free β- hCG Vs Miscarriage			No	yes	
Free β- hCG	<0.5	Count	23	1	24
		% within free β- hCG	95.8%	4.2%	100.0%
	>=0.5	Count	72	4	76
		% within free β- hCG	94.7%	5.3%	100.0%
Total		Count	95	5	100
		% within free β- hCG	95.0%	5.0%	100.0%
PAPP-A Vs Gest.HTN			No	yes	
PAPP-A	<0.52	Count	9	3	12
		% within PAPP-A	75.0%	25.0%	100.0%
	>=0.52	Count	81	7	88
		% within PAPP-A	92.0%	8.0%	100.0%
Total		Count	90	10	100
		% within PAPP-A	90.0%	10.0%	100.0%
PAPP-A with preeclampsia					
PAPP-A	<0.52	Count	8	4	12
		% within PAPP-A	66.7%	33.3%	100.0%
	>=0.52	Count	81	7	88
		% within PAPP-A	92.0%	8.0%	100.0%
Total		Count	89	11	100
		% within PAPP-A	89.0%	11.0%	100.0%
PAPP-A Vs Preterm delivery					
PAPP-A	<0.52	Count	9	3	12
		% within PAPP-A	75.0%	25.0%	100.0%
	>=0.52	Count	85	3	88
		% within PAPP-A	96.6%	3.4%	100.0%
Total		Count	94	6	100

		% within PAPP-A	94.0%	6.0%	100.0%
PAPP-A Vs Miscarriage					
PAPP-A	<0.4	Count	5	3	8
		% within PAPP-A	62.5%	37.5%	100.0%
	>=0.4	Count	90	2	92
		% within PAPP-A	97.8%	2.2%	100.0%
Total		Count	95	5	100
		% within PAPP-A	95.0%	5.0%	100.0%

Table-5: Nuchal Translucensy (NT)and Maternal outcome.

NT Vs gestational hypertension				**Total**
		No	**Yes**	
<2.5	Count	89	10	99
	% within NT	89.9%	10.1%	100.0%
>=2.5	Count	1	0	1
	% within NT	100.0%	.0%	100.0%
Total	Total	90	10	100
	% within NT	90.0%	10.0%	100.0%
NT Vs Preeclampsia				
<2.5	Count	89	10	99
	% within NT	89.9%	10.1%	100.0%
>=2.5	Count	1	0	1
	% within NT	100.0%	.0%	100.0%
Total	Count	90	10	100
	% within NT	90.0%	10.0%	100.0%
NT Vs Preterm delivery				
<2.5	Count	93	6	99
	% within NT	93.9%	6.1%	100.0%
>=2.5	Count	1	0	1
	% within NT	100.0%	.0%	100.0%
Total	Count	94	6	100
	% within NT	94.0%	6.0%	100.0%
NT Vs Miscarriage				
<2.5	Count	94	5	99
	% within NT	94.9%	5.1%	100.0%
>=2.5	Count	1	0	1
	% within NT	100.0%	.0%	100.0%
Total	Count	95	5	100
	% within NT	95.0%	5.0%	100.0%

The correlation is fetal NT and gestational hypertension, preterm labor and miscarriage not statistically significant (P value 0.738).

The correlation between fetal NT and preeclampsia is statistically significant (P value 0.004).

Table-6:Ductus venosus flow(DVF) and Maternal outcome.

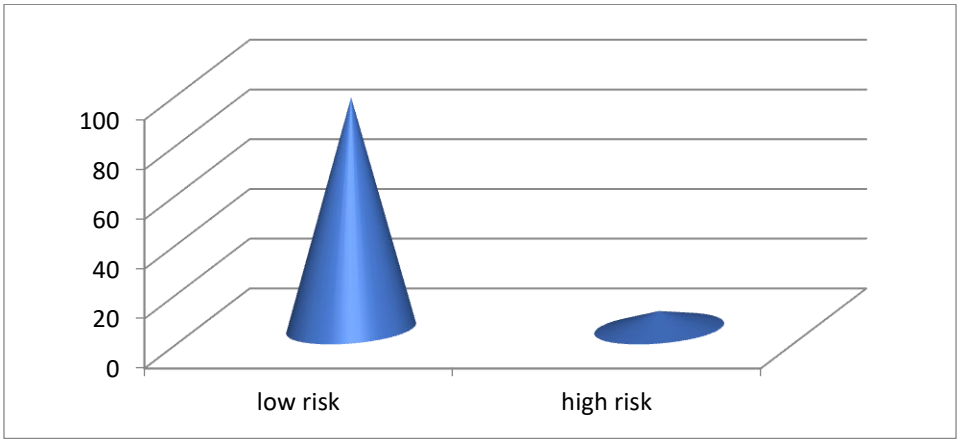
DVF Vs gestational hypertension				**Total**
		No	**Yes**	
abnormal	Count	3	1	4
	% within DVF	75.0%	25.0%	100.0%
normal	Count	87	9	96

	% within DVF	90.6%	9.4%	100.0%
Total	Count	90	10	100
	within DVF	90.0%	10.0%	100.0%
DVF Vs Preeclampsia				
abnormal	% within DVF	2	2	4
	Count	50.0%	50.0%	100.0%
normal	% within DVF	87	9	96
	Count	90.6%	9.4%	100.0%
Total	within DVF	89	11	100
	% within DVF	89.0%	11.0%	100.0%
DVF Vs Preterm delivery				
abnormal	% within DVF	4	0	4
	Count	100.0 %	.0%	100.0%
normal	% within DVF	90	6	96
	Count	93.8%	6.3%	100.0%
Total	within DVF	94	6	100
	% within DVF	94.0%	6.0%	100.0%
DVF Vs Miscarriage				
abnormal	% within DVF	3	1	4
	Count	75.0%	25.0%	100.0%
normal	% within DVF	92	4	96
	Count	95.8%	4.2%	100.0%
Total	within DVF	95	5	100
	% within DVF	95.0%	5.0%	100.0%

The correlation is DVF and gestational hypertension, preterm labor and miscarriage not statistically significant.

The correlation between DVF and preeclampsia is statistically significant.

Figure-1:Combined risk (free β-hCG ,PAPP-A,NT thickness) assessment and Maternal outcome .



The screening test results show: High risk category for chromosomal abnormalities 7%. Low risk pregnant women are 93%.On follow up of delivery, among these high risk women, 1% had abortion. The analysis of the abortus showed normal karyotype.

4% of these high risk pregnant women developed preeclampsia. 1% developed gestational HTN.1% women had uneventful pregnancies. But none of them had any babies with chromosomal abnormality, the babies had normal karyotypes.

Table: 6: Double marker combined high risk: 7/100

history	Free β- hCG (MoM)	PAPP-A(MoM)	NT mm	NB	DVF	others
Multi,13 wks	2.6	0.53	1.7	+	N	PE,EL.LSCS
primi,12 wks	2.56	1.25	3	+	abN	PE,NVD
primi,12 wks	3.05	0.18	1.2	**absent**	N	Spont. abortion. high risk, Normal karyotype
primi,14 wks	3.14	0.24	0.94	**absent**	N	PE.PTL(36wks), VD
primi,11 wks	3.12	0.2	0.92	**absent**	N	PE,NVD
Multi,14 wks	2.54	0.52	0.94	+	N	NVD
primi,11 wks	2.42	0.45	0.95	+	AbN	GestHTN,NVD

Table-7:Combined Risk and Maternal outcome.

Combined Risk Vs gestational hypertension					Total
			No	Yes	
Combined Risk	High risk	Count	6	1	7
		% within imp	85.7%	14.3%	100.0%
	Low risk	Count	84	9	93
		% within imp	90.3%	9.7%	100.0%
Total		Count	90	10	100
		% within imp	90.0%	10.0%	100.0%
Combined Risk **Vs Preeclampsia**					
High risk		Count	1	6	7
		% within imp	14.3%	85.7%	100.0%
Low risk		Count	88	5	93
		% within imp	94.6%	5.4%	100.0%
Total		Count	89	11	100
		% within imp	89.0%	11.0%	100.0%
Combined Risk **Vs Preterm delivery**					
High risk		Count	6	1	7
		% within imp	85.7%	14.3%	100.0%
Low risk		Count	88	5	93
		% within imp	94.6%	5.4%	100.0%
Total		Count	94	6	100
		% within imp	94.0%	6.0%	100.0%
Combined Risk **Vs Miscarriage**					
High risk		Count	6	1	7
		% within imp	85.7%	14.3%	100.0%
Low risk		Count	89	4	93
		% within imp	95.7%	4.3%	100.0%
Total		Count	95	5	100
		% within imp	95.0%	5.0%	100.0%

The correlation is Combined Risk and gestational hypertension, preterm labor and miscarriage not statistically significant.

The correlation between Combined Risk and preeclampsia is statistically significant.

Table-8: Variables in correlation with maternal outcome in study.

Parameter	Maternal outcome	Statistical significant
PAPP-A(<0.52MoM)	Preeclampsia	0.008
PAPP-A(<0.52MoM)	Preterm delivery	0.003
PAPP-A(<0.4MoM)	Miscarriage	0.0001
NT(>2.5mm)	Preeclampsia	0.004
NB(absent)	miscarriage	0.0001
NB(absent)	preeclampsia	0.0001
DVF(abnormal)	preeclampsia	0.011
Combined test assessment (high risk)	preeclampsia	0.0001

Statistically significant with all parameters Vs maternal outcome.

DISCUSSION

Chromosomal abnormalities are one of the most important causes of perinatal mortality, childhood handicap, lifelong difficulties & enormous socioeconomic burden. The risk of birth defects for all pregnancies is 2-3% and chromosome abnormalities account for approximately 10% of them.Trisomy 21, commonly known as Down syndrome is one of the commonest chromosomal anomalies occurring in approximately 1 in 500 live births[1].

As there is no cure available yet for chromosomal abnormalities, medical termination is the only available option for major congenital anomalies. The earlier the detection of these anomalies, the safer it is for the mother to take a decision either to undergo the procedure of termination or to continue for a natural course.

The mean age of pregnant women was 28yrs.According to **Ronald Wapner et al[5],** in their study, mean maternal age was 42 yrs. They found the prevalence of chromosomal anomalies (trisomy21) was 1:321. But in the present study we did not have trisomy 21, probably because of low mean age i.e 28yrs in the study group and low sample size. According to **Valerie J Rappaport et** al[6], the risk of down syndrome 1:1031 and risk of other chromosomal abnormality 1:435 at 28years of maternal age.

In present study all women are educated, 54% of them are graduates. 64% were primigravida, The pregnancies were followed up to term and postpartum period. They developed the following complications; preeclampsia(8%),gestational hypertension(4%), preterm delivery(4%) and miscarriage(2%). 36% were multiparous, in whom preeclampsia was found in 3% of women, gestational hypertension in 6%, preterm labour in 2% and miscarriage in 3%.

The analysis shows 14% with consanguinous marriages. On follow up, no chromosomal abnormality was detected. One miscarriage occurred at 14 wks of GA because of hydropsfetalis. Karyotyping of the abortus was found to be normal.There was One women who had previous child with Down syndrome, two women had family history of down syndrome, one woman had previous baby with NTD (neural tube defect) & mental retardation, one woman who had child with mental retardation but no chromosomal abnormalities. Other 95 women didn't give any history of previous abnormal child or family history of abnormal child.

It is known that drugs which are embryo toxic are categorized by US FDA into A,B,C ,D and X based on their severity of its toxicity based on evidence. Anticonvulsants ,anticoagulants, psychoactive drugs, retinoids and few analgesics etc., will cause teratogenicity. In this study none of the pregnant women took these drugs.All of them have taken folic acid and a few of them have taken pantoprazole, doxylamine and pyridoxine during the first trimester.Infections like toxoplasmosis, rubella, cytomegalovirus, herpes(TORCH), parvo virus and syphilis etc., will cause teratogenicity but none of the pregnant women had these infections & tested negative for TORCH screen.

The mean gestational age of pregnant women was 12wk. The analysis shows at 11wk,12wk,13wks and at 14 wks of GA the median PAPP-A levels were 0.98 MoM ; 0.94MoM; 0.75 MoM; 0.66 MoM respectively and median free β- hCG were 0.66 MoM, 0.84 MoM; 0.625MoM and 0.89MoM respectively. The women with weight ranges of 45-54kg, 55-64kg and 65-74kg had median PAPP-A and free β-hCG of 0.975 MoM, 0.65 MoM; 0.905 MoM, 0.74 MoM; 0.902 MoM.735 MoM respectively.

According to **K.spencer etal[7],** <11 wk mean GA the median PAPP-A was 0.396 MoM, free β- hCG was 1.82 MoM. According to K. spencer et al[27] at >/11wk mean GA the median PAPP-A was 0.437 MoM, free β- hCG was 1.95 MoM. In the same study they found women with weights in the ranges of 45-54 kg, 55-64kg and 65-74kg had median PAPP-A and free β- hCG values of 1.21 MoM, 1.21 MoM; 1.09 MoM, 1.01 MoM; 0.90MoM, 0.96 MoM respectively. therefore it may be inferred that PAPP-A levels are decreasing with increasing maternal weight.

The data showed 63% of women had free β-hCG in the range of 0.1-1.0MoM. Women with free β-hCG<0.54 MoM, 10.7% developed preeclampsia and 3.6% had gestational hypertension. According to **Audibert et al[8],** free β-hCG for diagnosis of preeclampsia is 0.548 (0.453-0.643). In the same study they found that gestational HTN developed at 1.16 (0.76-1.56) MoM values of free β-hCG.The women with free β-hCG of <0.5MoM, miscarriage occurred in 4.2%, and 10.7% had preterm delivery. According to **Gagnon A et al[9],** in the first trimester, low free β -hCG<0.5MoM was associated with an increased frequency of adverse obstetrical outcomes.

The data showed 60% of women had PAPP-A in the range of 0.1-1.0MoM. Women with PAPP-A <0.52 MoM, 33.3% developed preeclampsia and 25% had gestational hypertension.

According to **Uccella S et al[10], in** <0.52 MoM PAPP-A values, the risk of gestational hypertension or preeclampsia was 11.2% and risk of severe preeclampsia was 3.9%.

According to A**udibert et al[8],** PAPP-A for diagnosis of preeclampsia is 0.570 (0.482-0.657).

The analysis shows 25% of pregnant women with PAPP-A <0.52 MoM developed preterm delivery. According to **Uccella S etal[10]** the risk of preterm delivery <37wk of gestation developed in 11.8% of pregnant women with PAPP-A values <0.52 MoM.

Miscarriage occurred in 37.5% in those with PAPP-A <0.4MoM. According to **Gagnon Aet al[9]** in the first trimester unexplained low PAPP-A values of <0.4 MoM are associated with an increased frequency of adverse obstetrical outcomes.

According to **Markkuryynane et al[12]**maternal serum low PAPP-A values in the first trimester is an independent risk factor for adverse pregnancy outcome like miscarriage, SGA (small for gestational age), preeclampsia and aneuploidy.

Nuchal translucency (NT) thickness in 84% of pregnant women had NT 0.5-1.5mm. NT >2.5mm was seen in 1% of pregnant women. According to **Souka et al[13],** risk of adverse outcome including miscarriage and intrauterine death was 32% for those who had NT of 3.5 to 4.5mm, 49% for NT of 4.5 to 5.4mm, 67% for NT 5.5 to 6.4mm and 89% for those who had NT of 6.5mm or more.

In group with NT >2.5mm, preeclampsia developed in one (100%) pregnant women but not preterm delivery or gestational hypertension. No comparative data is available regarding association of NT with preeclampsia, gestational hypertension and preterm delivery.

In the present series, nasal bone was absent in 4% of pregnant women. According to **Langdon Down et al[18],** the nasal bone was absent in 1.4% of normal fetuses and 69% of fetuses who had trisomy 21. According to **Kagan KO et al[14]** the nasal bone was absent in 2.6% of the euploid fetuses, 59.8% with trisomy 21, 52.8% with trisomy 18, 45.0% with trisomy 13 and in none of the fetuses with turners syndrome.

In women with absent nasal bone, there was miscarriage (50%), Preeclampsia(75%) and preterm delivery(25%). No comparative data is available regarding association of nasal bone with preeclampsia, gestational hypertension, preterm delivery and miscarriage.
In ultrasonography absent/abnormal ductus venosus flow was found in 4% of pregnant women. Among them 50% had preeclampsia, 25% developed gestational hypertension and 25% had miscarriage. No comparative data is available regarding association of abnormal ductus venosus flow with preeclampsia, gestational hypertension, preterm delivery and miscarriage. **Matias et al**[15]showed that 90.5% of the chromosomally abnormal fetuses had reversed or absent flow during atrial contraction, whereas 3.1% of the chromosomally normal fetuses had abnormal ductus flow.
The combined test was offered to approximately 150 pregnant women in my study. Thorough counseling about the test was done in the woman's native language. 100 women accepted to undergo the test i.e 2/3rd of women choose to accept this test. Present study had women belonging to all socioeconomic strata. Out of the 50 women who declined the test, the socioeconomic status was also mixed. So this suggests that if proper counseling is done, most women choose to undergo this test irrespective of their socioeconomic status. Hence combined test is recommended as a screening test,in first trimester even though the cost is a limiting factor.

CONCLUSIONS

We conclude the following from present study that there were no chromosomal abnormal fetuses. Acceptability of the combined test in our population is high because of non invasive nature and possibility of early detection of chromosomal abnormalities.Low PAPP-A shows an association with preeclampsia, preterm labour and miscarriage. As the sample size of this study is small, there is a need of larger population studies for further analysis of prevalence of chromosomal abnormalities.Cost of the combined screening test is also a limiting factor of the study.

RECOMMENDATIONS

Based on the results of our study recommendations are suggested areall women should be offered the combined test of Double biochemical marker (free β-hCG and PAPP-A) with triple sonological markers(NT,NB,DVF). As the acceptability of the test is high even in low socioeconomic strata of at 11-14 wks gestation women.Thorough counseling regarding risks and benefits of the combined test is mandatory.Attention should be paid to individual MoM of free β-hCG and PAPP-A,as they correlate with adverse pregnancy outcomes.Performance of NT scan detection of NB & DVF requires training which every obstetric sonologist should strive to achieve as it is a noninvasive test. All women who are screen positive should have close monitoring of the pregnancy and offer institutional delivery.

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