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Prevalence of chromosomal abnormality in prenatal cases with high risk for chromosomal aneuploidy

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Abstract
Determination of fetal chromosomal patterns in high-risk prenatal cases using cytogenetic techniques was performed on 479 amniotic fluid samples. All cases were referred to Global Reference Laboratory and PCPNDT accredited centre- Metropolis Healthcare Ltd, Mumbai during year-2015 to year-2016. FISH and conventional karyotyping techniques were performed. Out of 479 amniotic fluid study samples, chromosomal abnormality was detected in 62 cases (12.94%) while aneuploidy was detected in 48 cases (77.42%). Amongst the aneuploidy cases, trisomy 21 was the most common abnormality detected in 31 (64.58%), followed by trisomy 18 in 9 (18.75%), monosomy of sex chromosome in 4 (8.33%), trisomy 13 in 3 (4%) and triploidy in 1 (2.08%) case. Apart from aneuploidies, structural abnormality was detected in 10 cases (16.13%) in the form of translocation, deletion, presence of derivative chromosome. cases. Fetal chromosomal karyotyping and FISH can be a useful tool for detection of fetal aneuploidies and structural chromosomal abnormalities.

Keywords: amniotic fluid, chromosomal abnormalities, fluorescence in situ hybridization (fish), GTG-banding, karyotyping, non-invasive prenatal screening (NIPS)

1. Introduction

Prenatal tests can be screening and confirmatory tests [1]. Screening test involve maternal serum test like double marker and NT scan is performed within the first trimester, triple or quadruple marker test performed within second trimester and non-invasive prenatal screening (NIPS) performed after the completion of ten weeks of pregnancy. Confirmatory test include chorionic villus sampling (CVS) performed at around 10-12 weeks, while, amniocentesis or cord blood sampling (CBS) performed after 16-18 weeks or after 20 weeks, respectively [2, 3]. According to the regulations of the Pre-Conception and Pre-Natal Diagnostic Techniques (PCPNDT) Act, the twentieth week is the legal limit for taking any irreversible action regarding to discontinuing of pregnancy [4]. Since, the karyotype reporting consumes almost 15 days; either CVS or amniocentesis is the preferred technique. As compared to CVS, amniocentesis is preferred as the procedure related risk of miscarriages is low [5]. Abnormalities of chromosomes are life time and unfortunately there is no treatment available to correct the chromosomal abnormality. The non-invasive test and USG are screening test and can identify the population at high risk. However, when there is a deviation from normal in any of the screening test option of invasive prenatal procedures like CVS, Amniocentesis or CVS should be discussed with the couple to study the fetal chromosomal pattern. Invasive testing's are confirmatory tests and helps the couple to take the decision. Pre and Post-test counselling forms an integral part of genetic testing and after appropriate counseling by a Genetic Counsellor the invasive procedure should be carried out [6].

The most common chromosomal abnormalities found in prenatal cases are numerical variations followed by structural and polymorphic variations. Amongst the numerical variation, Trisomy 21 is the most common variation followed by Trisomy 18 and, later by Trisomy 13 in autosomal aneuploidies. In the numerical sex chromosomal abnormalities, monosomy X is the most common abnormality. Polymorphic variations are usually familial and reported to be normal but may be reported in prenatal fetal karyotype as this fetal polymorphic variations in their adult hood after the birth has been reported to be associated (though rarely) with recurrent pregnancy loss or fetal chromosomal aneuploidy. The current retrospective study was conducted to determine fetal chromosomal patterns in high-risk prenatal cases using cytogenetic techniques. Also, this study was carried out to determine the frequency of chromosomal abnormality in prenatal cases with high risk for chromosomal aneuploidy in non-invasive screening tests.

2. Materials and Methods

This retrospective study was performed on amniotic fluid samples referred to Global Reference Laboratory - Metropolis Healthcare Ltd, Mumbai, Maharashtra, India during the period between year-2015 to year-2016. A total of 479 amniotic fluid samples were received from those centres who are PCPNDT accredited and all the norms of PCPNDT for specimen collection were followed. After receiving all the samples, they were processed for long-term cultures. The GTG banding was performed as per the standard protocol. While, cases were reported as per the guidelines of ISCN, CAP and NABL. Minimum of 20 metaphases were studied for each case and for mosaic cases minimum 50 metaphases were studied. Wherever applicable, further evaluation by FISH or molecular studies was also carried out.

3. Results

Amniotic fluid samples of 479 cases were studied for fetal chromosomal pattern within the age group of 20 to 43 years. The most common indications were advanced maternal age (AMA), abnormal USG findings (markers), abnormal maternal serum tests and others including previous babies with abnormalities, mother/father with balanced translocation. In or study, out of the 479 cases, 107 cases were identified to be of AMA, 79 cases had USG showing markers for aneuploidy and 115 cases had an increased risk for aneuploidy in Maternal Serum Testing (MST). Around, 23 cases had other indications such as previous baby/fetus with Downs/Trisomy 18/13 or other chromosomal abnormality. Moreover, 155 cases had an overlapping indication such as an advanced maternal age and an increased risk for fetal aneuploidy in maternal screening test or abnormal USG findings. Out of 479 cases 48 (10.02%) had chromosomal aberrations in the form of trisomy and monosomy. While, 10 cases showed structural abnormalities like balanced reciprocal translocations, unbalanced translocations leading to partial monosomy and partial trisomy of particular region. And, 1 case with presence of marker chromosome of unidentified origin was also recorded. Only 2 cases with trisomy in mosaic pattern and 2 cases with balanced translocation in mosaic form were detected. Almost 32 cases with polymorphic variation such as inversion of chromosome 9, increase in heterochromatic region or satellite and one case having inversion of both the chromosome 9.

Table 1: Frequency of chromosomal abnormality with respect to indication:

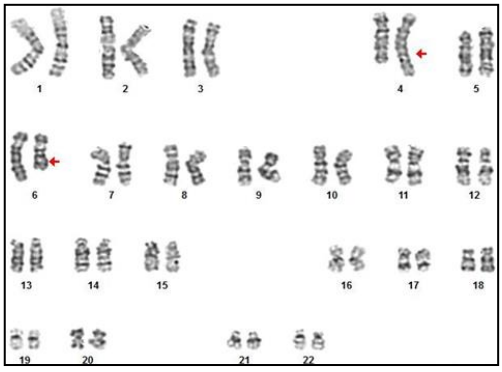
Indication	Type of chromosomal abnormality		
	Numerical	Structural	Mosaic
AMA	17	2	2
Maternal Serum Testing positive	22	2	1
USG showing marker	7	4	1
Others	2	2	-
Total	48	10	4

Table 2: Frequency of numerical chromosomal abnormalities seen with respect to MST positive:

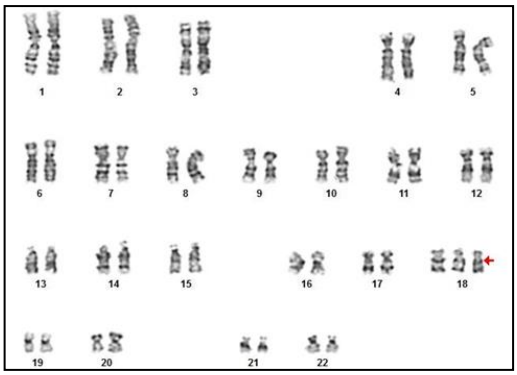
Abnormality	DMT	TMT	QMT
Trisomy 21	7	2	6
Trisomy 18	2	0	1
Trisomy 13	0	0	0
Monosomy X (accidental in MST positive for autosome)	2	0	2

Table 3: Type of structural abnormality with respect to indication:

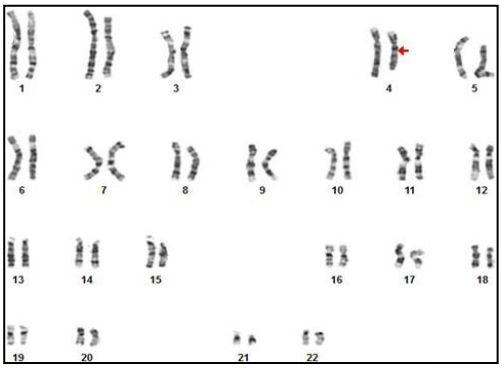
Indication	Type of fatal chromosomal abnormality	Parental karyotype done
QMT inconclusive	Triploidy	Normal karyotype
AMA	46,**,t(4;6)(q31;q15)	46,XX,t(4;6)(q31;q15)mat
Previous baby with chromosomal abnormality	46,**,t(11;12)(q23;q24.1)	46,XY,t(11;12)(q23;q24.1)pat
Previous baby with chromosomal abnormality	46,**, t(7;12)(p22:q11)	46,XX, t(7;12)(p22:q11) mat
AMA	46,**,der(6)t(6;?)(q23;?)	46,XY, t(6;15)(q23;24)pat
DMT positive	46,**,der(22)t(22;?)(q13;?)	46,XX, t(13;22)(q32;q13) mat
USG : Multiple congenital anomalies	46,**,der(10)t(10;?)(p13;?)	46,XX, t(3;10)(q21:p13) mat
USG : CHD	46,**,der(13)t(13;?)(q14;?)	Not willing/may have done elsewhere
USG: increased NT	46,**,del(9)(q22)	Normal karyotype
Prominent Nuchal translucency	46,**,der(4)t(4;?)(q31;?)	Not willing/may have done elsewhere



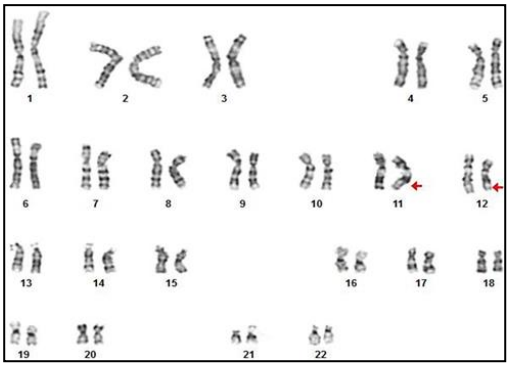
46,**,t(4;6)(q31;q15)



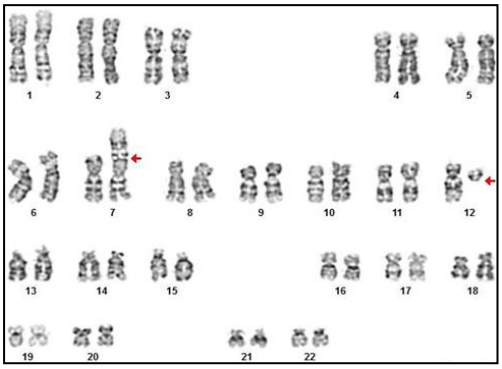
47,**,+18



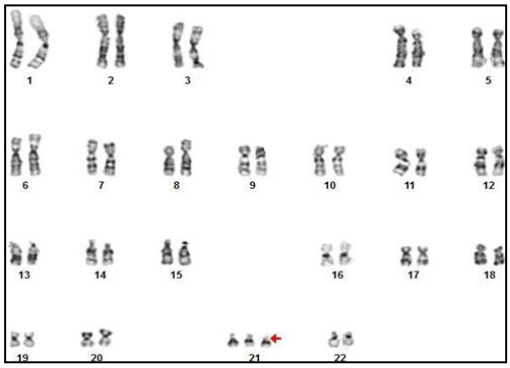
46,**,der(4)t(4;?)(q31;?)



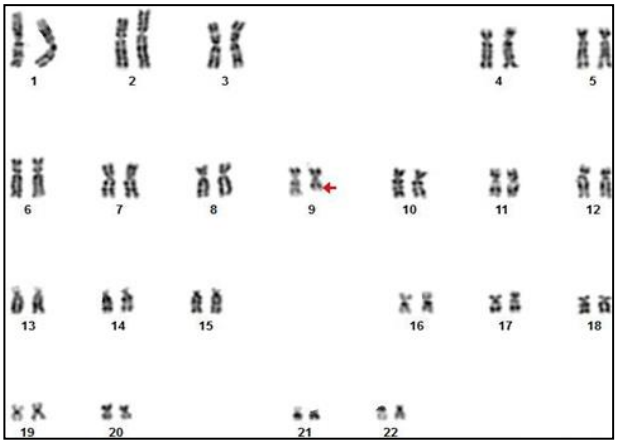
46,**,t(11;12)(q23;q24.1)



46,**, t(7;12)(p22:q11)



47,**,+21



46,**,del(9)(q22)

Fig 1: Fetal chromosomal abnormalities observed in our study

4. Discussion

As per the available literature studies, the percentage of pregnancy losses in first trimester of pregnancies due to aneuploidy (trisomy/monosomy X) is quite high [7, 8, 9, 10]. Majority of the conceptus affected with trisomy or monosomy either terminates during the first trimester abortion or if the pregnancy sustains up to full-term then the baby is born with congenital abnormalities leading to burden on the family. Patients affected with Down syndrome can survive up to 50 years but with various congenital abnormalities and systemic involvements [11]. Prenatal genetic testing is a confirmatory test which detects the fetal chromosomal pattern and helps the couple for taking any irreversible decision if fetal chromosomal abnormality is detected.

Genetic amniocentesis is comparatively a safe procedure as compared to CVS with a procedure with related risk of miscarriage at 0.5 %, while for CVS it is around 1% [12]. Also the possibility of maternal contamination is quite high in CVS. Since, Metropolis Healthcare Ltd is a Global Reference Laboratory, several amniotic fluid samples are received from all parts of India. This could be the reason for variation in the percentage of abnormality detected in our study and also because of the selection bias since only the highly suspected samples were referred to our laboratory for chromosomal studies.

5. Conclusions

It is important to examine the chromosomal pattern in the suspected cases because cytogenetic abnormalities are life-long concerns and unfortunately there are no treatments available till date. Hence, prenatal testing assists the couples to take the informed decision as the baby with chromosomal abnormalities may not only affect the parents' generation but may also the next generation and indirectly increases the burden on the society.

6. Acknowledgment

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