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Original Research Article

Frequency of down syndrome: an experience of a tertiary care diagnostic laboratory in India

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ABSTRACT

Background: Down syndrome or Trisomy 21 is a genetic condition involving the presence of extra copy of chromosome 21. It is the most common chromosomal abnormality within paediatric age group. The objective of our study was to determine the frequency of Down syndrome and its various cytogenetic types in cases with clinical suspicion of Down syndrome received at the Department of Cytogenetics, Metropolis Healthcare Limited, Mumbai, India.

Methods: Our study was performed on peripheral blood (2-3 ml) collected in Sodium Heparin Vacutainers obtained from 714 patients with clinical suspicion of Down syndrome. All the samples were requested for GTG staining and banding, while the cultures were set and analysed by GTG–banding at 450-550 band level. The period of our study was from January-2015 to December-2016.

Results: Out of 714 samples referred, about 657 showed trisomy of chromosome 21. While, out of 657 cases, 551 (83.87%) cases were detected with free trisomy, Robertsonian translocation in 52 cases (7.91%), Mosaic pattern in 16 cases (2.44%). Our study also recorded trisomy with additional polymorphic variation in 35 cases (5.33%) and 3 cases (0.46%) with additional abnormality.

Conclusions: According to the extensive literature available which states that the clinical diagnosis of Down syndrome is relatively easy, it is the pattern of chromosomal aberration that is extremely important. Identification of this pattern will assist in the estimation of the possibility of recurrence risk while counselling the parents. Overall, it will benefit the couple to arrive at an informed decision and will eventually minimize the frequency of disease in the society. Moreover, it will also assist the close blood relatives to know their risk of having baby with Down syndrome. It is to be noted that since the study was performed in a tertiary care laboratory, the percentage of cytogenetic.

Keywords: Karyotype, Metropolis healthcare ltd, Mosaic, Robertsonian translocations, Trisomy

INTRODUCTION

Down syndrome or Trisomy 21 is a genetic condition involving the presence of extra copy of chromosome 21.[1]

It is the most common chromosomal abnormality within paediatric age group. There are three types of Trisomy 21 which involve free trisomy 21, translocation trisomy 21 and Mosaic Trisomy 21.[2] This extra copy of chromosome 21 or additional genetic material in the form of chromosome 21 leads to clinical manifestations in cases with Down syndrome and involves various systemic defects such as Mental insufficiency, congenital cardiac anomalies, ophthalmic disorders, genital abnormalities and others.[3] The objective of our study was to determine the frequency of Down syndrome and its various

cytogenetic types in cases with clinical suspicion of Down syndrome received at the Department of Cytogenetics, Metropolis Healthcare Limited, Mumbai, India.

METHODS

Our study was performed on peripheral blood (2-3 ml) collected in Sodium Heparin Vacutainers obtained from 714 patients with clinical suspicion of Down syndrome.

All the samples were requested for GTG staining and banding, while the cultures were set and analysed by GTG–banding at 450-550 band level.

The results were reported as per International System for Human Cytogenomic Nomenclature (ISCN), and guidelines of College of American Pathologists (CAP) and The National Accreditation Board for Testing and Calibration Laboratories (NABL).

Around 20-30 metaphases per case while for mosaic cases 50 metaphases where studied.

The period of our study was from January-2015 to December-2016.

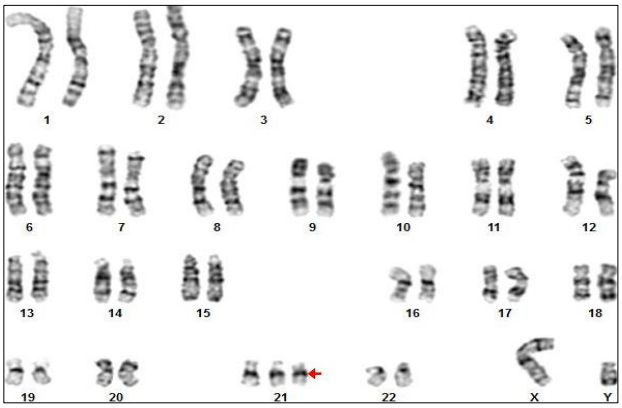

Figure 1: Patterns of karyotype 47, XY, +21.

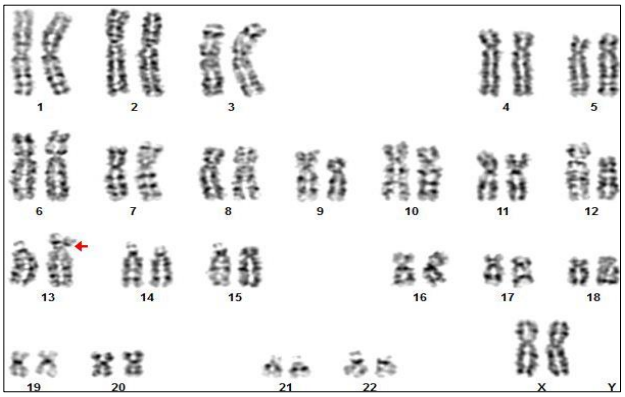

Figure 2: Patterns of karyotype 46, xx, der (13;21) t (13;21) (q^{10}; q^{10}), + 21.

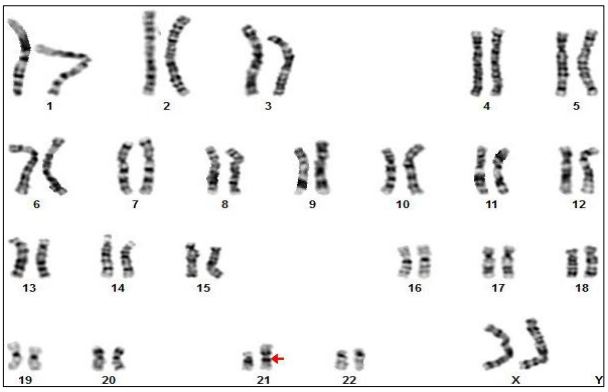

Figure 3: Patterns of karyotype 46, XX, +21, der (21;21) t (q^{10}, q^{10}).

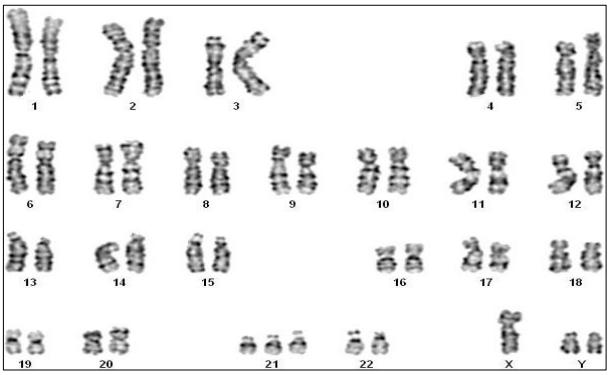

Figure 4: Patterns of karyotype 48, XYY, + 21.

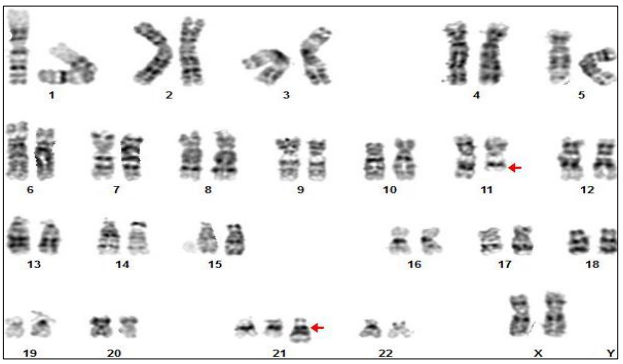

Figure 5: Patterns of karyotype 47, XX, t (11;21), +21

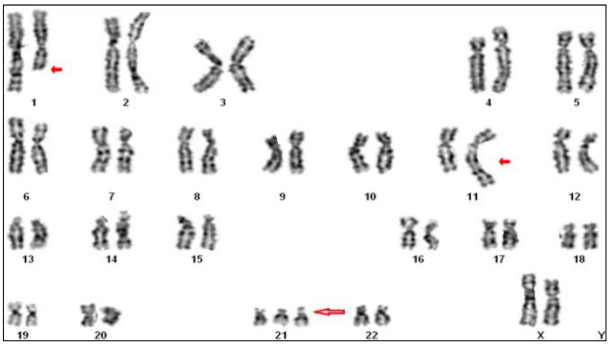

Figure 6: Patterns of karyotype 47, XX, t (1:11), + 21.

RESULTS

Out of 714 samples referred, about 657 showed trisomy of chromosome 21. While, out of 657 cases, 551 (83.87%) cases were detected with free trisomy, Robertsonian translocation in 52 cases (7.91%), Mosaic pattern in 16 cases (2.44%). Our study also recorded trisomy with additional polymorphic variation in 35 cases (5.33%) in the form of 13ps+, 14ps+, 15ps+, 21ps+, 22ps+, 9qh+1qh+, 16qh+ and 3 cases (0.46%) with additional abnormality like 48, XYY, +21, Downs with extra copy of X chromosome, 48, XYY, +21 Downs with extra copy of Y chromosome and 47, XX, t(1:11),+21 trisomy of 21 with translocation between chromosome 1 and 11. Male: female ratio was recorded to be around 1.39:1.00. Identification of the definite chromosomal pattern will assist in the estimation of the possibility of recurrence risk while counselling the parents. It is to be noted that since the current study was performed in a tertiary care diagnostic laboratory, the percentage of cytogenetic patterns may vary as per the established literature.

Table 1: Various patterns of trisomy reported in the current study.

Patterns of trisomy	Frequency out of 657
Free trisomy	551 (83.87%)
Robertsonian	52 (7.91%)
Mosaic	16 (2.44%)
Trisomy with Polymorphic variations	35 (5.33%)
Trisomy with other structural abnormalities	03 (0.46%)

Table 2: Frequency of Robertsonian translocation reported in the current study.

Type of Robertsonian translocation	Frequency out of 52 (%)
T (14;21)	29 (55.77%)
T (21;21)	17 (32.69%)
T (13;21)	04 (7.69%)
T (15;21)	02 (3.85%)

DISCUSSION

Down syndrome (DS) or Trisomy 21 is the most common autosomal aneuploidy seen in paediatric age group. Incidence of Down syndrome varies from 1 in 660 to 1 in 1000 in live birth4. The clinical presentation of DS patients is typical with various phenotypic and systemic involvement. In general, phenotypically the babies are hypotonic and have a tendency of keeping mouth open with protruding tongue, hyper flexibility of joints, comparative short stature.

This phenotypic feature is associated with systemic involvement most commonly mental insufficiency, fine lens opacity, refractory errors, hearing loss, cardiac anomalies like ventricular septal defects, endocardial cushion defect, patent ductus arteriosus, hyperkeratotic skin and genital abnormalities like relatively small penis and decreased testicular volume5. This characteristic presentation of DS patients makes clinical diagnosis relatively easy. However, the cytogenetic confirmation for the type of chromosomal pattern is very important as low-grade mosaicism may at times makes difficult to clinically diagnose the condition and knowing pattern of chromosomal abnormality helps to estimate the chances of recurrence risk in next pregnancy and also to know the potential of risk of having DS baby to close blood relatives6. This will help the couple to make an informed choice thus lowering the burden on the family and the society.

Genetic presentation of DS patients may present in three or more different form.[7] The most common form is Free trisomy where in there is extra copy of chromosome 21 in all the cells and its contribution is reported to be 95% which is usually caused due to error at meiotic cell division and usually advanced maternal age may be the cause8. Of all the detected trisomy, almost 4-5% is the contribution of translocation (Robertsonian/Translocation of 21 on other acrocentric chromosome) trisomy which is usually familial and transmitted from one of the parents and is second most common type with a recurrence risk of 50% except cases with one of the parent with translocation between 21 and 21 where the recurrence risk is almost 100%.[9] Third variant type of DS is Mosaic pattern which contributes 1-2% of total detected trisomies, where in some group of cells have trisomy and remaining cell are normal10.

Depending upon the percentage of normal and abnormal the consequence may vary but to best of our knowledge no clear-cut guidelines are available to predict the severity of manifestations. The fourth group could be trisomy with polymorphic variations is such cases along with trisomy 21 the karyotype pattern shows normal polymorphic variations. These polymorphic variations are usually familial and the one of the parents have these. It is reported that tough minimal these polymorphic variations in parents may lead to fetal chromosomal aneuploidies. The fifth group could be trisomy 21 with additional chromosomal abnormalities.

CONCLUSION

According to the extensive literature available which states that the clinical diagnosis of Down syndrome is relatively easy, it is the pattern of chromosomal aberration that is extremely important. Identification of this pattern will assist in the estimation of the possibility of recurrence risk while counselling the parents. Overall, it will benefit the couple to arrive at an informed decision and will eventually minimize the frequency of disease in the society. Moreover, it will also assist the close blood relatives to know their risk of having baby with Down syndrome. It is to be noted that since the study was

performed in a tertiary care laboratory, the percentage of cytogenetic patterns may vary as per the established literature.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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