ejpmr, 2016,3(6), 171-174

SJIF Impact Factor 3.628

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

CYTOGENETIC ANALYSIS OF CHILDREN DOWN SYNDROME PATIENTS IN WASIT

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Article Received on 08/04/2016 **Article Revised on 28/04/2016** **Article Accepted on 18/05/2016**

ABSTRACT

Trisomy 21 or Down syndrome(DS) is the most common type of autosomal chromosome abnormality. **Objective:** The present study is aimed to document the types of cytogenetic abnormality in DS children and their relation to maternal age in Wasit. **Method:** Cytogenetic study was done for 30 cases who presented with Down syndrome (DS). It was done in a private lab. Cells were studied using lymphocyte culture technique arrested at G-metaphase. **Results:** Among the 30 cases of Down syndrome presenting aged from 1 day to 14 years, free trisomy 21 was present in 28 cases (93.3%). two cases were mosaics(6.7%). The median maternal age of the Wasit mothers at the birth of the affected child was 36 years. **Conclusions:** The identification of specific types of chromosomal abnormalities in Down syndrome children is important. It also help in setting priorities of cytogenetic screening individual cases.

KEYWORDS: cytogenetic analysis, Down syndrome, karyotype pattern.

INTRODUCTION

Down syndrome is the most common type of chromosomal trisomy found in newborns, with an incidence of one out of 700.[1,2,3] Down syndrome is associated with mental retardation and characteristic facial features. A clinical diagnosis of Down syndrome may be unconfirmed in one third of cases.[4] Most individuals (95%) with trisomy 21have 3 separate copies of this chromosome (classicaltrisomy21). In approximately 4% of such people, one extra copy of the chromosome is translocated to another acrocentric chromosome, most often chromosomes 14 or 21[5] In 1-4% of cases with classical trisomy 21, there is recognizable mosaicism with parallel trisomic and normal cell lines. Warren et al. (1987) and Sherman et al.(1991) have described an association between trisomy 21 and reduced recombination at meiosis.

A significant proportion (at least 30%) of maternal meiosis I nondisjunction of chromosome 21 is associated with failure to recombine.[6] The cause of the non-disjunction error is not known, but there is a definite connection with maternal age. Advanced maternal age remains the only well-documented risk factor for maternal meiotic non-disjunction. The incidence of trisomy 21 conceptions increases with maternal age.[3,7] The present study aimed to evaluate the karyotype pattern in children with Down syndrome and to study the link between maternal age and trisomy 21 in the Wasit.

METHODS

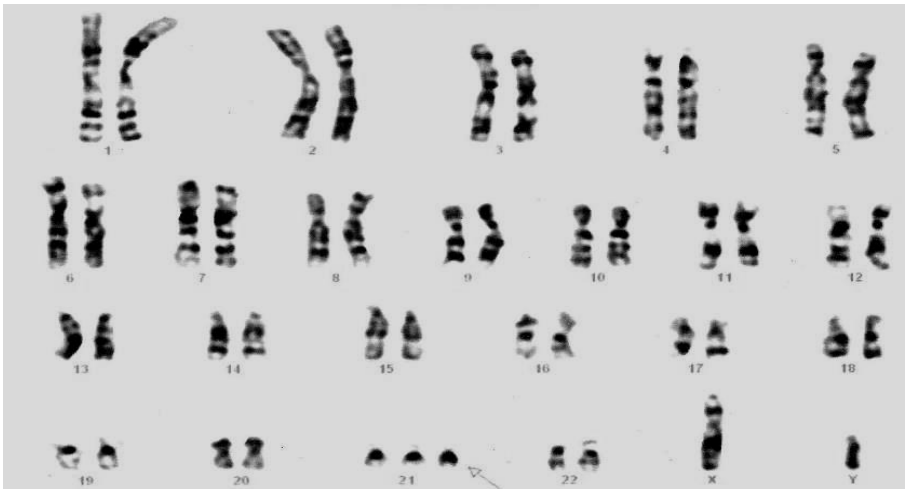
Study was conducted on all children with the diagnosis of Down syndrome who were referred to Al karma, Al zahraa and Al azezea hospitals to private laboratory, from January 2015 to January 2016. A total of 30 patients were included, aged from 1 day to 14 years because just of child patients. The data collected included maternal and paternal age at diagnosis. Chromosome preparation was carried out from peripheral blood collected in sodium heparin in all the subjects and cultures were harvested using standard cytogenetic procedures and some modification. Banding techniques were used to classify the chromosomes: the banding technique G-banding technique using Trypsin (GTG banding).[8] GTG-banded chromosomes were karyotyped according to the International System for Human Cytogenetic Nomenclature(ISCN2005).[9]

RESULT

There were 30 children with Down syndrome who attended the genetics clinic during the study period: 18from 30 case percent(60%) females and 12 from 30 case percent (40%) males. The median maternal age at the time of delivery was 36 years such as in table(1). Cytogenetic testing results revealed that 28 from 30 case percent (93.3%) had trisomy 21; 2from 30 case percent (6.7%) had showed mosaic pattern.

Table I. Correlation of maternal age and chromosomal aberration in Down syndrome

Maternal age (years)	n = 30	Ratio (male:female)	Cytogenetic profile	No. of cases	Total percentage (%)
20-25	3	1:2	Trisomy 21 Translocation Mosaic	3 - -	10
26-30	4	1:3	Trisomy 21 Translocation Mosaic	4 - -	13.1
31-35	6	2:4	Trisomy 21 Translocation Mosaic	5 - 1	20
36-40	7	3:4	Trisomy 21 Translocation Mosaic	7 - -	23.1
41-46	10	1:1	Trisomy 21 Translocation Mosaic	9 - 1	33.1



Figure(1): Metaphase and karyotype showing 21 chromosome trisomy.

DISCSSION

Trisomy 21 or Down syndrome is a common birth defect and is the most frequent and most recognizable form of mental retardation. Clinical diagnosis of this condition is usually done without difficulty. The diagnosis of Down syndrome, on the basis of clinical features in the neonatal period, has been reported to range from 73% to 100%.[10] The frequencies of the different karyotype patterns observed in these subjects are shown in Table I. The percentage of free trisomy 21 was 93.3% and mosaic trisomy 6.7%. The frequency of trisomy was higher than that of mosaic among our Down syndrome patients. This data is relatively compatible with the data from a few international studies (Table 2)[11-17] and slightly deviating from a few other studies. Thomas et al from Bangalore, India reported a higher frequency of mosaicism with 86.6% free trisomy, 7.7% translocation and 5.8% mosaicism.[18] Similarly, Jyothy et al from India reported a high prevalence of mosaicism (7.7%).[19] Contrary to this, Mutton et al from England and Wales reported trisomy in 95%, translocation in 4% and mosaicism in 1% children with Down syndrome Even though no specific reason could explain this discrepancy in the frequency of karyotype pattern in Down syndrome patients, differences in time period, the maternal age and population studied could be contributing factors.[17]

For non-disjunction trisomy 21, the most common error is maternal non-disjunction in the first meiotic division, with meiosis I error occurring three times as frequently as meiosis II errors. Most mosaic cases result from a trisomic zygote with mitotic loss of chromosome 21. The Down syndrome cases with unbalanced translocation usually are *de novo* and nearly 25% result from familial transmission.[20]

In our study population, median maternal age at birth of the affected child was 36 years. Out of the 30 Down syndrome patients, This clearly indicated that maternal age was a major contributing risk factor in a significant proportion of cases in this population (Table1). Almost a double increment was noted in the percentage of cases between the group of young mothers and the difference was reduced as the maternal age approaches 40 years

(Table I). This data is consistent with the exponential increment noted by Epstein. It is well known that aneuploidy can have major detrimental health consequences when it occurs in either germinal or somatic cells. Germinal aneuploidies, a major cause of pregnancy loss, aneuploid births and developmental defects are thought to arise *de novo*, through meiotic errors in germ cells of either parents, or mitotically shortly after fertilization. Both age-dependent and age-independent factors appear to be operating simultaneously. It could be due to age-dependent decay in the spindle fibres or their components, a failure in nucleolar breakdown or an accumulation of the effects of radiation, hormonal imbalances and infection.[21] On the other hand, clinical and experimental studies have shown that age-independent DNA hypomethylation is associated with chromosomal instability and abnormal segregation.[22,23]

Table (2). Frequencies of different karyotypes among the studied Down syndrome cases and pooled data from worldwide surveys.

Source	Total of case no.	Regular trisomy		Translocation		Mosaic		Non-classical	
		No.	%	No.	%	No.	%	No.	%
Wasit (current study)	30	28	96.4	-	-	2	4.6	-	-
Sudan(Khartoum)[11]	5	3	60	2	40	-	-	-	-
Jordan(Amman)[12]	33	28	85.0	3	9.0	2	6.0	-	-
Saudi(Riyadh)[13]	42	37	88.0	5	11.9	-	-	-	-
Malaysia[14]	149	141	94.6	1	0.7	7	4.7	-	-
France[15]	391	368	94.1	14	3.6	9	2.3	-	-
Egypt[16]	673	642	95.4	18	2.7	5	0.7	8	1.2
England and Wales[17]	5,737	5,411	94.3	220	3.8	66	1.2	40	0.7

In conclusion, free trisomy 21 was found in 93.3% of the subjects in this study. Karyotyping is essential for the confirmation of the clinical diagnosis and the determination of the recurrence risk, as well as to provide a basis for genetic counseling. A karyotype of the parents is required only if trisomy 21 is due to a translocation. Advanced maternal age is the principal risk factor for trisomy 21. This risk must be taken into account by couple candidates for medically-assisted procreation. Consultation with the geneticist is essential for these couples.

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