

# Down syndrome and consanguinity

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**Background:** Among the genetics disorders, Down syndrome (DS) is the major cause of mental retardation, congenital heart and intestinal disease. So far, no certain therapeutic method has been suggested for the treatment of this syndrome. The aim of the current survey was to investigate the frequency of parental consanguinity, maternal age in the patients with DS. **Materials and Methods:** This study was conducted on 38 consecutive patients with clinically and laboratory confirmed DS who referred to the genetic lab of a referral University Hospital. The G-banding method for karyotyping was employed. **Results:** The patients were 21 males and 17 females within the age of 16 days to 28 years old. Free trisomy (92.1%, n = 35) was the most common chromosomal abnormality. The frequency of DS was higher among the non-consanguine marriages (71.1%) in comparison with the consanguine marriages (28.9%). Mean age of the mothers in the consanguine marriages (mean = 27.1 ± 6.3) was lower than in the non-consanguine marriages (mean = 31.1 ± 7.7). **Conclusion:** Higher frequency of DS among the non-consanguine marriages in comparison with the consanguine marriages, may suggest that DS diagnostic tests might be done on all embryos regardless of the parents' familial relationship.

**Key words:** Consanguinity, chromosomal disorder, Down syndrome

**How to cite this article:** Rezaayat AA, Nazarabadi MH, Andalibi MS, Ardabili HM, Shokri M, Mirzaie S, *et al.* Down syndrome and consanguinity. *J Res Med Sci* 2013;18:995-7.

## INTRODUCTION

Down syndrome (DS) affects up to 1 in 700 live births<sup>[1]</sup> and among the mentally retarded population, its prevalence is reported to be approximately 15%.<sup>[2]</sup>

The incidence of DS is related to both genetic and environmental challenges.<sup>[3]</sup> An extra copy of the human chromosome 21 and its resulting dosage-related over expression of genes cause DS,<sup>[4]</sup> which is the most frequent genetic cause of mental retardation.<sup>[1]</sup> A number of clinical conditions and disorders such as: Congenital heart and gut disease, infectious diseases, increased nutritional intake, periodontitis, seizure disorders, sleep apnea, ocular motor or visual impairment, audiologic deficits, thyroid dysfunction, abnormalities of the immune system, an increased risk of leukemia, an Alzheimer-like dementia and rarely an imperforated anus, respiratory tract infection, abnormal brain development, skeletal problems and dermatoglyphics disorders usually befall at a higher prevalence among the affected to DS children. No specific treatment has been developed for DS so far.<sup>[5-9]</sup>

For many years, the study of karyotype from amniotic fluid cells has been a valuable criterion for the prenatal diagnosis of chromosomal anomalies in the developed

countries.<sup>[10-13]</sup> In addition, for the purposes of estimating the probability of DS in infants, prenatal screening and diagnosis have been employed. These are based on the factors, such as maternal age and serum concentrations of various analyses, such as triple test and ultrasound measurements which are have been found to be associated with Down syndrome and are known as screening markers for the disorder.<sup>[14,15]</sup>

Consanguinity is also reported to be associated with DS.<sup>[16]</sup> This finding is in contrast to another study claiming that the consanguinity was not a significant factor in the incidence of DS.<sup>[17]</sup>

Because of the controversy about this matter and a belief in our society that there may be a relationship between the consanguinity and Down syndrome, this study was performed to evaluate the frequency of parental consanguinity, maternal age in the patients with DS.

## MATERIALS AND METHODS

### Study design and subject selection

The current study was conducted among 38 consecutive patients with clinically and laboratory confirmed DS included 21 males and 17 females (55.3% males and

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**Received:** 25-11-2012; **Revised:** 13-02-2013; **Accepted:** 25-08-2013

44.7% females) within the age of 16 days to 28 years old. From June 2004 to November 2011 all subjects were referred to the Cytogenetic Lab of University Hospital, Imam Reza Hospital, after having received an early diagnosis by a specialist. The project was approved by the research ethics committee of the Mashhad University of Medical Science and the written informed consent was completed and signed by all volunteers or their parents prior to the study. Gender, maternal and paternal age, number of mother's pregnancy and parents' familial relationship of each patient were recorded as potential risk factors of DS. According to the parents' familial relationship, couples were categorized into two groups, included: Consanguine ("first cousin" and "second first cousin") and non-consanguine marriages. The subjects whose sanguine information was not complete were excluded from the study.

**Laboratorial analysis**

A blood sample of 3-5 cc was collected from the peripheral vein of each patient for cell proliferation process. After preparation, the cell cultures were incubated for 70 h at 37°C. For the preparation of the metaphase stage, G-banding method was employed for karyotyping by the use of commercial standard kits (The GIBCO diagnostics chromosome test kit/Life Technologies, Inc. Grand Island, New York, 14072, USA). After analyzing the karyotype map of all 46 chromosomes in the blood sampling of the patients, subjects with Down syndrome were determined.

**Statistical analysis**

All statistical analyses were performed using the SPSS for Windows™, version 16 software package (SPSS Inc., Chicago, IL, USA). At first, the quantitative data were assessed using Kolmogorov-Smirnov tests for normality. Data were expressed as means ± SD for parameters with a normal distribution. Group comparisons were performed using the sample T-test. A two-sided *P* value < 0.05 was considered statistically significant.

**RESULTS**

Within patients who referred (n = 38), a variety of chromosomal abnormality was evident, including:

Free trisomy (92.1%, n = 35), translocation form and double aneuploidy (48, XXX +21) (7.9%, n = 3). Through consanguine marriage group, 100% of the patients had trisomy chromosomal status which was higher than non-consanguine marriage group (88.9%). Fisher's Exact test shows no significant associations between the consanguine marriage and the patients' chromosomal status (*P* = 0.35). Among the subjects, 18.8% of the parents were first cousins, 10.8% were second first cousins and the remaining (70.3%) were of non-consanguine marriages.

The frequency of DS in the first and second childbirth was slightly higher (63.2%, n = 24) than the third childbirth and afterward (36.8%, n = 14). The mean of maternal and paternal ages was 29.8 ± 7.5 and 35.5 ± 8.3 respectively. The maternal age, at the time of giving birth, in non-consanguine marriages was 31.1 ± 7.7, while in consanguine marriages; it was 27.1 ± 6.3 [Table 1]. The majority of the patients were male in non-consanguine marriage. In contrast with consanguine marriage; however, this difference was not statistically significant [Table 2].

**DISCUSSION**

In this investigation, free trisomy was more prominent than the translocation form. This finding was in agreement with other studies conducted by Ghosh S and *et al.*<sup>[3]</sup> Although, the previous study indicated that the incidence of DS was more pronounced in the consanguine marriages than non-consanguine marriages,<sup>[3]</sup> nevertheless no significant difference was evident between these two groups.

In regard to the effect of maternal age on DS in the consanguine and non-consanguine marriage, in contrast with some previous studies,<sup>[16,18]</sup> this study did not find any significant differentiation between these two groups.

According to the maternal age at the time of a DS child's birth, the comparison between the groups, with and without familial relationship, showed that parents in non-consanguine marriages are older without any familial relationship. Although these results were not significant,

**Table 1: The difference between parental age and familial relationship**

	Parent status	P-value	Mean	Std. error	95% Confidence interval of the differences	
					Lower	Upper
Maternal age	Consanguine marriage	P~0.15	27.1	1.54	-1.4	9.3
	Non-consanguine marriage		31.4	1.92		
	Total		30.1	1.90		
Paternal age	Consanguine marriage	P~0.2	32.4	1.73	-2.1	9.8
	Non-consanguine marriage		36.3	2.02		
	Total		35.1	1.29		

**Table 2: Consanguinity and gender of the patient with Down syndrome**

Groups	Gender		Total (%)	P value
	Female (%)	Male (%)		
Non consanguine marriage	10 (37)	17 (63)	27 (100)	0.12
Consanguine marriage	7 (63.6)	4 (36.4)	11 (100)	
Total	17 (44.7)	21 (53.3)	38 (100)	

nevertheless these indicate the possible effect of parental consanguinity on giving birth to a DS child.

Moreover, almost all the Down syndrome children of the consanguine marriages were born when the maternal age was under 33. This age is lower when compared with the maternal age of Down syndrome parents without any familial relationship.

In this study's population the majority of DS cases occurred in the children of young mothers under 30 years of age, which is in contrast with previous studies.<sup>[18]</sup> On one hand, this may be due to the higher frequency of delivery by mothers between the ages of 20 to 30 years and on the other hand, to the social and cultural customs of the country of Iran where consanguine marriage is frequent in adolescence and among younger ages.<sup>[19]</sup>

## CONCLUSION

Higher frequency of DS among the non-consanguine marriages in comparison with consanguine marriages, may suggest that DS diagnostic tests might be done on all embryos regardless of the parents' familial relationship.

Of course the small number of cases may be a limitation of this study.

## ACKNOWLEDGEMENTS

The authors would like to express their appreciation to Z. Rabbani and F. Hassanzadeh for their excellent technical assistance. The authors declare that they have no conflicts of interest in the research.

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**Source of Support:** The Cytogenetic Lab of University Hospital, Imam Reza Hospital, **Conflict of Interest:** None declared.