Sys Rev Pharm 2021;12(3):76-79
A multifaceted review journal in the field of pharmacy

Maternal Prenatal History And Consanguinity Among Families Of Children With Down Syndrome: A Retrospective Case Control Study

Radwa Ezzat Amin[1], Iman Ehsan Abdel-Meguid[1], Nihal Mohamed El-Refaie[1], Hala Ahmed El-Gindy[1]

Department of Pediatrics, Faculty of Medicine, Cairo University, Egypt
Corresponding Author: Radwa Ezzat Amin, E-mail:radwa.ezzat.amin@gmail.com

ABSTRACT

Introduction: Down syndrome (DS) is one of the most common causes of intellectual disability. Many studies reported the relationship between antenatal history of spontaneous abortion and the risk of having DS children. Consanguineous marriage is common and preferrable in most of the Arabic countries, but its relation to DS remains controversial.

Objective: Evaluating the association between antenatal maternal history, spontaneous abortions and consanguineous marriage in relation to the risk of giving DS live births.

Subjects and Methods: This case control study included 306 patients diagnosed as DS, and their caregivers, presented to Clinical Genetics clinic, Cairo University Children Hospitals, from February 2018 to February 2020. The patients' ages ranged from 1 to 5 years old and 306 families with healthy children as controls. They were evaluated by full history and examination.

Results: Among DS children 67.6% were males, 22% of mothers of DS gave history of antenatal illness. History of previous spontaneous abortions was statistically significant higher among mothers with DS children with P- value <0.001, while there was no statistical difference in the prevalence of consanguinity among families of DS and controls with P-value 0.186.

Conclusions: There is significant association between maternal history of spontaneous abortions and DS live births. However, there is no relationship between DS and consanguinity, these findings may be considered on providing genetic counselling.

Keywords: Down syndrome, Consanguinity, Spontaneous abortions, Prenatal illness)

Correspondence:
Radwa Ezzat Amin
Department of Pediatrics, Faculty of Medicine, Cairo University, Egypt

*Corresponding author: Radwa Ezzat Amin email-address:
radwa.ezzat.amin@gmail.com

INTRODUCTION

Down syndrome (DS) is one of the most common causes of intellectual disability [1], affecting up to 1 in 700 live births [2]. Its incidence is attributed to both genetic and environmental factors [3], an extra copy of the chromosome 21 leads to dosage-related genetic over expression which results in DS [4]

Furthermore, there are a number of medical conditions associated with DS, the most common being cardiac defects, leukemia, gastrointestinal issues, vision and hearing disabilities, dental, thyroid disease, obstructive sleep apnea, epilepsy, and Alzheimer disease [5].

It is well established that karyotyping from amniocentesis is valuable for antenatal diagnosis of chromosomal disorders in developed countries [6 7 8 9]. In addition, antenatal screening and diagnosis have helped estimating the probability of DS. These tests are based on age of the mother, serum levels of different screening markers of triple test, and ultrasound which are considered as valuable screening tools in DS and other trisomies [10]. However, the choice of antenatal diagnosis with selective termination of an affected fetus is uncommon and slowly evolving in most Arab countries [11].

Many studies have reported that there is a relationship between antenatal history of spontaneous abortion or still births of unknown karyotyping and the risk of having DS children. However, results are still inconclusive [12]

Consanguineous marriage is common and preferrable in most of the Arabic countries, first-cousin marriage are specially familiar representing almost 25% of all marriages in many Arab comunities [13]. The association between consanguinity and DS has been reported [14] However, other studies claimed that the consanguinity has no significance in DS incidence and does not predispose to it [15].

Objective

The aim of the current study is evaluating the association between antenatal maternal history, spontaneous abortions and consanguineous marriage in relation to the risk of giving DS live births.

SUBJECTS AND METHODS

This case control study included 306 patients diagnosed as DS, ascertained using karyotyping, and their caregivers, who presented to the Clinical Genetics clinic, Cairo University Children Hospitals, from February 2018 to February 2020. The patients' ages ranged from 1 to 5 years old. Same number of Families (306) with phenotypically normal age and sex matched children were recruited from outpatient clinics as controls. All patients and controls were evaluated by full history including personal data; age, sex, residence, phone number, presentation, consanguinity, age of the parents at conception, full prenatal history including history of abortions, still birth and maternal illness. Full examination and reviewing patients investigations including karyotyping was done.

Ethical considerations

Ethical approval was obtained from Ethical Committee, Faculty of Medicine, Cairo University before starting the study (approval number: I-250218). Informed consent was received from the participant's caregivers, and they were assured of confidentiality. The purpose of the study was explained in addition to their rights to terminate their participation, without affecting care and services offered to their children.

Statistical analysis

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 25 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. For comparing categorical data, Chi square ($\chi 2$) test was performed. P-values less than 0.05 were considered as statistically significant.

RESULTS

A total of 306 children with DS were recruited of which 204 (67.6%) were males and 102 (32.4%) were females. Age of mothers of DS children at conception was >35 years in 171 (56%) of them, while 216 (71%) of fathers were >35 years. The majority of DS patients 244 (80%) had no family history of DS or any neurological deficits, while 40 (13%) and 22 (7%) gave family history of neurological impairment and DS respectively. There is history of unsafe drug intake during pregnancy in 16 (5.2%), radiation exposure during pregnancy in 10 (3.4%).

On reviewing prenatal maternal history in mothers with DS children, 67 (22%) of them gave history of antenatal illness as shown in table (1), hypertension was the most frequently reported in 24 (7.8%), followed by diabetes in 12 (3.9%).

Table (1): History of Prenatal Maternal Illness

	Count (n=306)	%
Hypertension	24	7.8%
Diabetes	12	3.9%
Bronchial asthma	6	2%
Antiphospholipid Syndrome	2	0.7%
Prenatal Thyroid Dysfunction	5	1.6%
Prenatal bleeding	5	1.6%
Prenatal fever or infections (hepatitis C, varicella)	6	2%
Prenatal Tumor	2	0.7%
Prenatal Rheumatoid Arthritis	2	0.7%
Others(fracture, electric exposure, cardiac)	3	1.0%

Among DS families, consanguineous marriage was found in 81 (26.5%) of them. There is positive history of previous abortions, still birth and dead siblings in 104 (34%), 7 (2.4%) and 24 (7.9%) respectively.On comparing prenatal maternal history of spontaneous abortions and consanguinity between families of DS children in relation to controls, history of previous spontaneous abortions was statistically significant higher among mothers with DS children with P- value <0.001, while there was no statistical difference in the prevalence of consanguinity among families of DS and controls with P-value 0.186 as shown in table (2).

Table (2): Consanguinity and History of Abortions among DS and Controls

		DS		Control		
		Count	%	Count	%	P value
Consanguinity	yes	81	26.5%	67	21.9%	0.186
	no	225	73.5%	239	78.1%	
Abortions	yes	104	34.0%	44	14.4%	<0.001
	no	202	66.0%	262	85.6%	

DISCUSSION

The most known established risk factor in DS is the maternal age, incidence of DS can be affected either in maternal age dependent group that occur in women with older age or maternal age independent group that occur in younger women below 35 years [12]. In this study's population most of DS cases occurred in the children of older mothers above 35 years of age, which was in agreement with previous studies [16] and in contrast with others [17] in Iran where marriage is frequent in adolescence and among younger ages [18]

The main aspects in women's reproductive health are contraception, abortion, maternal morbidity, sexually transmitted diseases, and infertility. An increased risk of aneuploidy is present in women who had many spontaneous abortions [19]. Maternal health and reproductive potential are significant factors in the incidence of DS [20].

In our study, history of previous spontaneous abortions was statistically significant higher among mothers with DS children with P-value <0.001. This was in agreement with many prior studies. Increased incidence of fetal loss is associated with increased risk of nondisjunction and, the highest fetal loss in pregnancies occurs closest to DS births [21]. [12] as well reported that the abortions clustered nearer to DS births. The relative risk of having DS child is associated with increased frequency of abortions in younger women [22]. Women at risk of having DS may be identified by history of spontaneous abortions, maternal age and translocation carrier status in both maternal age groups. The highest percentage of abortions is seen before DS births in younger women and after DS births in older women [12]

The rates of consanguinity are high in the Middle East ranging from 20% to 50% [23] [24]. In many Middle East communities, consanguineous marriages are culturally preferred with old traditions [25]. In Egypt prevalence of consanguinity differs in various residence areas, ranging from 29 to 39% [26] [27]. It differs with various cultural and moral perspectives, especially in rural areas [23].

In the current study, there was no statistical difference in the prevalence of consanguinity among families of DS and

controls this was in agreement with [28], they found no association between consanguinity and DS. On the other hand, [29] reported an increased risk of chromosome 21 nondisjunction during meiosis II in young mothers with consanguineous mating this finding was first published by [30]

CONCLUSIONS

This study supports the significant association between maternal history of spontaneous abortions and DS live births. However, there is no relationship between DS and consanguinity, these findings may be significant on providing genetic counselling.

Funding: No specific funding was received.

ACKNOWLEDGMENTS

The authors thank Clinical Genetics clinic,Cairo University Children Hospitals, all patients, and their caregivers for their participation.

Potential Conflict of Interest: No potential conflicts of interest to disclose.

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