

MATERNAL AGE AND CONSANGUINITY AS RISK FACTORS FOR MENTAL RETARDATION AMONG CHILDREN IN SOUTH JORDAN

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Abstract

The incidence of childhood mental retardation (MR) remains an alarming situation in South Jordan. The current retrospective study was designed to determine whether consanguinity and maternity age are major risk factors to educate the population and define intervention methods. A total of 108 children diagnosed with MR of unknown etiology were included in this study. Systemic neurological examination and Stanford Binet Intelligence test was conducted for each participant. Overall prevalence of consanguinity was 54.6%, and 75.9% of mothers were less than 30 years old. Consanguinity and mother's age does not predict mental retardation of unknown etiology. Though the finding of our study is concurrent with the published studies, there is no report from South Jordan. It is important to monitor if there is any impact on consanguinity due to social change. We also believe that findings of this study will be useful in creating awareness and thereby educating people of the genetic deformities associated with consanguinity.

Keywords: Mental retardation, mother's age, consanguinity, South Jordan

Introduction

According to the report of the Ministry of Social Development, in a population of 4.5 million people, Jordan has over 130,000 citizens suffering from various forms of disabilities, including mental and physical retardation ("Societal, financial constraints limiting disabled rights activists' awareness campaigns," .1998).

Mental retardation (MR) is a serious and lifelong disability that has devastating effects on society and the health system. About 3% of children worldwide manifest some degree of MR (Zeldin & Kao, 2012) but its pathogenesis is poorly understood. Causes of MR are numerous and include genetic and environmental factors. Despite thorough evaluation, the etiology could not be determined in 30–50% of cases (Daily et al.2000).

Down syndrome is the best-known example of a prenatal genetic disorder The causes of mental retardation can be grouped from most to least common as follows (Sebastian et al.2012) alterations in embryonic development (for e.g. those caused by chromosomal abnormalities or fetal exposure to drugs or toxins; environmental deprivation and other mental disorders (for e.g. autism); problems of pregnancy and the perinatal period (for e.g. fetal malnutrition, hypoxia, infection, trauma, or prematurity); hereditary abnormalities (for e.g. inborn errors of metabolism or chromosomal aberrations); or medical conditions of infancy or childhood (for e.g. Central nervous system (CNS) infection or trauma, or lead poisoning).

An initial study documenting Jordanian children from 1975 to 1985 revealed that the two main factors of severe MR were: (1) sequel from the high frequency of perinatal morbidity or meningitis in infancy leading to a combination of severe mental retardation and cerebral palsy; (2) a high degree of consanguinity and a high frequency of retarded siblings (Janson et al.1999). The aim of this study was to determine whether the situation has changed over the past 30 years, and whether maternal age is also an important risk factor of severe MR in Southern Jordan.

Advanced maternal age is a well-established risk factor for trisomy 21 (Down syndrome); however, the impact of maternal age on the children for attaining MR is still conflicting.

Establishing an etiologic diagnosis of patients with MR is usually a challenge for every specialist as the spectrum of possible underlying disorders is enormous and the range of available additional investigations is extensive (Vashist et al.2011). Maternal age and consanguinity are debatable causes of MR among children (Sridhara et al. 1976), and the existing literature reports conflicting findings. In South Jordan, the consanguinity rate still high (Sueyoshi et al.1997). Therefore, the present study aimed to evaluate whether maternal age and consanguinity are risk factors for MR among children of South Jordan.

Subjects and Methods

This retrospective study was conducted on 108 children diagnosed with MR of unknown etiology from South Jordan with a mean age of 6.5 years (range: 2–17 years), 54

(50%) male and 54 (50%) females were enrolled. Children having known underlying cause (such as Down syndrome, fragile x syndrome, antenatal, and environmental causes) were excluded. All the study participants attended a specialized center for the diagnosis of early childhood disabilities in Al-Karak province in the period of September 2009 to September 2011.

Data collection

All the evaluation was done through an official request. Information on maternal age at the time of birth of the child and consanguinity was obtained from the medical records. Maternal age was then divided into 6 groups ranging from 15 to 45 years. (1) 15–20 (2) 20–25, (3) 25–30, (4) 30–35, (5) 35–40, (6) more than 40 years.

The consanguinity between their parents could be categorized into 4 groups: (a) first cousins, (b) far cousins, (c) far relatives, and (d) not related. Most patients that came to our specialized center for diagnostic evaluation were referred from schools or education authorities.

All data were collected from the medical records of these children, which contains extensive clinical and family history, including antenatal as well as pre and postnatal evaluation. Developmental and neurological exams were conducted by the same pediatric neurologist. The evaluation also included hearing assessment, speech assessment, and the Stanford Binet Intelligence test done when suitable by a specialized psychologist. Thyroid function tests, were done for all children, and it was normal and imaging investigation such as brain CT scan or brain MRI was done only when indicated.

Results

The 108 children with mean age of 6.5 years (SD: 3.9, range: 2–17 years), 54 (50%) males and 54 (50%) females were classified according to the age of their mother at birth.

Table 1: Number of mothers in different age groups

Age Groups	Number of Mothers	Percent
15–20	11	10.2
20–25	35	32.4
25–30	36	33.3
30–35	16	14.8
35–40	6	5.6

40+	4	3.7
Total	108	100.0

Table 1 shows that only 10% of the mothers were teenagers. In contrast, about 80 % were within normal range for maternal age, with equal representations for the 20–25 and 25–30 age groups.

Table 2: Distribution of study participants according to the degree of consanguinity

Degree of Consanguinity	Number of Participants	Percent
First cousin	25	23.1
Far cousin	19	17.6
Far relative	15	13.9
Not related	49	45.4
Total	108	100.0

Fifty five percent mothers were related to the father to some degree (Table 2), the closest relatives being first cousins. Each class of relatives were equally represented, namely first cousins, far cousins and far relatives. These data indicate that the parents of children with severe MR in South Jordan are generally mothers of normal age group with extremely high incidence of consanguinity.

Table 2 shows the number of participants in each consanguinity group. Strong consanguinity was observed in 23.1% (n = 25) of the parents (first cousins); 17.6% (n = 19) were far cousins; 13.9% (n = 15) were far relatives; about 45.4% (n = 49) were not married to any of their relatives and thus showed no consanguinity. These results indicate that neither consanguinity nor mother's age at birth predicted the presence of mental retardation of unknown causes amongst group of patients in Jordan.

Data analysis

Frequency, valid percentage, mean, and SD were reported for all the variables as appropriate Chi square test was performed for comparing non categorical variables among the groups. A p value of <0.05 was considered statistically significant.

In this study 108 children with mental retardation of unknown cause and 135 controls matched for age, location and socioeconomic class. Based on Chi square analysis, there was no statistically significant between patients with mental retardation and controls in the consanguinity of their parents (P = 0.3) (table 3).

Table 3: consanguinity between patients and control group

Status	First cousin	Far cousin	Far relatives	Not relatives	Total
Control	22	30	27	56	135
Patient	25	19	15	49	108
Total	47	49	42	105	243

$$\text{Pearson } \chi^2 = 3.6006, \text{ Pr} = 0.30$$

The analysis was also done when consanguinity was limited first degree relatives and also indicated that there was no statistically significant difference between them ($p = 0.2$).

The logistic regression analysis performed on 243 samples keeping the presence of mental retardation as dependent variable and maternal age at birth and consanguinity as independent variables are projected in table 4.

Table 4: Logistic regression analysis**Dependent variable:** Presence of mental retardation**Independent variable:** Maternal Age and Consanguinity.

Variable	β	Se β	95% Confidence Interval [Range]	P value
Constant	1.163239	.8012159	-0.4071153–2.733593	0.147
Maternal age	-.0445972	.0253476	-0.0942776–0.0050831	0.079
Consanguinity	-.0558347	.1110274	-0.2734445–0.1617751	0.615

These results indicate that neither consanguinity nor mother's age at birth predicted the presence of mental retardation of unknown cases amongst group of patients in Jordan.

Discussion

Severe MR remains an alarming situation for the children of South Jordan, both in terms of incidence and consequences. The present study was designed to shed more light on the factors driving such high incidence of MR in this region. Based on the current literature on MR, this study was focused on two parameters: maternity age and consanguinity. This study exposes the current situation and identifies the most pressing interventions to reduce the incidence of childhood MR in South Jordan.

The present study suggests that the high incidence of MR in the children of Southern Jordan is associated with a normal maternal age distribution, but an extremely high rate of consanguinity. More than 50% of the fathers were family relatives, with equal representation

from first cousins, far cousins and far relatives. Similar studies were conducted in other areas. A study conducted in Iran (Jazayeri R, et al. 2010). reported 77% of the consanguineous marriage resulting in MR children were among relatives with half of them being among first cousins. An earlier global profile of Jordan (2002-2006) revealed that 20-30% of all marriages occur between first cousins. Incidentally, they constitute 69% of the marriages bearing children diagnosed with autosomal recessive conditions, 22% of marriages bearing children diagnosed with dominant X-linked and chromosomal conditions, and 41.7% of marriages with sporadic undiagnosed conditions (Hamamy et al. 2007). We found the similar results reporting 23% of all consanguineous marriages bearing childhood MR were between first cousins.

Older maternal age was associated with increased risk of mental retardation. This age effect was only seen in the lowest education group. In terms of risk for the population, it was younger mothers with 12 years of education or less whose births were associated with the greatest proportion of mental retardation. From a public policy point of view, children born to mothers with low level of education are an important group to target for prevention/early intervention efforts (Chapman et al.2002) .

In a study from Unites States, children of teenage mothers were not at increased risk for either form of retardation (concomitant developmental disabilities or birth defects affecting the Central Nervous System (co-developmental retardation) or disabilities like isolated retardation. While the children of mothers aged <30 years were not at increased risk for isolated retardation, when compared with children of mothers aged 20–29 years. A markedly increased risk of co developmental retardation was seen among black children of mothers aged <30 years which was not attributable to Down syndrome (Williams et al.1999).

In a Chinese study (Zhang et al. 1992), maternal age had no significant effect. Birth order was also found to be a non-significant factor after adjusting for other factors. Similar to the findings of the Chinese study, our study reported that 90.7% of the participant's mothers were under the age of 35 years, and therefore maternal age was not a significant factor for MR.

An epidemiological study of MR in Pakistan reported no association between consanguinity and MR (Hasan et al.1981). In Bangladesh, 60% of mentally retarded children were offspring of consanguineous parents. The overall prevalence of serious MR was extremely high and no association between consanguinity and MR was reported (Islam et al.1993).

Another study conducted in a selected region of the Israeli Arab community found that 68% of children with mental retardation were the offspring of consanguineous marriages (Sharkia et al. 2010) However, in Jordan, the rates of consanguinity vary. The prevalence of consanguinity in North Jordan (Al-Salem et al.1993) was reported to be 63.7%. In another study, the incidence of marriage with first cousins was 32.03%, second cousins 6.8%, and distant relations 10.5%; the partners were not related in 50% of all marriages (Khoury et al. 1992)], the incidence of consanguinity was high 54.6% of our cases but it is not higher than the usual in our community Therefore, in the present study, we could not find any association between consanguinity and MR.

Conclusion

Mental retardation affects both males and females equally. The overall prevalence of consanguinity was 54.6%, and 75.9% of mothers were less than 30 years old. Consanguinity and mother's age does not predict mental retardation of unknown etiology. Though the finding of our study is concurrent with the published studies, there is no report from South Jordan. It is important to monitor if there is any impact on consanguinity due to social change. We also believe that the findings of this study will be useful in creating awareness and thereby educating people of the genetic deformities associated with consanguinity.

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