



*Full Length Research Paper*

# The impact of consanguinity on children health in Jordan Valley

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Abstract

Consanguineous unions have been associated with an increased susceptibility to various forms of inherited recessive disease in many parts of the world, including Arab populations. First cousin unions where the individuals share 1/8 of their genes are very common in Middle East cultures and could affect disease risk. Although consanguinity is known to contribute to hereditary and congenital diseases, the incidence of such diseases is still not clear in Jordan population. This study was performed to determine the prevalence of genetic, congenital/mental disorders (ex. Congenital Heart Diseases (CHD), cleft lip, mental and sensory handicap) and chromosomal aberration disorders and their association with parental consanguinity in a selected sample of children in Jordan Valley. The present study was undertaken to determine the prevalence of and their association with parental consanguinity in a sample of children selected from Jordan Valley. The study also explored incidence of children with hereditary diseases, congenital abnormalities and handicaps in Jordan valley in relation to other factors such as sex and mode of transmission. A descriptive analysis of all children with hereditary and congenital diseases among 100 affected children ages 6 months - 15 years was conducted. The study consisted of a 100 children-parents of children whom were having a child affected by a genetic abnormalities and/ or congenital malformations/ diseases. Families-children dyads were approached through local health centres and school. Data were collected through questionnaire which was adopted from health centre. The questionnaire provided information on consanguinity status and date of marriage among two generations: the affected children, and their parents. Data on consanguinity status among 100 children was obtained. Descriptive quantitative analysis was used to analyse data. The overall consanguinity of parents was 74% and the inbreeding coefficient was (0.025). Consanguineous marriages remain an important factor associated with hereditary abnormalities in northern Jordan. The closer the relationship of mates, the greater genetic effect and its associated abnormalities were found. This result is similar to other places with similar social features.

**Keywords:** Consanguinity, Inbreeding, Jordan Valley.

## INTRODUCTION

Consanguinity, which is marriage between biological relatives, has been recognized as the main social factor related to a high prevalence of genetic and congenital disorders worldwide including Arab communities' (Teebi and Teebi, 2005; Sharkia, Zaid, Athamna et al., 2008, Assaf and Khawaja, 2009, Kanaan, Mahfouz and Tamim, 2008, Yunis, Mumtaz, Bitar et al., 2006, Sawardekar, 2005). Arab populations have a long tradition of consanguinity due to socio-cultural factors like

maintenance of family structure, and properties or ease of marital arrangements (Bittles, 2008, Assaf et al., 2009 El Mouzan, Al Salloum, Al Herbish et al., 2009). Many Arab countries such as Jordan, Palastine, Qatar, Oman, Yemen, Saudi Arabia and UAE, still display the highest rates of consanguineous marriages in the world, specifically first cousin marriages which may reach 25-30% of all marriages (Tadmouri et al., 2008, Obeidat et al., 2008, Assaf et al., 2009, Sawardekar, 2005, El Mouzan et al., 2009).

Consanguinity rates in various societies were found to be dependent on multiple factors e.g. religion, educational level, local traditions socio-economic status

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and demography (Fuster, 2003, Assaf et al., 2009). Consanguineous couples are at high risk of conceiving a child with a genetic disorder and many other health problems such as inherited genetic disease and congenital malformation (Bittles, 2008, Kanaan et al., 2008, Yunis et al., 2006). The main impact of consanguinity is an increase in the rate of homozygotes (even common alleles.) for autosomal recessive genetic disorders such as beta-Thalassemia (Bittles, 2008). Worldwide, known dominant disorders are more numerous than known recessive disorders (Bittles, 2008). However, data on genetic disorders in Arab populations indicate a relative abundance of recessive disorders in the region as compared to western communities that is clearly associated with the practice of consanguinity (Tadmouri et al., 2008).

Various forms of congenital malformation of the central nervous system, speech and infertility were found at a higher frequency in those individuals whose parents are family related, than those with unrelated parents (Kanaan et al., 2008, Yunis et al., 2006, Bromiker, Glam-Baruch, Gofin, 2004). Recently, it was found that the prevalence of neurological hereditary diseases and mental retardation was associated with consanguinity in selected samples of Arab communities (Sharkia et al., 2008, Assaf et al., 2009, Sawardekar, 2005). A high proportion of infant mortality due to congenital malformation in the Arab community is mainly caused by the high frequency of consanguineous marriages (Kanaan et al., 2008, Yunis et al., 2006, Zlotogora, 2002).

The present study was undertaken to determine the prevalence of various genetic, congenital and mental disorders (ex. CHD, cleft lip, mental and sensory handicap) and chromosomal aberration and their association with parental consanguinity in a selected sample of children Jordan Valley. The study also explored incidence of children with hereditary diseases, congenital abnormalities and handicaps in Jordan valley in relation to other factors such as sex and mode of transmission. This study is important as investigation of hereditary disorders is vital for improving overall health care. This can be achieved by identifying and diagnosing their molecular genetic basis, with a view to developing preventative intervention measures aimed at reducing the occurrence of these inherited genetic disorders among children.

The disadvantages (ex. high frequency of infant mortality, beta-Thalassemia, congenital malformation of the central nervous system and mental retardation) of consanguineous marriage were assessed by primary investigator and discussed with parents through short interview, with specific consideration given to the consequences on children health in selected study setting (that is Jordan valley), among whom first cousin marriage remains preferential. The result of this study presented incidence of children with hereditary diseases, congenital abnormalities and handicaps in Jordan valley

and showed their relation with parental consanguinity and other factors such as sex and mode of transmission.

## **METHODS**

### ***Design***

Descriptive quantitative study was used to determine the relationship between consanguinity and health disorders among children.

### ***Ethical Considerations***

#### **Informed consent**

Consent was obtained from the Director of health department at selected areas, nursing services and from the management of the participating centres to conduct this research, after ethical clearance had been granted by the Ethics and Research Committee of Department of Health Studies. All participants consented verbally to show their willingly to be interviewed by the researcher and for the collected data to be filled at study tool. All filled questionnaires was sealed in an envelope and placed into a sealed container. .

All participants were ensured that no personal information would be revealed. No names would be mentioned in any report nor attached to the transcribed interviews. Only numbers were used in an effort to maintain anonymity. The data were kept locked up by the researcher. Only the researcher, a data analyst and the supervisor had access to the raw data. All participants were interviewed by way of numbers and no real names were used. Prior to the interviews all participants were requested not to make any reference to anyone's name.

### ***Setting***

The community in Valley of Jordan is characterized by some unique features: most of the population lives in villages which were founded by small numbers of originators and the majority of families have a large number of children. It was also believed that the favourite marriage at such setting is the consanguineous one (Jaber, Halpern and Shohat, 2000). We believe that the high consanguinity rate in our study is partly a result of regional and social factors. Residents of 5 towns in Jordan valley were included in this study. These specific towns were selected to be included in this study as consanguinity is common among such rural area including first and second cousins. This is because these towns are the poorest and least educated families in Jordanian society. Agriculture is primary source of earning money there and most of families are engaged in

agriculture, while others either working in military services or governmental institutions.

### **Study sample**

The target population consisted of all families having children with hereditary and/or congenital diseases live at selected area in Jordan Valley. The study group comprised the full pediatric population (6 months-15 year old), that was affected with one or more types of any diseases, abnormalities or mental disabilities caused by congenital and/ or hereditary illness since birth. The sample excluded children with disorders caused by accidents (like birth accident) or environmental factors. The sample recruited through referral by local community contacts at 5 selected towns.

The recruitment process was a multi-stage random sample which was designed in three stages: selection of enumeration five areas, selection of health centre in the chosen enumeration area and selection of two persons at selected health centres to review health history of children and to find those who are having hereditary and congenital problems and whom their age was ranged 6 months -15 years.

Parents of selected children were approached by researcher and were asked to participate in study. As primary researcher was a teacher of nursing at governmental school at Jordan Valley, that facilitated access and contact of families. Primary researcher visited selected families and interviewing included families. The included families were informed one day before interview about study aim and verbal approval were sought. On the day of interview researcher meet parents and their children and they were informed again about purpose of study. They were also reassured that their responses and any collected data would be confidential. Verbal approval was taken and study purpose was explained.

The total number of the study group was 100 affected children whom their age ranges from 6 months and up to 15 years. This age group were selected the sample was compromised of children under the age of 15 because life expectancy of affected children with chromosomal or other congenital abnormalities would die before adult hood so that there would not be a rise in incidence at adulthood (Othman and Saadat, 2009, Kanaan et al., 2008, Yunis et al., 2006). Accordingly, 100 children and their parents who were living in northern Jordan valley were approached and included during study time. Participants age ranged from 6 months to 15 years with 39% were less than 2 years, 36% between 2 and 5 years, 25% over 5 years and up to 15 years. The sample is believed to be a reasonable sample from the population

of families with affected children in 5 selected areas.

### **Data Collection and Instrument**

The used instrument was taken from the socio-economic survey that was used by health centre at selected area. This survey was covering the following areas:

- a. Identification information for the child (ex. gender, age, type of delivery, Birth Weight, Medical diagnosis, and cause of disability).
- b. Parental status information: included marital status, whether husband and wife are related, and the degree of consanguinity, level of education parents, mothers' age, and the number of other affected offspring.
- c. Health status information: included incidence of chronic diseases, disabilities, kinds of disabilities, and causes of disabilities, availability of supplementary health insurance, and places of treatment

Before going to the study field and start of collecting data the content of study tool were reviewed and discussed with experts, after approval on all contents, primary investigator collected and filled data using instrument after taking verbal approval from parents. Questionnaires were completed through face to face interviews and information on consanguinity between the parents was obtained through the interviews. The duration of data collection was three months.

Relationships were grouped into two major categories: a consanguineous and Non-consanguineous marriage which was defined as follows:

Consanguineous marriage: This group included two main levels of relationships:

- a. First cousins and closer. These include double-first cousins (in which all grandparents are shared) and first cousins in which the couple are parallel or cross cousins of either paternal or maternal descent;
- b. Distant relative marriages, in which the members of the couple were relatives but not with first-degree relations, for example they were first cousin once removed, second cousin, second cousin once removed.

Non-consanguineous marriage: The couple is not related.

### **Data Analysis**

Data from the questionnaires were coded and entered in SPSS version 10. Descriptive statistics were used to describe the sample in demographic data and other data relating to asking about child and family history and consanguinity. The statistical significance of associations between consanguinity and various types of disorders

**Table 1.** Frequencies of consanguinity and level of educational (LOE) of parents

| LOE                         | Consanguinity |        |        |        |        |        |             |        |                    |        |
|-----------------------------|---------------|--------|--------|--------|--------|--------|-------------|--------|--------------------|--------|
|                             | First         |        | Second |        | Third  |        | No relation |        | Total for each LOE |        |
|                             | Father        | Mother | Father | Mother | Father | Mother | Father      | Mother | Father             | Mother |
| Illiterate                  | 10            | 10     | 5      | 6      | 5      | 5      | 5           | 5      | 25                 | 26     |
| Primary                     | 9             | 10     | 6      | 7      | 4      | 4      | 3           | 3      | 22                 | 24     |
| Total                       | 19            | 20     | 11     | 13     | 9      | 9      | 8           | 8      | 47                 | 50     |
| Secondary                   | 4             | 4      | 6      | 5      | 5      | 5      | 5           | 5      | 20                 | 18     |
| High                        | 8             | 8      | 3      | 3      | 2      | 1      | 1           | 2      | 14                 | 14     |
| Total                       | 12            | 12     | 9      | 7      | 7      | 6      | 6           | 7      | 34                 | 32     |
| Diploma                     | 2             | 1      | 2      | 2      | 1      | 1      | 6           | 6      | 11                 | 10     |
| BA andpost                  | 1             | 1      | 1      | 1      | -      | 1      | 6           | 5      | 8                  | 8      |
| Total                       | 3             | 2      | 3      | 3      | 1      | 2      | 12          | 11     | 19                 | 18     |
| Total for types of marriage | 34            | 34     | 23     | 23     | 17     | 17     | 26          | 26     | 100                | 100    |

**Table 2.** Percentage distribution of affected children (n=100), divided according to diseases and handicaps and known means of transmission

| Types of diseases or handicaps        | Percentages |
|---------------------------------------|-------------|
| Mendelian genetic inheritance         |             |
| Thalassemia                           | 20%         |
| Progeria                              | 2%          |
| Total                                 | 22%         |
| Multifactorial causation              |             |
| CHD                                   | 10%         |
| Cleft lip                             | 5%          |
| Mental retardation                    | 20%         |
| Sensory handicap                      | 25%         |
| Total                                 | 60%         |
| Chromosomal aberration                |             |
| Trisomy21                             | 18%         |
| Total number of cases and percentages | 100%        |

was examined by means of the  $\chi^2$  test.

## RESULTS

Of 100 children, 74% were of consanguineous parents and 26% were non-consanguineous (See Table 1). The various subtypes of consanguinity was observed; The total numbers of affected children of varying degrees of disabilities separated into those from consanguineous and from non-consanguineous marriages are presented in Table 1.

More than half of affected children (74%) were found to be products of parental consanguinity; 34% of this prevalence was offspring of first cousins marriage, 23% were second-cousin marriage, and 17% were third cousin type. The incidence for distant relative marriage was only

26% (Table 1).

Of the 100 total children from all the family samples, children were found to have one or more kinds of various types of disorders. About 22% of the affected children were having Mendelian genetic inheritance (ex Thalassemia (20%), progeria (2%), 60% Multifactorial disorders (ex. CHD (10%), Cleft Lip (5%), Mental retardation (20%), Sensory Handicap (25%)), and 18% were having chromosomal aberration (trisomy 21). This indicates that there is an associated familial background (Represent in Table 2).

There was a significant difference in the prevalence between the offspring of consanguineous versus non-consanguineous mating for various types of examined disorders especially Mendelian genetic inheritance (17% vs. 5%, respectively) and chromosomal aberration (14% vs. 4% respectively). All reported disorders were more

**Table 3.** Percentage distribution of affected children (n=100) by sex and type of disease or handicap, divided according to known means of transmission

| Types of diseases or handicaps | Male | Female | % of total cases |
|--------------------------------|------|--------|------------------|
| Mendelian genetic inheritance  |      |        |                  |
| Thalassemia                    | 10%  | 10%    | 20%              |
| Progeria                       | 2%   | -      | 2%               |
| Total                          | 12%  | 10%    | 22%              |
| Multifactorial causation       |      |        |                  |
| CHD                            | 6%   | 4%     | 10%              |
| Cleft lip                      | 3%   | 2%     | 5%               |
| Mental handicap                | 15%  | 5%     | 20%              |
| Sensory handicap               | 15%  | 10%    | 25%              |
| Total                          | 39%  | 21%    | 60%              |
| Chromosomal aberration         |      |        |                  |
| Trisomy 21                     | 12%  | 6%     | 18%              |
| % of total by sex              | 63%  | 37%    | 100%             |

frequent in consanguineous marriages indicating that there is a significant association between consanguinity and types of disorders and that genetic factor are probably the main underlying cause the prevalence of disorders' types was higher in boys (63%) than in girls (37%), and this difference was significant (Table3).

## DISCUSSION

Consanguineous marriage refers to unions contracted between biologically-related individuals who are related as second cousins or closer (Bittles, 2008). Although rate of consanguineous marriage decreased, in Jordan consanguinity is still common especially among traditional rural area, the poorest and least educated families in society. Our study, which is based on data obtained from small rural area of Jordan community, showed that the incidence of consanguinity there is relatively high and prevalence of congenital malformations and genetic diseases still affecting children.

The most preferred types of consanguineous marriage vary according to tradition, so that in Arab societies first cousin marriage between a man and his father's brother's daughter is most common, In this study 34% of consanguineous marriages are including first and second cousins marriage type. This study finding supported that the phenomenon of consanguineous marriages could still common in Jordan and its prevalence is considered to be much higher (35% - 55%) as compared to that (1%) of Western countries (Sharkia et al., 2008; Tadmouri et al., 2008).

Generally, the highest rates of marriages to close relatives are consistently reported in the more traditional rural areas and among the poorest and least educated in

society, and this is the situation in Jordan (Hamamy, Jamhawi, Al-Darawsheh and Ajlouni, 2005, Hamamy, Masri, Al-Hadidy and Ajlouni, 2007, Obeidat et al., 2008). Among Jordanian, this would include first cousins, second cousins, and third cousins. Uncle-niece marriage is prohibited in Islam and so is absent among Arabs. Reports from some Arab countries have shown that consanguinity rates are lower in urban when compared to rural settings (Zaoui and Biemont, 2002, Othman et al., 2009, Obeidat et al., 2008).

Consanguinity rates are not declining in some Arab countries because it is generally accepted that the social advantages of consanguinity could outweigh the disadvantages, and consanguinity is regarded as a deeply rooted cultural trend. It is believed that the practice of consanguinity has significant social and economic advantages. Consanguineous marriages among Arabs are respected because it is thought that they promote family stability, simplify financial premarital negotiations, offer a greater compatibility between the spouses and other family members, offer a lesser risk of hidden financial and health issues, and maintain the family land possessions (Bittles, 2008). Among 390 women attending reproductive health clinics in Jordan, consanguinity was protective against violence during pregnancy (Clark, Hill, Jabbar, Silverman 2009, Obeidat et al., 2008).

Worldwide, marriage between first cousins, who on average have co-inherited 1/8 of their genes from one or more common ancestors, is the most common form of consanguineous. First cousin offspring will therefore be homozygous at 1/16 of all loci (Bittles, 2008). Consanguinity is still the most common risk factor for a high frequency of autosomal recessive diseases and congenital malformations within Arab communities (Kanaan et al., 2008, Sharkia et al., 2008, Yunis et al.,

2006). In addition, several studies among Arab societies show that there is a higher occurrence of consanguineous marriages among parents of offspring with congenital malformations than in the general population (Kanaan et al., 2008, Bener and Hussain, 2006; Teebi et al., 2005). A strong association between most of the examined disorders and consanguinity was demonstrated in the present study; approximately 56% of the children with one or more disorders were the offspring of consanguineous marriages, and in approximately 68% of these marriages the parents were first cousins or closer. This association between consanguinity and disorder rate as well as the familial effect of most disorders' types that were obtained by the current results indicate that genetic factors are involved with the underlying cause.

In addition, we found that the frequency of the disorders' types were higher among males (63%) than females (37%) in our studied sample, possibly reflecting the elevated levels of X-chromosome homozygosity inheritance. The relationship between consanguinity and genetic disorders is attributed to the fact that a high prevalence of consanguinity increases homozygosity and reduces the genetic variation which may protect against the expression of recessive genes that can lead to genetic disorders in a group (Tadmouri et al., 2008). When a new mutation is inserted in such a population, it will rapidly spread, leading to an increased prevalence of carriers, and a high number of affected homozygous individuals

We believe that the genetic conditions of the disorders in the present studied sample probably relates to homozygosity autosomal recessive diseases. These results demonstrated that implementing various health interventions and genetic counselling services in order to improve public health issues in the Israeli Arab community will have a positive effect, even if only partial. Therefore, such programs are needed, particularly, for identifying and diagnosing the molecular genetic basis of the most common disorders so that a preventive program can be launched, with the aim of minimizing the occurrence of different spectrum disorders in future generations.

## CONCLUSION AND RECOMMENDATION

Research on effect of consanguinity on individual health in Arab countries is limited, both in quantity and in quality. Many studies fail to indicate clearly the different effects of consanguineous marriages in all aspects of children daily activities. As consanguinity could lead to anatomical, physiological and/ or neurological abnormalities, this will lead to multiple burdens that could affect activities of daily living, which in turn will negatively impact on quality of children life. For example, children will have limited ability to perform the normal activities of daily living and would

rely upon others to meet their needs. They may also be unable to fulfil normal roles in their family and society thus they may become isolated and marginalized. Beside that if the child has an abnormal appearance or altered functionality that would cause low self esteem, feelings humiliation, and shame which prevent them of participation with others. This was supported by the literature in which many rare and bizarre skeletal, muscle, cardiac and rare syndromes abnormalities were related to consanguineous marriage among young children (Al Hosani, Salah, Abu-Zeid et al., 2005, Madi, Al-Naggar, Al-Awadi et al., 2005, Bromiker et al., 2004, Dawodu, Al-Gazali, Varady, Varghese et al., 2005).

Consanguineous marriages are widely practiced in several global populations, with some of the highest rates observed in the Arab World. Reports abound on both the negative and positive biological effects of consanguinity. In net terms, the reproductive criteria related to consanguineous versus non-consanguineous couples include earlier parental age at marriage, younger maternal age at first live birth, higher number of infants born to consanguineous parents, similar rates of abortions, and higher rates of postnatal mortality and birth defects in offspring of consanguineous parents. Furthermore, consanguineous unions lead to increased expression of autosomal recessive disorders. Studies on the association of consanguinity with chromosomal abnormalities such as Down syndrome and other mental abnormalities among children are presently non conclusive with the recommendation of performing standardized research in the future. Likewise, studies on the association of consanguinity with traits such as intelligence quotient and stature are scanty among Arabs and results of studies performed in Western countries cannot be applied directly to societies with high consanguinity rates such as the Arab society. Research on inbreeding is considered a priority in societies with high consanguinity rates to help understand and prevent the deleterious impact of consanguinity on health, and to provide standardized and evidence-based guidelines for health care providers to assist them in counselling for consanguinity.

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