

Consanguinity, fertility, reproductive wastage, infant mortality and congenital malformations in Jordan

Sami A. Khoury, MD, MPH, Diana F. Massad, MD, MPH.

ABSTRACT

Objectives: Consanguinity is a wide spread practice in Jordan. The objective of this study is to explore the health effects of consanguinity, in particular fertility, reproductive wastage, infant mortality and congenital malformations.

Methods: A stratified 2 stage cluster sample of 1867 married couples, representative of all population groups and all geographic locations of Jordan were randomly selected. A questionnaire was specially designed to explore each of the objectives set for the study and was field tested. A group of field workers were thoroughly trained on the implementation of this instrument. All 1867 couples were interviewed by these field workers and completed questionnaires were reviewed before data entry. Data analysis was carried out using SPSSX statistical package. Significance tests were performed wherever appropriate.

Results: The study showed that fertility, as measured by

the number of pregnancies, taking into consideration marriage duration, was not affected by consanguinity. Twin pregnancies and abortions did not show any significant difference between consanguineous and non-consanguineous marriages. Consanguineous marriages showed significantly higher rates of still births and infant mortality in general. Within the consanguineous group, female infant mortality rates were significantly higher than those of males. Congenital malformations as reported by mothers of consanguineous marriages were significantly higher than those reported by mothers of non-consanguineous marriages.

Conclusion: This study showed that consanguinity has a detrimental effect on many aspects of reproductive health.

Keywords: Consanguinity, fertility, reproductive wastage, infant mortality, congenital malformations.

Saudi Medical Journal 2000; Vol. 21 (2): 150-154

Consanguineous marriage is a wide spread traditional practice in Jordan. In order to study this phenomenon, a comprehensive community based study was carried out in 1980. In a first paper,¹ consanguinity was investigated at length including selection of the sample, magnitude of the problem, types of consanguineous marriages and variables affecting consanguinity, namely: consanguinity of parents, education of husband and wife, place of residence, religion and marriage arrangement modalities. The study sample was selected by the Department of Statistics on the basis of blocks,

stratified by population size in each governorate. After stratification, a randomly selected sample of 120 blocks was drawn from all blocks in a way to allow for all population settlements in all governorates an equal chance of representation in the final sample. At a rate of 60 households in each block, it was expected to end up with approximately 7200 households from which the final sample was drawn. All 7200 households were visited by trained interviewers and date of marriage recorded. Couples married since 1969 were selected. The reason for this selection was that couples married recently

From the Department of Community Medicine, University of Jordan, Amman, Jordan.

Received 22nd June 1999. Accepted for publication in final form 16th October 1999.

Address correspondence and reprint request to: Dr. S. A. Khoury, Department of Community Medicine, University of Jordan, Amman, Jordan. Tel. +962 (6) 5355000 ext. 2393. Fax. +962 (6) 5355111. e-mail: admin@ju.edu.jo

tended to be younger and better educated. The total group married in that period of time amounted to 2007 couples.

A specially constructed self-weighting questionnaire was developed for the study. It covered, for both husband and wife, the following variables: Age, place of birth, educational level and religious affiliation. For the couple, it explored dwelling, length of current marriage, type of relation consanguineous and non-consanguineous. Consanguinity was divided into: double first cousins, first cousins types 1, 2, 3 and 4 cousins once removed and from the family. Consanguinity of the couple's parents and their date of marriage was also explored. This information was intended to construct a time trend. Modalities of marriage arrangement were also investigated and covered a spectrum extending from opposition of the husband and/or the wife to parents' opposition. The instrument was field tested before actual use. Female interviewers trained on this instrument visited all 2007 households selected for the study and completed 1983 questionnaires with housewives representing 86% of respondents. The remaining 24 couples did not respond, yielding a non-response rate of 12 per 1000. The most prevailing type of consanguineous marriage was found to be first cousins type 1 (paternal cousins) with 20% of the total sample. No relationship comprised approximately 50% of all marriages. Double first cousin relationship had an inbreeding coefficient of 0.001, first cousins (type 1, 2, 3, 4), 0.020, first cousins once removed, 0.001 and second cousins, 0.0005.

Several investigators stressed the relationship of consanguinity and health. The objective of this second part of the initial study is to explore the effect of consanguinity on: fertility, reproductive wastage, infant mortality and congenital malformation, using the data collected in the comprehensive community based study already mentioned.

Methods. Sample. All women with a history of pregnancy and/or delivery are included in this analysis. The total number of women who satisfied

this condition amounted to 1867. This final sample included 947 (51%) consanguineous marriages.

Operational definitions. For the purpose of this study, fertility was measured by the number of pregnancies. Since the number of pregnancies is primarily a function of the duration of marriage, the sample was divided into intervals of 2 years to avoid bias based on length of marriage. Pregnancy outcome included either a full term or premature live birth or reproductive wastage i.e. stillbirth and abortion. Infant mortality was defined as death of an infant before one year of age. The study of congenital malformations was not intended to establish causality but the relationship of consanguinity and congenital malformations as reported by the mother. A pediatrician experienced in congenital malformations reviewed and checked the list of reported malformations and familial diseases. Cardiac septal defect, cleft lip and palate, imperforate anus, hypospadias, congenital hip dislocation, blindness, spina bifida, limb anomaly, strabismus, oesophageal atresia, breast anomaly, ear anomaly, asthma and diabetes were accepted for analysis.

Methods of Analysis. Analysis of results was carried out by using SPSSX statistical package. Chi-square and t tests were used to assess, at the 95% confidence level, statistical significance of relationships for categorical and continuous variables. All variables under study were recorded as reported by the housewife.

Results. Age. Mean age of women in consanguineous marriages was 24.6 years as compared to 25.8 years in non-consanguineous marriages. This difference was statistically significant ($P < .001$).

Fertility. Fertility as measured by number of pregnancies is shown in Table 1. This table shows the total number of pregnancies and number of pregnancies per woman in both consanguineous and non-consanguineous relationships by intervals of marriage duration. No significant difference was observed in number of pregnancies per woman,

Table 1 - Fertility by duration of marriage and consanguinity.

Duration of marriage/years	1-2		3-4		5-6		7-8		9-10		11-12		TOTAL	
	P	P/W	P	P/W	P	P/W	P	P/W	P	P/W	P	P/W	P	P/W
Consanguineous	227	1.44	399	2.31	577	3.39	746	4.58	987	5.45	593	5.93	3529	3.73
Non-consanguineous	244	1.47	444	2.36	579	3.35	624	4.52	875	5.30	582	6.33	3348	3.63
TOTAL	471	1.45	843	2.34	1156	3.37	1370	4.55	1862	5.38	1175	6.12	6877	3.68
P - Number of pregnancies P/W - Pregnancies per woman														

neither in the total sample nor in each interval of marriage duration tested.

Pregnancy outcome. Table 2 shows pregnancy outcome (numbers and rates) by consanguinity. Significance tests were performed for all categories by consanguinity. Stillbirths were the only pregnancy outcome that showed a statistically significant difference between consanguineous and non-consanguineous relationships ($P < .05$). Twin pregnancies deserved a separate study. The results are shown in Table 3. The birth order of twin pregnancies showed a bimodal distribution with the first peak occurring at the first birth and the 2nd at the 5th. The highest percentage of twin pregnancies 47% (25) occurred among mothers in the age group 24-29 years.

Infant mortality. Table 4 shows infant deaths (numbers and rates) by consanguinity. The difference was statistically significant ($P < .01$). All types of consanguineous relationships were tested separately against non-consanguinity and the only type which showed a significant difference in infant mortality was first cousins (types 1,2,3,4), ($P < .01$), as shown in Table 5. Infant death by gender and consanguinity are also shown in Table 5, significance tests were performed, and non-consanguineous relationship showed a significantly higher male mortality ($P < .02$). Separate comparison of male infant deaths in first cousins, and other consanguineous marriages with those in non-consanguineous relationship did not show any significant difference. Similar comparison of female infant deaths, however, showed a significantly higher female death rate in first cousins ($P < .01$) as well as in other consanguineous relationships ($P < .01$).

Congenital malformations. In the total sample, 77 instances of congenital malformations were reported by mothers at a rate of 13.7/1000 live births. Malformations reported in the consanguineous group amounted to 50 (17.5/1000 consanguineous live births) as compared to 27 (9.8/1000 non-consanguineous live births). This difference was significant ($P < .01$). As demonstrated previously in infant mortality, among consanguineous marriages, only first cousin relationship showed a significant difference in the reported congenital malformations

Table 2 - Adverse pregnancy outcome by consanguinity in the total sample.

Relationship	Premature alive		Still birth*		Abortion	
	No.	Rate/LB	No.	Rate/LB	No.	Rate/LB
Consanguineous	24	8.40	32	11.20	345	97.80
Non-consanguineous	29	10.60	16	5.80	328	97.80
TOTAL	53	9.50	48	8.60	673	97.90

* Significant difference ($P < .05$)
 LB - 1000 live births (consanguineous n = 2857, non-consanguineous n=2746).
 P - 1000 pregnancies (consanguineous n = 3529, non-consanguineous n=3348)
 NB: Total number of pregnancy outcome does not correspond to the total number of pregnancies. Twins were allocated to one or another category according to the condition of the twin infants at birth and still pregnant women are not included.

Table 3 - Twin pregnancies by consanguinity in the total sample.

Relationship	Number	Rate/1000 Pregnancy
Consanguineous	21	5.9*
Non-consanguineous	32	9.6**
TOTAL	53	7.7

Difference was statistically not significant.
 * Rate is from 1000 consanguineous pregnancies (n=3529)
 ** Rate is from 1000 non-consanguineous pregnancies (n=3345)

Table 4 - Infant death by consanguinity in the total sample.

Relationship	Number	Rate/1000 LB
Consanguineous	186	65.1*
Non-consanguineous	134	48.8**
TOTAL	320	57.1

Significant difference ($P < .01$)
 * Rate is from 1000 consanguineous live births (LB) (n=2857)
 ** Rate is from 1000 non-consanguineous live births (LB) (n=2746)

Table 5 - Infant deaths by gender and consanguinity.

Relationship	Males	Rate/1000 LB	Female	Rate/1000 LB	Total	Rate/1000 LB
* First cousins (all types)	63	66.5	67	74.6	130	70.5(a)
** Other consanguineous	31	58.4	25	51.8	56	55.3
*** Non-consanguineous	79	57.9	55	39.8	134	48.8(b)
**** Total sample	173	60.9	147	53.2	320	57.1

* Gender difference was not significant - rate for males is from 1000 1st cousin male live births (n=947) - rate for females is from 1000 1st cousin females live births (n=898). ** Gender difference was not significant - rate for males is from 1000 other consanguineous male live births (n=530) - rate for females is from 1000 other consanguineous female live births (n=482). *** Gender difference was significant $P < .02$ - rate for males is from 1000 male non-consanguineous live births (n=1364) - rate for females is from 1000 female non-consanguineous live births (n = 1382). **** Gender difference was not significant - rate for males is from 1000 total male live births (n = 2841) - rate for females is from 1000 total female live births (n=2762). a,b show significant difference $p < 0.01$

when compared with non-consanguineous relationship ($P < .05$).

Discussion. The discussion herein refers to community-based studies and does not include case reports of individuals with a presumed relationship between consanguinity and abnormality. Japanese researchers were the first to draw attention to the health effects of consanguinity.²

Fertility did not show any significant difference between consanguineous and non-consanguineous marriages. This result is supported by several research findings.³⁻⁸ Khlaf,⁹ in Beirut, Lebanon, initially reported a significantly higher fertility rate among consanguineous couples, however, when controlled for socioeconomic status, religious affiliation and specially marriage duration, no difference was found. Another study in India¹⁰ showed a significantly higher fertility among consanguineous marriages, but this study did not control for duration of marriage when calculating fertility. Twin pregnancies did not show any significant relationship with consanguinity. Review of literature failed to show any relationship between the two groups as well.

Prematurity was not affected by inbreeding, and no significant relationship was found with consanguinity. This finding is supported by the studies of the Old Order Amish.¹¹ Consanguineous marriages produced a significantly higher number of stillbirths. This finding had been supported by several reports.^{8,12-14} One study in India¹⁵ found that stillbirth rates were significantly higher in consanguineous groups irrespective of the mother's socioeconomic status and that stillbirths were also higher in uncle-niece matings in both poor and upper middle classes.

In the present study, abortions were not significantly affected by consanguinity. Comparison of several studies seems to indicate that the effect of consanguinity on abortion may differ with locality. Some studies support our findings,^{6,7} while others¹⁶⁻¹⁹ found that abortions occurred more frequently in consanguineous marriages. With regard to the apparent local variance of the effect of consanguinity on abortion rates, one should note that in some districts of India, uncle-niece marriages may constitute as much as 24% of marriages among Hindus.²⁰ This type of marriage is rarely seen in other parts of the world.^{21,22}

Infant mortality, an important indicator of community health was analyzed thoroughly. As is shown in table 4, consanguineous marriages had a significantly higher rate of infant mortality than non-consanguineous marriages. Analysis of infant mortality by gender and consanguinity did not show any significant difference in mortality rates between males and females in the sample as a whole, nor in

first cousin marriages (types 1, 2, 3, 4), and in other consanguineous groups as well (Table 5). Non-consanguineous marriages, however, showed a significant difference. This difference, with a higher rate of male mortality follows the usual pattern of infant mortality,²³ thus this group was taken as a reference in comparing gender deaths in other groups. Male and female deaths in first cousins and other consanguineous marriages were compared to male and female deaths in non-consanguineous relationships. The results seem to indicate that inbreeding increases the female infant mortality to a point where there is no significant difference in infant mortality between genders. Although Ansley Coale²⁴ and Hill and Upchurch²⁵ made the same observation, they attributed this increase in female infant mortality to cultural gender discrimination. This fact needs further in-depth genetic and cultural studies.

Several researchers observed increased occurrence of congenital malformations in offspring of consanguineous marriages, both in Arab countries²⁶⁻²⁹ and other parts of the world.^{11,14,17,30,31} According to some observers, congenital malformations increased with a closer consanguineous relationship, first cousins,³² and uncle-niece marriages in India.¹⁵ Organ specific malformations have also been associated with consanguinity in Saudi Arabia³² and France.³³

In conclusion, this comprehensive community based study showed that 51% of marriages in Jordan were consanguineous. Health effects of consanguinity showed a significant relation of inbreeding with stillbirths, infant mortality in general and female infant mortality in particular. Congenital malformations as reported by the mother occurred more frequently in consanguineous marriages. This study has shown that consanguineous marriage is an important social and health problem which should be addressed by an intensive health education campaign. The study also provides a baseline for further investigations.

References

1. Khoury SA, Massad D. Consanguineous marriage in Jordan. *Am J Med Genet* 1992; 43: 769-775.
2. Imaizumi Y, Shinozaki N, Aoki H. Inbreeding in Japan: Results of a Nation-Wide Study. *Jpn J Hum Genet* 1975; 20(2): 91-107.
3. Edmond M, DeBrackeleer M. Inbreeding effects on fertility and sterility: A case control study in Saguenay-Lac-Saint-Jean (Quebec, Canada) based on a population registry 1838-1971. *Ann Hum Biol* 1993; 20(6): 545-555.
4. Shami SA, Schmitt LH, Bittles AH. Consanguinity, spousal age at marriage and fertility in seven Pakistani Punjab cities. *Ann Hum Biol* 1990; 17(2): 97-105.
5. Hann KL. Inbreeding and fertility in a South Indian population. *Ann Hum Biol* 1985; 12(13): 267-274.
6. Saha N, Hamad RE, Mohamed S. Inbreeding effects on reproductive outcome in a Sudanese population. *Hum Hered* 1990; 40(4): 208-212.

7. Jain VK, Nalini P, Chandra R, Srinivasan S. Congenital malformations, reproductive wastage and consanguineous matings. *Aust N Z J Obstet Gynaecol* 1993; 33(1): 33-36.
8. Verma IC, Prema A, Puri RK. Health effects of consanguinity in Pondicherry. *Indian J Pediatr* 1992; 29(6): 685-692.
9. Khlal M. Consanguineous marriage and reproduction in Beirut, Lebanon. *Am J Hum Genet* 1988; 43(2): 188-196.
10. GovindaReddy P. Effect of consanguineous marriages on fertility among 3 groups of Andhra Pradesh. *Soc Biol* 1987; 34: 68-77.
11. Khoury MJ, Cohen BH, Diamond EL, Chase GA, Mckusick VA. Inbreeding and prereproductive mortality in the Old Order Amish III. Direct and indirect effects of inbreeding. *Am J Epidemiol* 1987; 125(3): 473-483.
12. Basaran N, Hassa H, Basaran A, Artan S, Stevenson JD, Sayli BS. The effect of consanguinity on the reproductive wastage in the Turkish population. *Clin Genet* 1989; 36(3): 168-173.
13. Stoll C, Alembik Y, Dott B, Feingold J. Parental consanguinity as a cause of increased incidence of birth defects in a study of 131,760 consecutive births. *Am J Med Genet* 1994; 49(1): 144-147.
14. Magnus P, Berg K, Bjerkedal T. Association of parental consanguinity with decreased birth weight and increased rate of early death and congenital malformations. *Clin Genet* 1985; 28(4): 335-342.
15. Kulkarni ML, Kurian M. Consanguinity and its effect on fetal growth and development: A South India study. *J Med Genet* 1990; 27(6): 348-352.
16. Baki A, Karaguzel A, Beser E, Cakmakci T, Ucar F, Omeroglu A. Consanguineous marriages in the Province of Trabzon, Turkey. *East Afr Med J* 1992; 69(2): 94-96.
17. Guz K, Dedeoglu N, Luleci G. The Frequency and medical effects of consanguineous marriages in Antalya, Turkey. *Hereditas* 1989; 11(1): 79-83.
18. Shami SA. Inbred and non-Inbred first cousins marriages. *JPMA J Pak Med Assoc* 1983; 3-6.
19. Asha Bai PV, Jacob JT, Subramaniam VR. Reproductive wastage and development disorders in relation to consanguinity in South India. *Trop Geogr Med* 1981; 33: 275-280.
20. Radha Rama Devi A, Appaji Rao N, Bittles AH. Inbreeding in the state of Karnataka, South India. *Hum Hered* 1982; 32: 8-10.
21. Costeff H, Dar H. Consanguinity analysis of congenital deafness in Northern Israel. *Am J Hum Genet* 1980; 32: 64-67.
22. Fraccaro M. Consanguineous marriages in Italy. *Eug Q* 1957; 4(1): 36-39.
23. Mausner JS, Bahn AK. *Epidemiology*. 2nd ed. Philadelphia (USA): WB Saunders Company; 1985. p. 123.
24. Coale AJ. Excess female mortality and the balance of the sexes: an estimate of the number of missing females. *Population and Development Review* 1991; 17(3): 517-523.
25. Hill K, Upchurch DM. Gender differences in child health: Evidence from the demographic and health surveys. *Population and Development Review* 1995; 21(1): 127-151.
26. Hamamy HA, Al-Hakkak ZS. Consanguinity and reproductive health in Iraq. *Hum Hered* 1989; 39(5): 271-275.
27. Khrouf N, Spang R, Podgorna T, Miled SB, Moussaoui M, Chibani M. Malformations in 10,000 consecutive births in Tunis. *Acta Paed Scand* 1986; 75(4): 534-539.
28. El-Shafei A, Rao PS, Sandhu AK. Congenital malformations and consanguinity. *Aust N Z J Obstet Gynaecol* 1986; 26(3): 168-172.
29. Gev D, Roguin N, Freundlich E. Consanguinity and congenital heart disease in the Rural Arab population in Northern Israel. *Hum Hered* 1986; 36: 213-217.
30. Moreno-Fuenmayor H, Champin J, Alvarez-Arratia M, Sanchez O. Epidemiology of congenital malformations in Bolivar City, Venezuela. Analysis of the consanguinity factor. *Invest Clin* 1993; 34(1): 5-14.
31. Gordon M, Gorman DR, Hashem S, Stewart DG. The health of travelers' children in Northern Ireland. *Public Health* 1991; 105(5): 387-391.
32. Al-Faran MF, Tabbara KF. Corneal dystrophies among patients undergoing Kerato plasty in Saudia Arabia. *Cornea* 1991; 10(1): 13-16.
33. Stoll C, Alembik Y, Dott B, Roth MP. Epidemiological and genetic study in 207 cases of oral clefts in Alsace, North-eastern France. *J Med Genet* 1991; 28(5): 325-329.