Asian Journal of Pharmaceutical and Health Sciences
www.ajphs.com

Consanguineous marriages and their malformation in F_1 generation

Farzana Perveen*, Shagufta Rehman

Department of Zoology, Hazara University, Garden Campus, Mansehra-21300, Pakistan

ARTICLE HISTORY

Received: 12.05.2012

Accepted: 15.06.2012

Available online: 10.08.2012

Keywords:

Blood relatives, congenital, consanguineous marriages, F_1 generation.

***Corresponding author:**

Email : farzana_san@hotmail.com
Tel : 0300-2253872

ABSTRACT

This paper describes the malformation in F_1-generation of parents having consanguineous marriages. The purpose of research is to produce awareness in public about prevalence of genetic disorders in offspring increased with passage of time due to consanguineous marriages. The present survey was conducted from January-March 2010, in Bajaur-Agency, Pakistan. Data was collected from 123 consanguineous married couples through questionnaire comprised of information about complete history and risk factors of malformation from the following different localities: Sadiq Abad, Chamerkand, Loisam, Anatkali, Nawagai, Manudera, Raghagan, Nawaikali, Alijan, Gandaw where cousin marriages are dominant. They have healthy children 26%, abnormal 8.2%, both healthy and abnormal 39% and no children 27%. They have abortion 35.7%, still birth 21.1%, live birth 81.3% and dead one 25.2%. The children were died due mental retardation, cardiac anomalies, heamoglobinopathies, jaundice, fits, meningocele and other multiple malformations. The live children were also suffering from diseases. The couples having such children, their percentage was in descending order: diseases deafness and speech disorders: 13%, cleft lip and palate 11%, asthmatic diseases and mental retardation: each 10%, cardiac anomalies 8% and obesity and ophthalmic anomalies: each 7%. Comprehensive genetic education and premarital genetic counseling programs can help to lessen the burden of genetic diseases in such communities.

INTRODUCTION

The consanguineous marriage is defined as "a union between a couple who are blood relatives", i.e., to marry paternal or maternal uncle and aunt's daughter/son [1]. They occur throughout the world with varying degrees. Worldwide they are between first and second cousins, about 20 and 10.4%, respectively. It is particularly prevalent in Middle East, Africa, Asia and Saudi Arabia [2]. In Pakistan, they are extremely common, about 60% of the marriages are reported to be consanguineous and among them 80% are between first cousins [3].

In many cultures, they are preferred option for both economic and social obligations. In many parts of the world, a dowry is an integral part of the wedding process and a substantial amount of money or property involved. Those who cannot afford a sizeable dowry may choose to marry within the family to relieve the cost. Some families have a tremendous inheritance and are reluctant to spread the resources outside of the family; therefore, cousin marriage is favorable to them [4-5]. It is believed that consanguineous marriage will strengthen family ties. In addition, marrying with in family ensures that everyone is familiar with the couple and their history [6].

Consanguinity means shared the genetic material, i.e., identical DNA. First cousins have four times the consanguinity of second cousins. First cousins once removed half the shared DNA as full first cousins. Half-fourth cousins sometimes cannot be detected at the DNA level. Finally, double first cousins share twice the consanguinity as first cousins and are as related as half-siblings. Parental consanguinity increases the autosomal recessive conditions through the expression of recessive deleterious alleles, especially, in the offspring of first cousins. Medical research has shown that they should be avoided, because children born from such marriages are adversely affected. The consanguinity has been associated with increased risk of pediatric disorders including: stillbirth, abortion, dead children and perinatal mortality, congenital birth defects, malformations,

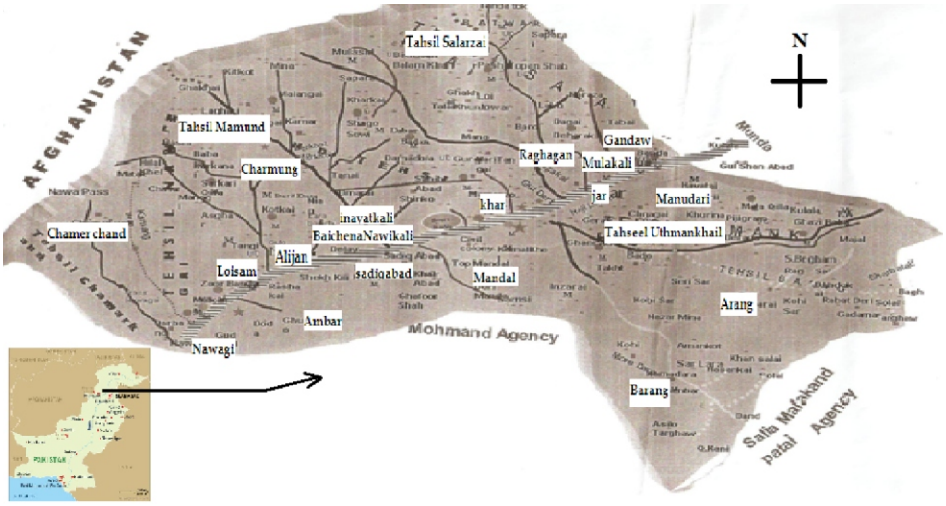

Fig. 1 : Map of Bajaur Agency [11] where questionnaires were filled by consanguineous married couples visited to Ar-Rehman General Hospital during January to March 2010

mental retardation, blood diseases (e.g., hemophilia, thalassemia), cystic fibrosis, chronic renal failure and neonatal diabetes mellitus [7]. In order to prepare ourselves to accept the challenges regarding congenital malformations due to them, the first step is to get complete information of their prevalence and risk factors [8-9].

Bajaur is the smallest agency of the Federally Administered Tribal Areas (FATA) of Pakistan with a hilly terrain. It is located from 34°41′ to 71°30′ northeast, 34.683° to 71.5° north latitudes. Annual growth rate is 4.33 with total population of Bajaur agency 595, 227 with female and male are 290,090 and 305,137, respectively. People of Bajaur agency are 100% pathan with Sunni Muslims. They are hardworking having strong religious belief; however, poverty is widely spreaded. Due to lack of education they are conservative in their customs and traditions. People live and die for their honors and dignity. They feel pride in taking revenge from their enemies, however, jirga and hospitality is very dear to them (Fig. 1) [10].

The trends in cousin marriages show a decline in the practice among people in the Jordan, Lebanon, Morocco, Mauritania and Israel. An increasing trend is found in the Qatar, United Arab Emirates and Yemen. In the North America, Europe, Russia and Australia less than 1% of consanguinity was calculated. Other areas including the South America, North India and Japan, it was 1-10%. While higher rate of consanguinity was calculated in Arab countries, Turkey, Iran, Pakistan and south India, it was 20-50% [12]. Avoiding cousin marriages will result in a real reduction of the frequency of birth defects and genetic diseases in general. The carrier testing and to create a plan for prevention medical and genetics complications their doctors would help the couples [13-14]. The objectives of the present research are to determine the frequency of malformation in first and second cousin marriages and to know the main effects of consanguinity in Bajaur Agency.

MATERIALS AND METHODS

Area study

Bajaur Agency is the backward area of FATA, Khyber Pakhtunkhwa, Pakistan, where the literacy rate is very low. Therefore, the present research was conducted to aware the people about later harmful effects of cousin marriages in different areas of Bajaur Agency.

Study design

This study is a small effort towards guidance of the people of Bajaur Agency. The data was collected through questionnaire which consists of fifteen [15] items related to the cousin marriage was designed in such a way to get complete history of family in which cousin marriage was held. These questionnaires were filled by 123 consanguineous couples from different areas of the Bajaur Agency including Anatkali, Khar, Nawagi, Barang, charmang, Manuderai Mamund, Jar, Raghagan, Hajiluang, Salarzo, Mandal, Shamozo, uthmankhail, Arang, Loisam, Gardai, Biechena, Hiati, Saddiq abad, Alizae, Ambar, Bartras, Ali jan, Gandaw, Nawae kali (Figures 5). As the people of Bajaur agency are illiterate, therefore, questionnaires were filled by help of the local doctor. First, the patients who were the local residents of Bajaur Agency informed about the study and purpose of the study. Then they were requested to cooperate in filling the questionnaires. Some pictures of children affected by cousin marriages were also taken. The data was analyzed by computer program Microsoft Excel.

RESULTS

The present survey was conducted to estimate the number of *cousin marriages and their* malformation during January to March 2010 in Bajaur Agency. The data for such purpose were collected through questionnaire which consisted of fifteen (15) items. As the people of Bajaur Agency are illiterate, therefore, questionnaires were filled with the help of a local doctor. There were 52% couples' parents that were married to their 1st cousin while 47.9% couples' parents were 2nd cousin.

In the present study, it was found that the couples having percentage of healthy children were about the same as having no children. While couples having abnormal children were less as compared to have both healthy and abnormal children suffering from some sort of abnormalities (Table 1).

According to estimation, the couples having different medical complications during birth were in descending order: abortions > dead children > still birth > live birth (Table 2).

It was observed that the couples' children were died with the following diseases given here in descending order: mental

Table 1 : The couples having healthy, abnormal and both healthy and abnormal children found in the present survey done during January to March 2010 in Bajaur Agency, Pakistan.

SNo	Health of children	n[1]	Percentage (%)[2]
1.	Healthy children	123	26
2.	Abnormal children	123	8.2
3.	Both normal and abnormal children	123	39
4.	No children	123	27

[1]n: Questionnaires were filled by 123 consanguineous married couples from different areas of Bajaur Agency, FATA, Khyber Pakhtunkhwa, Pakistan
[2]%: Percentage of consanguineous married couples having children with different health conditions

Table 1 : The couples having healthy, abnormal and both healthy and abnormal children found in the present survey done during January to March 2010 in Bajaur Agency, Pakistan

SNo	Medical complications	n[1]	Percentage (%)[2]
1.	Abortion	123	35.7
2.	Dead children	123	25.2
3.	Live birth	123	18.0
4.	Still birth	123	21.1

[1]n: Questionnaires were filled by 123 consanguineous married couples from different areas of Bajaur Agency, FATA, Khyber Pakhtunkhwa, Pakistan
[2]%: Percentage of consanguineous married couples having different medical complications.

retardation: 20% > jaundice and fits: 17% > meningocele diseases: 16.6% > cardiac anomalies: 13% > heamoglobinopathy: 12.5% > deafness and speech disorders: 11.5% > multiple malformation: 9.4% (n=123; Fig. 2).

It was also observed that the couples' children who were alive were suffering from different disease. The couples having such children, their percentage was in descending order is given here: diseases deafness and speech disorders: 13% > cleft lip and palate: 11% > asthamatic diseases and mental retardation: each 10% > respiratory diseases: 9% > cardiac anomalies: 8% > obesity and ophthalmic anomalies: each 7% > heamoglobinopathy: 6% > diabetes: 5% > bone diseases and congenital malformation: each 4% > mild anemia and multiple malformation: each 3% (n=123; Fig. 3). Some photographs of alive children of consanguineous couples who were suffering from cleft lip (a), deafness (b), mentally retarded disorder (c), speech disorder (d), mentally retarded and speech disorder (e) and deafness and mentally retarded (Figure 4f) are given here (Fig. 4).

The present survey was conducted in the following different localities of Bajaur agency in descending order: Alijan: 14% > Anatkali: 13% > Gandaw: 12% > Manudera and Nawaikali: each 11% > Loisam: 10% > Chamerkand: 9% > Raghagan and Nawagai: each 8% > Sadiq Abad: 4%; where *cousin* marriages were performed predominantly (n=123; Fig. 5).

DISCUSSION

The consanguineous marriage attracts considerable attention as a causative factor in the prevalence of genetic disorders in F_1 Generation [5]. It is estimated that globally over 20% of the human population live in communities with a preference for them and over 8.5% of all children have consanguineous parents [13]. As in Pakistan mostly arrange marriages are held especially between cousins and a list of diseases related to them is very long, therefore, it is very important to make people aware of it.

The present study comprises of questionnaire which was filled by 123 one partner of consanguineous married couples visited in the local clinic from different areas of the Bajaur Agency. The questionnaire was designed in such a way to get complete history of his/her family in which cousin marriage was held. It was reported that its prevalence was 30.6% in Kahramanmaras with first (22.6%) and second cousins (8%) [14]. *While in another study, in which* its frequency in the population was 21%, among them 20.3% were first cousin and 29.4 % between distant relatives [15]. In the present study, out of 123 couples 87% were 1st while 13% were 2nd cousins, the frequency was higher as compared to aforementioned studies.

In the present study, it was observed that the couples' children were died with the greatest percentage of congenital

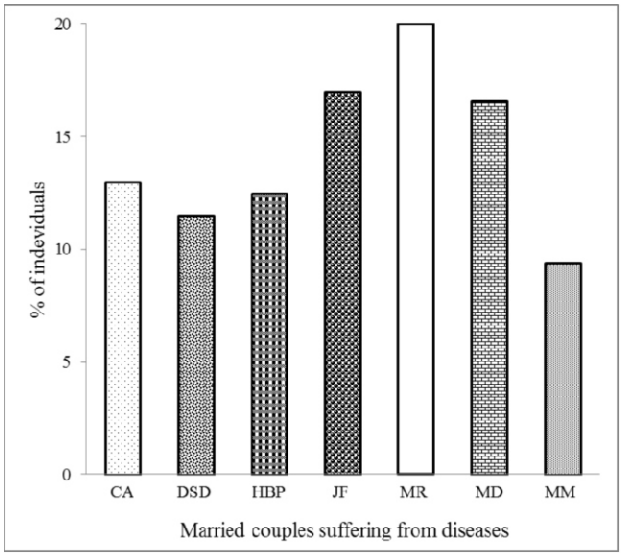

Fig. 2 : The percentage (%) of malformations found in consanguineous married couples in their dead children: CA: cardiac anomalies; DSD: deafness and speech disorders; HBP: heamoglobinopathy; JF: jaundice and fits; MR: mental retardation; MD meningocele diseases; MM: multiple malformation; n= questionnaires were filled by 123 consanguineous couples in the present survey done during January to March 2010 in different localities of Bajaur Agency FATA, Khyber Pakhtunkhwa, Pakistan.

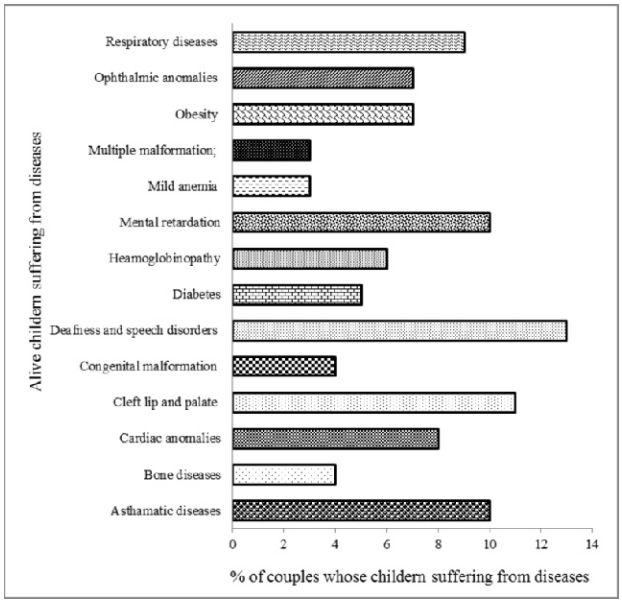

Fig. 3 : The percentage (%) of malformations found in the live children of consanguineous married couples (n=questionnaires were filled by 123 consanguineous couples) in the present survey done during January to March 2010 in different localities of Bajaur Agency, FATA, Khyber Pakhtunkhwa, Pakistan

malformations (n=123; Fig. 2), however, their parents did not know the exact age of children and name of diseases at the time of death because they are mostly illiterate, moreover, they are aware of the signs of diseases. On the basis of signs, it was suggested that children were died with cardiac anomalies, heamoglobinopathy, multiple malformations, jaundice, fits and meningocele. [16] reported that cystic fibrosis and von Gierke's disease (glycogen

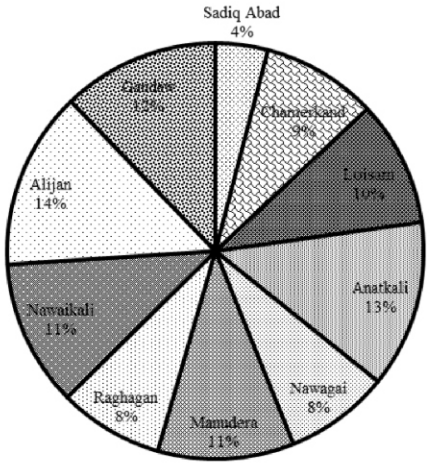

Fig. 5 : The cousin marriage in different localities of Bajaur agency in the present survey done from January to March 2010; Alijan, Anatkali, Chamerkand, Gandaw, Loisam, Manudera, Nawagai, Nawaikali, Raghagan and Sadiq Abad; n= questionnaires were filled by 123 consanguineous couples from different localities of Bajaur Agency, FATA, Khyber Pakhtunkhwa, Pakistan

storage disease of the liver) were attributable to the action of recessive genes. Six children in a family of 11 were died with muscular dystrophy. Although the autopsy recorded from the fifth child made no mention of this condition, it is possible that the first, fifth and sixth children were died because of homozygosity for the same gene. It is likely that other deaths were also due to the effect of specific recessive genes, but this was not ascertainable for the present cases. [17] showed that congenital heart disease was the main cause of death in the malformed children (36 cases) among which interventricular septal defects showed by the highest rate of children which was 15. [18] reported that the most of the children, females born with normal weight were died from interventricular septal defects. [19] reported that malformations usually were very common and seen on all body organs and skeletal systems; however, the bones and joints malformations were the most prevalent.

Hijazi and Haider [20] reported that in live children, it was observed the joints and bone diseases 0.0083%, cardiac anomalies 0.005%, ophthalmic anomaly 0.05%, however, cleft lip (without cleft palate disorders) 0.4-0.8, respiratory tract infection 0.0012% and deafness or acoustic disorder 0.003%. Since prevalence of congenital heart diseases was approximately 0.4-0.8. In another study from Kuwait, the consanguinity rate in the parents of children with asthma was 42%. [19] reported that bone and joint diseases were 0.0083% whereas in the present study, it was 0.8% which was higher. Other diseases like respiratory disease and speech disorder were mentioned by Rehmani were 0.0012% and 0.003%, respectively, which was lower than in the present study as they were 9 % and 13%, respectively. The rate of cleft palate and ophthalmic anamolies were higher in the present study as compared to both studies. They reported asthma which was 42% whereas in the present study it was 4.8%. It shows that the ratio of asthmatic disease was higher in Hijazi and Haider [20] study as compared to the present study. The ratio of depression in a pilot study was noted as 5.66% while in the present study it was lower as 1.6%.

According to the present study, 35.7% abortions and 21.1%

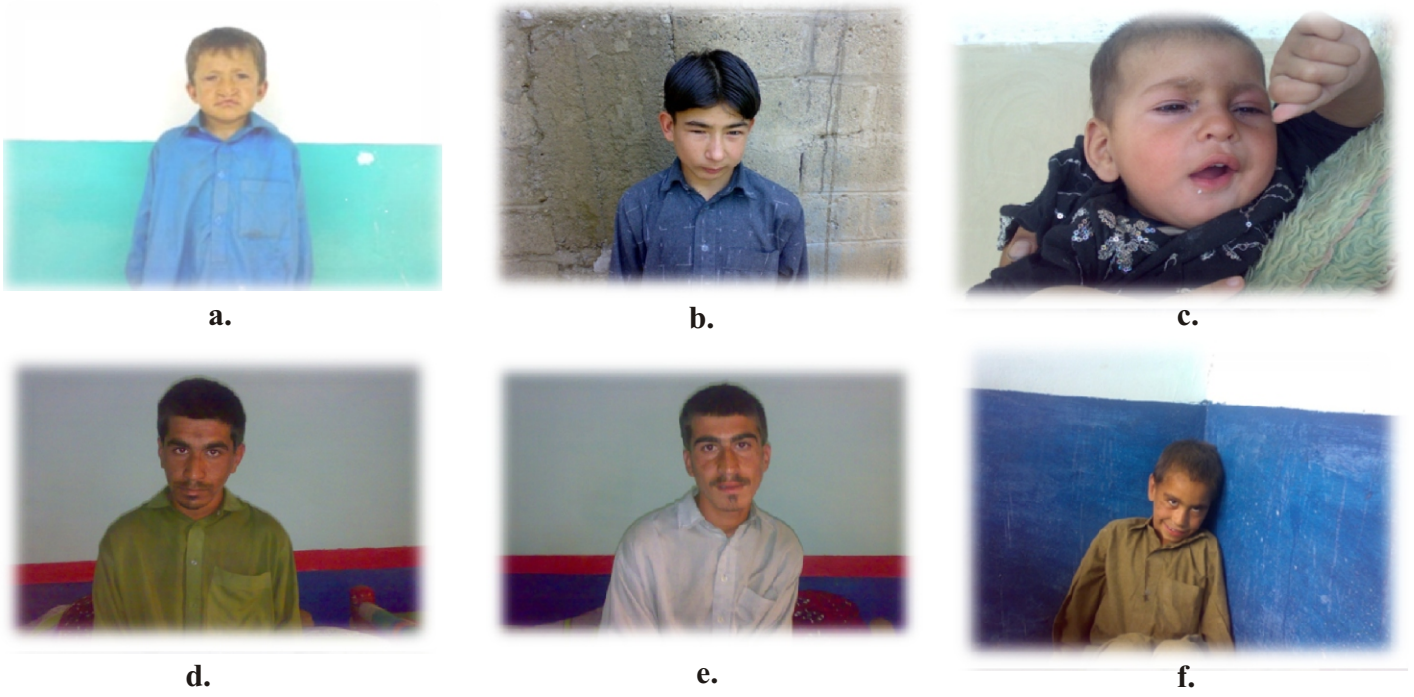

Fig. 4 : The malformation in the live children of consanguineous married couples (n= questionnaires were filled by 123 consanguineous couples) a: cleft lip; b: deafness; c: mentally retarded disorder; d: speech disorder; e: mentally retarded and speech disorder; f: deafness and mentally retarded in the present survey done from January to March 2010 in different localities of Bajaur Agency, FATA, Khyber Pakhtunkhwa, Pakistan

still births were noted. Weiss et al. reported that the World Health Organization (WHO) estimated 15% all clinically recognizable pregnancies end in an abortion [21]. *reported that the* positive history of abortion which had significant correlation with congenital malformations. Among 373 couples, 278 abortions and 95 still births and fetal losses rate was significantly higher than the present [19]. According to Brent rate of abortion was 15%, however, according to Rahmani et al. this rate was 74% while in the present study it was 35.7% [19]. In present study, the rate of still births was lower compared with Rahmani et al. it was 25% [19].

In the present study, it was found 48% were weak, 18% normal while 34% were obese couples during marriage (results are not shown). Weiss et al. reported that the obese woman was at risk for a multitude of potential medical and obstetric problems during gestation, which may had adverse short-term effects on her fetus. There was an increased risk of miscarriage in obese women, whether they conceived after natural conception or assisted reproductive measures [21]. Labayen also claimed that both maternal and paternal body mass index (BMI) increased cardiovascular disease risk factors of their offspring. Total and central body fat and higher maternal BMI were associated with poorer cardio respiratory fitness. The present findings gave further support to the concept that in parents' adiposity transmitted susceptibility to cardiovascular disease risk to descendants, which was detectable even in the absence of overweight in offspring [22]. The present study showed 10% obese couples; however, the study of. [21] claimed that obesity of women caused multiple problems during gestation. Another study of Labayen [22] showed that both maternal and paternal high and low BMI associated with poorer cardio respiratory fitness and increase cardiovascular disease risk factors in their offspring. Bajaur Agency is a remote area of FATA, Pakistan with very high rate of illiteracy. There is need to educate the people and create awareness about the medical and genetics prospects of cousin marriages are prime important in reducing them.

CONCLUSIONS

Cousin marriages remain culturally, socially favored and respected in many countries, mostly in Arab, Iran, Pakistan, Turkey and India. The risks of cousin marriage are the highest among families with severe segregating autosomal recessive conditions. These data suggest that premarital genetic, social counseling and mass media efforts needed to increase public awareness about genetic risks associated with cousin marriage. Those female whose age is below 20 years should not get married because according to Hamamy et al [17] younger female age at marriage leading to increased maternal reproductive span and congenital malformation. The frequency of consanguineous marriages correlates with an increase in recessively transmitted diseases congenital malformations and infant mortality. First cousin marriage in inbred families carries an even higher risk for autosomal recessive genetic diseases than first cousin marriage in non-inbred family.

ACKNOWLEDGEMENT

We are grateful Doctors and Employees, Ar-Rehman General Hospital, Bajaur Agency FATA, Khyber Pakhtunkhwa, Pakistan for cooperation in the present research. The experiments comply with the current laws of the country in which they were performed. We also attest that any human and /or animal studies undertaken as part of the research from which this manuscript was derived are in compliance with regulation of our institution(s) and country and with generally accepted guidelines governing such work.

REFERENCES

1. Bittles AH, Makov E. In human mating patterns, Inbreeding in human populations: An assessment of the costs, Edited by Tyalor, MCGN and Boyce, A. Cambridge University Press, Cambridge, UK, 1988: 153167.
2. Bittles AH, Neel JV. The costs of human inbreeding and their implications for variation at the DNA level. Nat. Gene. 1994: 8: 117-121.
3. Abdulkareem A, Al-Abdulkareem A, Seifeddin G, et al. Consanguineous marriage in an urban Area of Saudi Arabia: Rates and adverse health effects on the offspring. J. Commu. Health. 2004: 23: 75-83.
4. Mansoor H. Types of marriages in Pakistan. 2010: Online: http://EzineArticles.com/?expert =Hayi_Mansoor (Accessed: 12/01/2012).
5. Alwan A, Modell B. Disorders EMRO and community control of genetic and congenital Eastern Mediterranean region Egypt. Technical publication Series 24. WHO Regional Office, New York, USA, 1997: 1-40.
6. Rao TS, Prabhakar AK, Jagannatha R. Relationship between consanguinity and depression in a South Indian population. Ind. J. Psych. 2009: 51(1): 50-2.
7. Tunçbilek E, Koç I. Consanguineous marriage in Turkey and its impact on fertility and mortality. Ann. Hum. Gene. 1994: 58: 321-329.
8. Temtamy SA, Meguid AN, Mazen I, et al. A genetic epidemiological study of malformations at birth in Egypt. East. Medit. Heal. J. 1998: 4 (2): 252-259.
9. Shami SA, Qaisar R, Bittles AH. Consanguinity and adult morbidity in Pakistan. Lance. 1991: 338: 954955.
10. Bittles AHA. community genetics perspective on consanguineous marriage. Commu. Gen. 2008: 11: 324330.
11. Hussain R. Community perceptions of reasons for preference for consanguineous marriages in Pakistan. J. Bios. Sci. 1999: 31: 449-461.
12. Teebi A. WCMC-Q Physician Explores the Social and Health Implications of Cousin Marriage. Wie. Cor. Med. Col. QR. 2009: 155.
13. Modell B, Darr A. Genetic counseling and customary consanguineous marriage. Nat. Rev. Gene. 2002: 3: 225229.
14. Donbak L. Consanguanity in Kahramanmaras city, Turkey, and its medical impact. Sau. Med. J. 2004: 25(12): 1991-1994.
15. Wahab A, Ahmad M, Consanguineous marriages in the Sikh Community of Swat, NWFP, NWFP, Pakistan. J. Soc. Sci. 2005: 10(3): 153-157.
16. Bener, A, Hussain R, Teebi AS. Consanguineous marriages and their effects on common Adult disease: Studies from an endogamous population. Med. Princ. Pract. 2007: 16: 262267.
17. Hamamy HA, Masri AT, Al-Hadidy AM, et al. Consanguinity and genetic disorders. Profile from Jordan. Sau. Med. J. 2007: 28: 1015-1017
18. Herman, M, Raymond, RH, Reis, Hoene, RE. Consanguineous marriages in the Chicago region. Amer. J. Hum. Gen. 1958: 10(4): 446-464
19. Rahmani SA, Aboualsoltani F, Pourbarghi M, et al. The frequency of consanguineous marriages and their effects on offspring's in Tabriz City. Shi. Med. J. 2010: 11: 12.
20. Hijazi, Z, Haider, MZ. Influence of consanguinity and Ig E receptor genotypes on clinical manifestations of asthma in Kuwaiti children. J. Trop. Pediat. 2001: 47: 13-6.
21. Weiss JL, Malone, FD, Emig D. Obesity, obstetric complications and cesarean delivery rate a population based screening study. Amer. J. Obst. Gyne. 2004: 190: 10917.
22. Labayen I, Ruiz JR, Ortega FB, et al. Intergenerational Cardiovascular Disease Risk Factors Involve both Maternal and Paternal BMI. Diab. J. Org. 2010: 33: 4-36.