

Consanguineous Marriages in the Middle East: Nature Versus Nurture

Bowirrat Abdalla* and Armaly Zaher

EMMS Nazareth-The Nazareth Hospital Nazareth, Zip code: Postal. O. Box: 11; Zip code: 16100, Israel

Abstract: Family is societal institution that is conceptualized as “Vital” and “Valid” its importance is emphasized by social conservatives across cultures. Consanguinity is usually socially motivated and can be genetically harmful; it is a state of being descended from a common ancestor. It has been practiced by many societies around the globe from time immemorial, and a part of most civilizations as far back as the Old Testament of the Bible, and in the Arab world before the emerging of the Islam, and therefore, it is not monopoly where Islamic faith prevails.

We scrutinize the effect of consanguinity on family health, its benefits and its detriments, and how should be tackled on medical and policy levels. We also pursue the Islamic attitude and discourses on the marriage custom, law, ethics and principles. Attention is then drawn to the cultural influences and challenges in the Arab word.

Keywords: Consanguineous Marriages, Family Health, Arab word.

INTRODUCTION

While marriages between close biological kin are customary in many parts of the world, particularly in Middle Eastern countries, where consanguinity has been a long-standing habit, a vast gap in understanding this central feature of human kinship structure persists.

Historically, the term consanguinity is derived from the Latin words: *con* – “shared” and *sanguis* “blood”. A marriage is said to be consanguineous where the marriages are solemnized among persons descending from the same stock with close biological relations [1]. A relationship between two cousins is the most common of consanguineous mating [2].

Marriage between two such individuals who have at least one traceable common ancestor is said to be ‘consanguineous’ and offspring of such mating ‘inbred’ (Fig. 1 and Fig. 2).

The terms *inbreeding* and *consanguinity* are used interchangeably to describe unions between couples. Inbreeding in population genetic terms refers to a departure from nonrandom “mating” in that individuals “mate” with those more similar (genetically) to them than if they “mated at random” in the population. In fact, inbreeding is a pejorative term when applied to humans, because of its negative impact on the society and health system and *coefficient of inbreeding (F)* is a term used in population genetics [3] to describe this phenomenon.

It is widely perceived that consanguinity is more prevalent among the underprivileged in the society [4-6]. However, it is possible that factors that are not genetically

determined, such as education level and socio-economic status of the subjects, have a confounding effect in the studies on consanguinity [7]. Traditionally, some cultures have practiced and continue to practice marriage between relatives as a means of strengthening family ties and retaining property within the family [5, 8].

Intermarriages are usually socially motivated and can be genetically harmful. The study and consequences of inbreeding are considerable concerns in the field of genetics. Mating of relatives, leads to increased genetic homogeneity of inbred individuals, due to similarities between contributing paternal and maternal genetic material. The detrimental effects of inbreeding are the consequence of homozygosity of harmful genes.

Different studies reported that offspring’s of consanguineous parents had higher rates of congenital malformation [9, 10] and neonatal, post-neonatal, child, and infant mortality than those of non-consanguineous parents [11-15].

In addition, consanguineous unions were more likely to result in genetic diseases of childhood (and primarily focused on early-onset diseases, mainly recessively inherited monogenic (Mendelian) diseases), most of which had a distinctive phenotype that was readily identifiable. Therefore, the great majority of research on inbreeding effects had been focused on pre-reproductive health problems, and the risks have been thoroughly evaluated by numerous groups and individual authors [16-23].

Substantial uncertainty exists regarding the genetic architecture underlying common late-onset human diseases. In particular, the contribution of deleterious recessive alleles has been predicted to be greater for late-onset than for early-onset traits [24, 25].

Unfortunately, in spite of the considerable effect of inbreeding on post-reproductive human health in different

*Address correspondence to these authors at the Clinical Neuroscience & Population Genetics, EMMS Nazareth-The Nazareth Hospital Nazareth, Zip code: 16100, Israel; Tel: +972-4-6356133; Fax: +972-4-6356133; E-mail: bowirrat@netvision.net.il

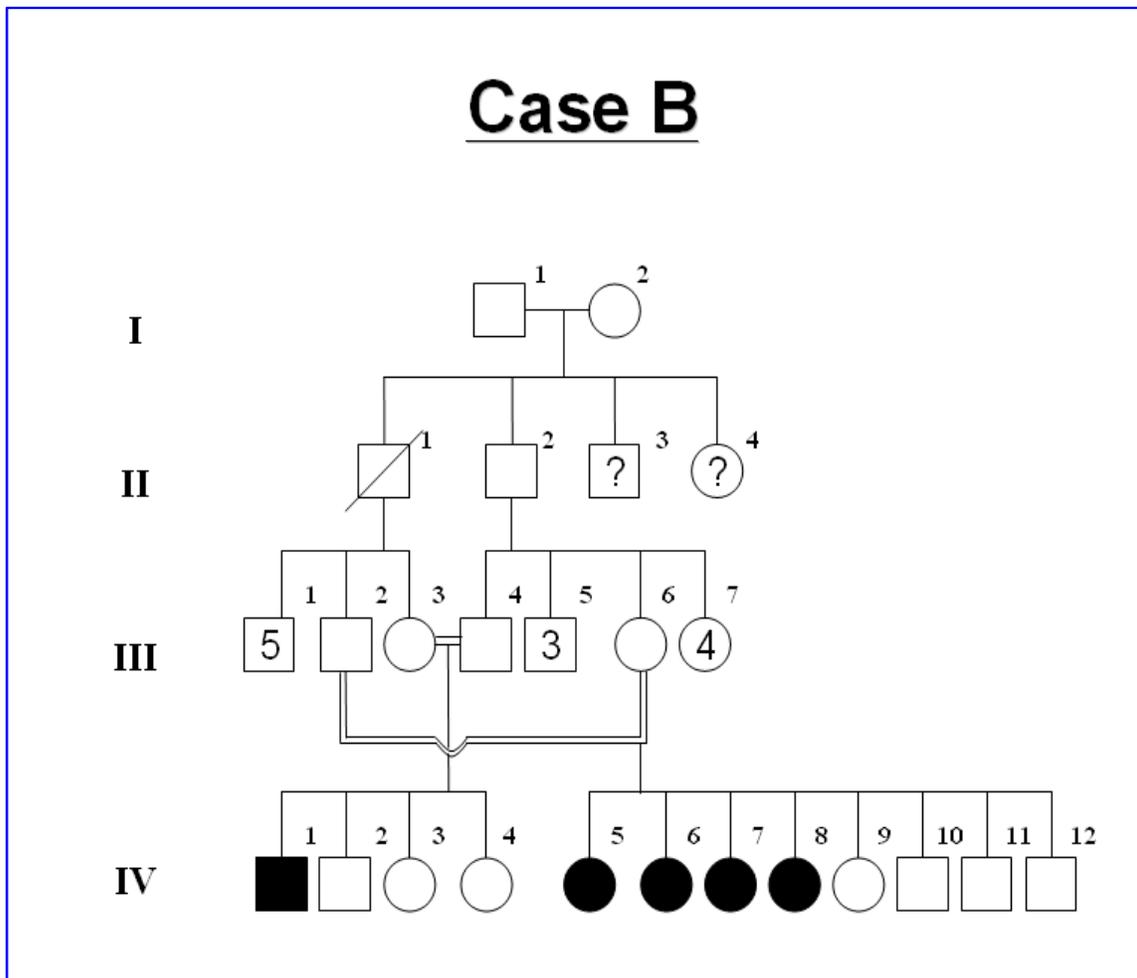
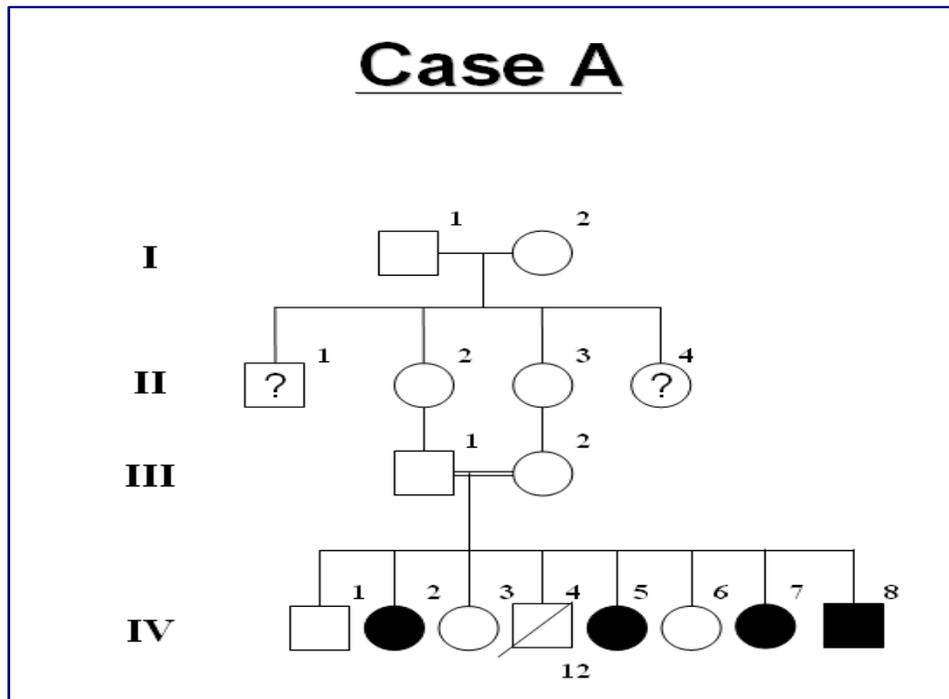


Fig. (1). Two Family Pedigrees Showing High Level of Consanguinity, Large family size, and Several Affected Children in Different Sibships.

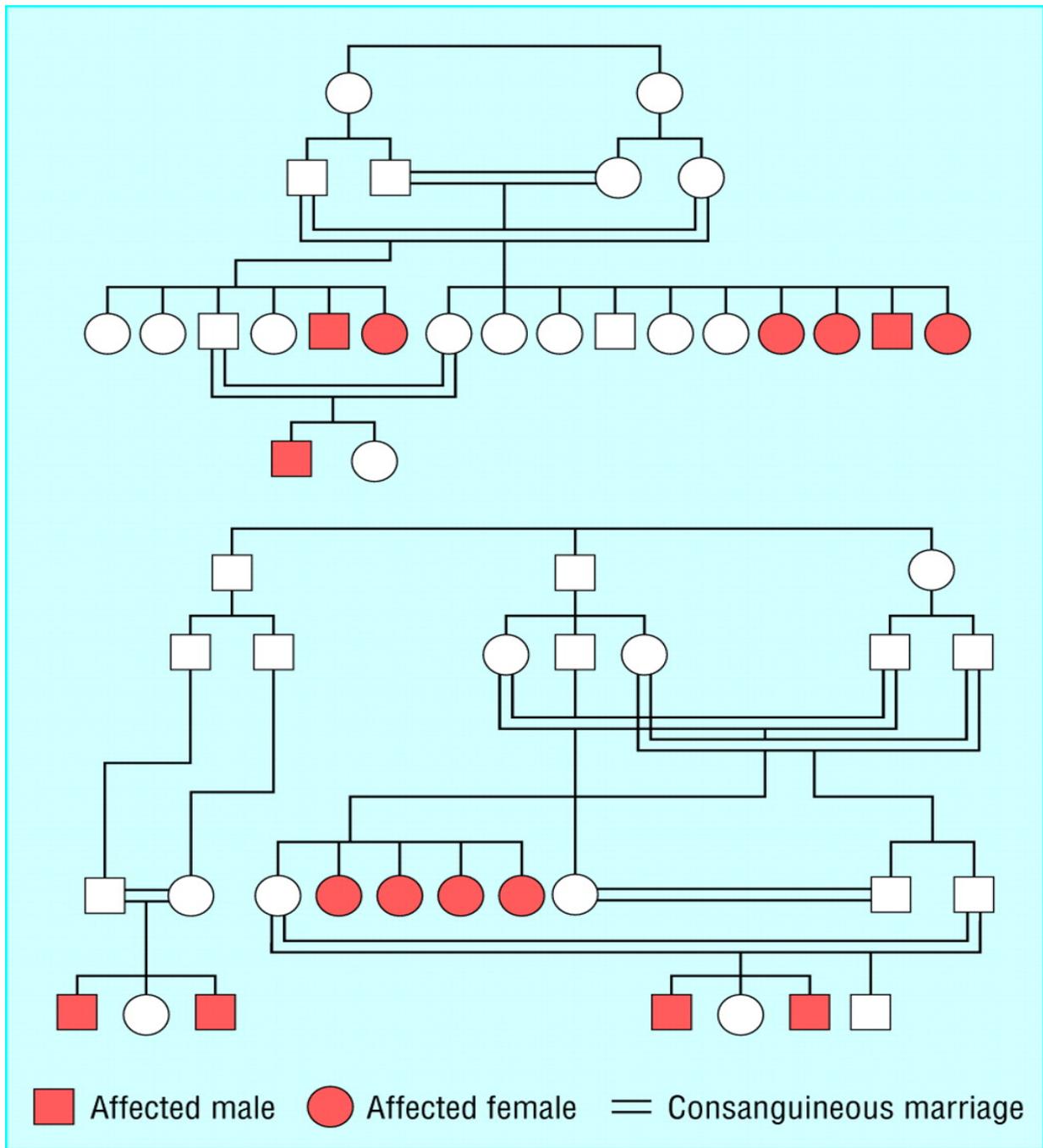


Fig. (2). Extended family showing Consanguineous marriage.

regions of the world where consanguineous marriages are very frequent, [26] few studies investigated the effect of consanguinity on complex diseases [27-33].

These studies reported considerable relative risks associated with inbreeding, flanked by 2.0–5.0, typically persisted after adjustment for suspected confounding factors [33] Nonetheless, complex diseases research still neglectful, in areas of the world where inbreeding prevails, and late-onset diseases have not until recently represented the main public health problem (e.g. Asia and Africa) [33].

Therefore, it is possible that this may be explained to some extent by the fact that offspring of consanguineous unions may be at increased risk for disorders of

multifactorial inheritance [33]. However, studies to date are controversial and as to whether consanguinity increases the risk for multifactorial disorders during the adulthood span [34-37].

Indeed, studies of the prevalence of Dementia of Alzheimer’s type (DAT) among elderly population, demonstrated a high prevalence of DAT, [38, 39] this high prevalence might be related partially to consanguineous undiscovered recessive genes, where inbreeding exceeds 36% in these communities [40, 41].

Other associated feature related to consanguinity is the inbreeding depression, assumed to reduce fitness in a given population; it is a recognized phenomenon that is common to

polygenic traits in all living organisms [42]. It is thought to result from increased homozygosity of recessive alleles that act in the same direction at loci that influence the phenotype of interest (directional dominance) [43]. Another mechanism responsible is over-dominance of heterozygous alleles leading to a reduction in the fitness of a population with many homozygous genotypes, even if they are not deleterious.

Inbreeding is predicted to have larger effects on the population-attributable fraction of disease if the underlying variants are rare rather than common. This is because common recessive variants will infrequently become homozygous in the population by chance, without a need for inbreeding to bring them together. This was demonstrated to be the case with population attributable fraction of early-onset monogenic (Mendelian) diseases in the presence of inbreeding. It has been shown that the prevalence of autosomal dominant Mendelian disorders is constant in all world populations, but the prevalence of autosomal recessive Mendelian disorders is increased by 3–4 fold in regions where inbreeding is prevalent [19, 44]. Therefore, the majority of Mendelian diseases that are caused by rare recessive variants of large effect and early age of onset are due to inbreeding in those countries. However, these diseases manifest in pre-reproductive period, so they are “clear” to selection.

CONSANGUINITY IS A GENETICS DILEMMA AND A SOCIAL PROBLEM

The incidence of deleterious genes mutations is universal; essentially every person has several harmful alleles on their chromosomes [45].

There are approximately **500 -1200** deleterious mutations in the genome of any given person, most of which are offset by a second, properly functioning, copy of the gene, and most of which are rare and present in heterozygous form [45]. Consanguinity increases the likelihood that some of these harmful recessive traits will reveal themselves, giving credence to the scientific caveat against incestuous relationships. In an offspring of first-cousin marriage, 30–75 of these variants mutations would be expected to become homozygous, with uncertain effects [33, 46].

The risk that unrelated parents will have a child with a birth defect or disability is between 2% – 3% (2 to 3 births out of every 100) [47, 48]. On the other hand, blood relatives share a greater proportion of the same genetic material than unrelated individuals because they have a common ancestor such as a grandparent from whom they inherited their genes through a parent. The closer the biological relationship between relatives increases the likelihood that both individuals will carry the same gene mutation [49]. In the absence of a known genetic disease in the family, children of first cousins have an excess risk in the order of 3% (1 in 30). This fact is often a relief to couples who expect a significantly higher figure [47,48].

The excess risk is a result of autosomal recessive conditions arising due to homozygosity by descent – that is, the risk of a recessive mutation present in an ancestor being passed down two branches of the family, and coming together in the consanguineous marriage. It is thought that

we all carry at least one mutated allele which would cause an autosomal recessive disorder if present in 2 copies (homozygosity). If this mutant allele is passed down to both members of a consanguineous couple from a shared ancestor both will be carriers for this condition, and therefore will have a 1 in 4 (25%) chance of having an affected child.

The probability of both parents being carriers for a recessive condition is determined by how closely they are related. For example, if parents are first cousins, the risk is approximately two times greater, i.e., between 5% – 6% (5 to 6 births out of every 100) versus between 2% – 3% (among unrelated). Theoretical calculations predict that 6% (1/16) of the genome of a child of first cousins will be homozygous with the average homozygous segment will be 20 cM in size. Looked at another way, where parents are first cousins, there is about a 94% chance that they will have a baby unaffected by a condition due to the parents’ faulty genes [47, 48].

Additional studies conducted by, [14, 50-52]. verified that, the increased risk for a significant birth defect in offspring of a first cousin union range between 1.7 and 2.8% above the risk of the general population risk. There is an estimated 4.4% risk for pre-reproductive mortality (to median age of 10 years) above that of the background population risk (this number includes birth defects resulting in mortality) [50].

If there is a family history or the parental ancestry suggests a greater risk of a faulty gene for a specific condition, such as Thalassaemia, it may be possible to determine if both parents are carriers of the same genetic mutation by carrying out genetic testing [53-55].

COEFFICIENT OF INBREEDING (IF)

Consanguinity increases the inbreeding coefficient (F), thereby increasing the chance that an individual will inherit two identical alleles by descent [56]. In other words, Consanguinity has the effect of increasing the frequency of homozygotes and of reducing that of heterozygotes, relative to the proportions given by the Hardy-Weinberg Law [57].

Inbreeding is unions between two persons who share at least one recent common ancestor [26]. As a working definition, unions contracted between persons biologically related as first cousins ($F \geq 0.0156$) are categorized as consanguineous [44] http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11972160&dopt=Abstract that is, the progeny are predicted to have inherited identical gene copies from each parent at 6.25% of all gene loci, exceeding the baseline level of homozygosity in the general population. Certain populations also favour uncle-niece and double first cousin unions, where the level of homozygosity in the progeny is equivalent to $F = 0.125$ [35].

Globally, the most common form of consanguineous union is between first cousins, in which the spouses inherited $1/8$ of their genes from a common ancestor, thus their progeny are homozygous (or more correctly autozygous) at $1/16$ of all loci [47, 48].

The coefficient of inbreeding (F) provides a numerical estimate of the degree of inbreeding of an individual. F values are higher for unions between closer relatives, that is,

the offspring of an incestuous relationship have a greater F value than do those of a first-cousin relationship. The mean inbreeding coefficient can also be calculated for entire populations in which a proportion of marriages are consanguineous, and for individuals who are related through multiple loops of consanguinity. Populations with a high mean inbreeding coefficient do not necessarily represent a community of close cousin marriages, and in fact cousin marriage may be discouraged [15].

The F value is calculated from genealogical information and it amounts to about 6% in the offspring of first cousin parents and 25% in the offspring of incestuous unions of first-degree relatives [58, 59]. The apparent risk in the individuals with a considerable proportion of their genes homozygous for identical allelic variants is the occurrence of “Mendelian” (monogenic) diseases caused by rare and recessive deleterious autosomal mutations of large effect [8, 15, 17-20].

In clinical practice, F rarely is calculated with confidence, because of incomplete knowledge of a sufficient ancestry [60].

Generally, in human genetics, the closest relationship between parents is used to Estimate F , under the assumption that all grandparents are only distantly related.

RELATIONSHIP BETWEEN RELIGIONS, CULTURES AND CONSANGUINITY

It is well known in human history that religions influence cultures and have been considered the cornerstone of any region's culture. This power of the religions determined the initial culture roles and regulations. That our existing own cultures owe what little beauty and harmony they possess entirely to them.

These early initial cultures are governed and arose by natural or geographically confined areas or a result of borders that are artificially created for example, islands such as Cyprus, Sardinia and Japan, peninsulas such as Greece and Italy, naturally isolated areas like countries in South America and Egypt, and more or less artificially enclosed areas like China and Palestine.

With the advent of globalization, consanguinity is decreasing but it still remains popular cultural phenomena in certain regions of the world today.

Intermarriages occur and sometimes dominate in Middle-Eastern and Asian population, with rates that exceed 40% of all marriages, also high incidence reported in India that go beyond 5-60% [61]. Marriage choice and decision-making is a complex interaction of various social and cultural standard pattern of behavior and norms, the main reasons for a continuing preference for consanguineous unions are: Historical, cultural, socioeconomic, geographical proximity, tradition, restricted mobility, and maybe an additional unconscious, instinctive and unintentional political unrest and behavioral that is influenced by this...which according to our opinion that should be mentioned as adjunct reason for the high frequency of this habit among different populations and especially Middle-Eastern populations. The trend of intermarriages among ethnic minorities in Europe with a tradition of consanguineous marriage, for instance, people of North

African origin in France and Belgium and people of Turkish origin in Germany and the Scandinavian countries still apparent - this tendency probably follows from constraints imposed by migration, disintegration and cultural diversity. Indeed, ethnic minorities face two problems: the limited availability of suitable persons in the restricted local community [62] and the fact that their circle of acquaintance in the country of origin tends to shrink within the limits of the extended family. Therefore, for groups with tradition intermarriage, it is only natural for the choice of partner to fall progressively closer within the family circle.

There appears to be no particular rationale for the subdivision of human populations into opposing forms of marriage preference, and even within the major religions there are quite marked differences in attitude toward close kin marriage. Thus in Christianity, the Orthodox churches prohibit consanguineous marriage, the Roman Catholic church currently requires Diocesan permission for marriages between first cousins, and the Protestant denominations permit marriages up to and including first cousin unions [58]. A similar degree of non-uniformity exists in Hinduism. The Aryan Hindus of northern India prohibit marriage between biological kin for approximately seven generations on the male side and five generations on the female side. By comparison, Dravidian Hindus of South India strongly favor marriage between first cousins of the type mother's brother's daughter and, particularly in the states of Andhra Pradesh, Karnataka and Tamil Nadu, uncle-niece marriages also are widely contracted.

Muslim regulations on marriage parallel the Judaic pattern detailed in Leviticus. However, aunt-nephew and uncle-niece marriages are prohibited strongly by Islam and by state laws [63]. Yet they are forbidden by the Koran, even though double first cousin marriages, which have the same coefficient of inbreeding ($F = 0.125$).

It is commonly and somewhat erroneously believed that Islam favors marriage between close relatives other than the proscribed ones such as those between siblings, parent and child, uncle and niece or aunt and nephew.

However, no passage in the Koran can be interpreted as encouraging intermarriages. Moreover, according to one of the *hadith* (a record of the pronouncements of Prophet Mohammad “*PBUH*”, the Prophet “*PBUH*” discouraged marriages to cousins who, because of the closeness of the relationship, were almost like siblings [51]. After the spreading of Islam through Arabia, Islam did not prohibit, or encourages cousin marriages as a civil law, intermarriages was kept under the verdict of permissibility and absolutely not in the canon of obligatory. In fact, marriages outside the clan were highly desirable and pleasing to increase cultural exchange and religious influence. The preponderance of consanguineous marriage in Arab world predates Islam. Does Islam discourage it? A hadith is cited: “marry from afar (not nearby relatives) so that the offspring is not weakened”. The second Caliph Omar is reported to have given this advice to (Bane-Saeeb tribe), because offspring weakness in that tribe (“strange hadith” - Abu- Maleka).

In fact the custom of consanguinity has nothing to do with Islam entirely as many criticizers believe; it is just a time-honored tradition [64].

MARRIAGE REGULATIONS IN ISLAM

Islam recognizes value of sex and recommends marriage and does not believe in celibacy.

Islam places more emphasis on spirituality and the control of sexuality in marriage. The Koran explicitly allows Muslim men to marry chaste women of the People of the Books, a term which includes Jews and Christians. Marriage is forbidden between certain blood relations and between those individuals who were both breastfed by the same woman. Recognition or celebration of same sex marriage is sternly forbidden in the view of Islamic law. Homosexuality is strictly strappingly forbidden by Koran's injunctions and Islamic tradition and remains a forbidden and anti-nature roles according to Muslim scholars. [65].

Marriage in Islam is essentially a contract. However, the distinction between sacred and secular was never explicit in Islam. Any action or transaction in Islam has religious implications. It is not quite accurate, therefore, to designate marriage in Islam simply as a secular contract. The appropriate designation of marriage could be a "Divine Institution".

The summarizing Koran's simile (You are a garment to them, and they are a garment for you) [66] condenses the primary aims of marriage—to provide warmth, comfort, and protection and to beautify. Within the Islamic vision, children have a right to be conceived and reared in a stable and secure environment; marriage is deemed to provide such an environment. In contrast, sex outside of marriage is strongly forbidden because it is considered a behavioral extreme that is not conducive to a wholesome society [67].

REPORTED AND PROFESSED "BENEFITS" OF CONSANGUINEOUS MARRIAGE

Whilst, the disadvantages; intermarriages remain the rule in more traditional societies worldwide and strongly favored in many migrant communities in western countries, [62] for different apparent genuine advantages:

1. Strengthening family ties and retaining property within the family [44, 58, 68].

2. Improving the position of women by decreasing the chances of maltreatment from a husband bound by family ties; and also decreases the chance of divorce [8, 69].

3. Consanguinity ensures the unity of lands. Inheritance of land by males and females is kept within the same family, and this is of great importance for peasants because small pieces of land are inefficient in agricultural economies. This pattern is common among Lebanese, Egyptians, Palestinians, and Jordanians [70].

4. Consanguinity offers the best opportunity for compatibility between the husband and wife, and the bride and mother-in-law, also undisclosed problems regarding health or other unfavorable social characteristics of either bride or groom will be effectively avoided [8].

5. Consanguineous marriages create a mean of equilibrium in the lineage within the families by guarantying the wedding of young's women within the family's men, which mean decreasing the spinster and celibacy problems.

6. Anthropologists have long agreed that the main achievement of consanguineous marriages is the inheritance of family structure and property, (families with specific features of intelligence) [21, 70, 71, 72].

7. The most important and overriding reasons for consanguineous marriages, both in South Asia and the Middle East, therefore appear to be social and cultural considerations. Despite increasing urbanization and nucleation of families, as well as increases in female literacy, marriage choice continues to be strictly the domain of parents, reinforced by the vocal or tacit support of elder married siblings [73, 74].

GENETICS CONSIDERATIONS

Consanguineous marriage is a special form of assortative mating leading to an increase in the frequency of homozygous genotypes and allowing the less common alleles to become manifested homozygous [75].

With rare recessive traits, the parents of affected offspring are often consanguineous, because they are more likely to carry the same genes they inherited from a common ancestor [76]. Impairment of function due to homozygosity of recessive alleles has been reported through inbreeding effects on a wide range of traits, suggesting a large number of deleterious alleles in the genome. As most identified genetic variants causing complex disease in humans are partially recessive [77, 78].

Offspring of second cousins are predicted to have children with 1/64 of their genome homozygous; offspring of first cousins, 1/16; offspring of double-first cousins, 1/8; and offspring of incestuous union, 1/4 [79]. Furthermore, in the case of first-cousin offspring, it has been calculated that the average homozygous segment will be 20 cM [80]. This degree of homozygosity is far greater than that seen in apparently out-bred populations [81].

A study of quantification of homozygosity in consanguineous individuals with autosomal recessive disease was conducted recently and [82] found that in individuals with a recessive disease whose parents were first cousins, on average, 11% of their genomes were homozygous (n p 38; range 5%–20%), with each individual bearing 20 homozygous segments exceeding 3 cM (n p 38; range of number of homozygous segments 7–32), and that the size of the homozygous segment associated with recessive disease was 26 cM (n p 100; range 5–70 cM). These data imply that prolonged parental inbreeding has led to a background level of homozygosity increased ~5% over and above that predicted by simple models of consanguinity. It is important to have a high index of suspicion for inborn errors of metabolism in children of consanguineous parents, as most of these conditions are inherited in an autosomal recessive manner, and while individually rare, collectively they represent a significant burden of disease, including some conditions which are treatable if caught at an early stage. A number of recessive genes cause pre-lingual deafness, and it is important for babies of consanguineous parents to receive their routine hearing tests [83, 84].

Aside from autosomal recessive conditions which cause learning difficulties, consanguinity does not have any effect on intelligence, [85] but there is a lesser extent evidence that

consanguinity affects fertility [86, 87]. In contrary, other studies reported that consanguinity is generally associated with increased fertility, partly a result of younger maternal age at marriage. It could be argued that the greater genetic compatibility between the mother and the developing fetus in a consanguineous pregnancy might lead to reduced rates of involuntary sterility and prenatal losses. In addition, there is a strong possibility that greater fertility may be observed among consanguineous unions as a compensatory mechanism for infant and childhood losses [8].

CONSANGUINEOUS MARRIAGES SHOULD BE TACKLED ON THE MEDICAL AND POLICY LEVELS.

The need to disseminate recommendations for genetic counseling and screening for consanguineous unions is extremely important; It's should be a public demand and should commove the interest of health policy makers authorities.

Consanguineous marriage is deeply-seated and deeply-rooted in many communities, but leads sometimes to painful consequences by increasing birth prevalence of infants with sever recessive disorders. It is therefore often proposed that consanguineous marriage should be dissuaded on medical grounds.

However, several researchers have pointed out that this suggestion is inconsistent with the initiative ethical principles of genetic counseling, neglects the social importance of consanguineous marriage and is ineffective. Instead, they suggest that the custom increases the possibilities for effective genetic counseling, and recommend a concerted effort to identify families at increased risk, and to provide them with risk information and carrier testing when feasible [44].

The main propel towards a reduced frequency of consanguineous unions remains in the field of preventive genetics in the form of general education of society. The public education may have to be taken at school level during adolescence to instill the biological risk of close marriages. Parents must be aware of the close associations of their children with the children of their brothers and sisters during their adolescence [88].

A preventive program and serious recommendations are necessary to limit the number of children affected through public health education regarding the possible outcome risks of consanguineous marriage. Recommendations are intended to assist health care professionals who provide genetic counseling and screening to consanguineous couples, their pregnancies and their offspring. The recommendations focus on the offspring of first cousin unions, because it is the preferred marriages almost everywhere [34, 89].

The aims of these recommendations are to provide risk assessment and reproductive options to consanguineous couples who request genetic counseling in a preconception setting, improving safe pregnancy outcome and provide reproductive options when parental consanguinity is identified in a pregnancy, also, reducing morbidity and mortality in the first years of life for children from consanguineous unions [3].

Aside to the preventive genetics, more practical steps at the level of legislation, decision makers and policy makers must be taking to enhance the knowledge, create a professional health facilities, capable to orientate and assists motherhood, by giving genetics counselling, and overprotects marriages at high risk of genetics diseases. Professional centres must be available, which can examine confidentially families at high risk.

1. Inter marriages between couples, who have family history of genetics diseases, need a special concern: A laws act must be legislated in all the countries where consanguineous marriages are common and must indicate: That all close couples planning to marriage are obligate to perform genetic counseling as a condition prior to marriage.
2. Cousin couples, who intended to marry, must have a legal certificate indicating clearly their state of health, and the absence of any genetic disorder before marriage contract.
3. Women over 40 years of age should be included in the category of high risk for genetic diseases (Down's syndrome...ecc...). These rules must be extremely respected and implemented by law.

DISCUSSION

In the Arab World, the custom of consanguineous marriage results from cultural and historical, rather than religious reasons. Unlike what is widely thought, Islam does not advocate or encourage consanguineous marriages.

Islam is a religion which encompasses the secular with the spiritual, the mundane with the celestial and hence forms the basis of the ethical, moral and even juridical attitudes and laws towards any problem or situation including marriage. In fact, Islamic teachings carry a great deal of instructions for health promotion and disease prevention including hereditary and genetic disorders.

Marriages - a socio - cultural custom, is the basis for reproduction and symbol of permanence and therefore, certain marriage practices of assortative nature deviating from panmixis - especially those between relatives, have been receiving widespread attention at various fields including, genetics, anthropology, sociology, demography and even politics [90].

Consanguineous marriage has long been a controversial topic, with particular attention focused on adverse health outcomes. Unfortunately, the studies that have been conducted on consanguinity to date have usually lacked control for important sociodemographic variables, such as maternal age and birth intervals, and in estimating specific disease gene frequency; they have ignored the influence of population sub-division. The need for comprehensive and more balanced investigations into all aspects of consanguineous marriage is pressing and merits a substantial international collaborative research effort.

Different studies over-exaggerate when dealing on issues like inter marriages, the risk still "tolerable". As we point out before, if parents are first cousins, the risk is approximately, between 5% - 6% (5 to 6 births out of every 100) versus between 2% - 3% in general population. Theoretical

calculations predict that 6% (1/16) of the genome of a child of first cousins will be homozygous. Looked at another way, where parents are first cousins, there is about a 94% chance out of 100 (94%) that they will have a normal child [3, 47, 91].

In the end, and in the era of Genome project, genetics engineering and biotechnology, issue like consanguinity should be evaluated carefully at all the level, for the benefit of the new generations.

Because of improved health care facilities and reporting, genetic disorders predictably will account for an increase in the proportion of disease worldwide, and it is evident that this burden will fall disproportionately on countries and communities where consanguinity is relatively frequent [23, 24]. Consanguinity as a cultural routine and socially driven custom must be resolved by overwhelming the awareness, knowledge, education and the understanding its consequences on the whole health. By discussing the disadvantages of this habit at the level of health systems and Policy Makers, novel solutions will arise which will resolve or decrease the suffering of many unfortunate families in different societies. Ultimately, the campaign against consanguinity should proceed with determination, because, this is a growing public health that should be actively discouraged, not passively tolerated. It should, however, be discussed as a purely medical endeavor, and should engage further consideration as a yet-unexamined mechanism for achieving greater peace and abiding stability.

LIST OF ABBREVIATION

Consanguinity

The term consanguinity is derived from the Latin words: *con* – “shared” and *sanguis* “blood”. Relationship by blood, whether lineal (for example, by direct descent) or collateral (by virtue of a common ancestor). The degree of consanguinity is significant in laws relating to the inheritance of property and also in relation to marriage, which is forbidden in many cultures between parties closely related by blood.

Inbreeding

Production of offspring from within a limited genetic pool, as when generations of royalty are married among members of the same families.

Coefficient of Inbreeding

F is the symbol for the coefficient of inbreeding, a way of gauging how close two people are genetically to one another. The coefficient of inbreeding, F, is the probability that a person with two identical genes received both genes from one ancestor.

Population Attributable Risk: (PAR)

The disease incidence in a population that is attributable to a particular risk factor. Studies commonly report the PAR percentage to estimate what proportion of the disease is explained by associated variants.

Homozygosity

The state of possessing two identical forms of a particular gene, one inherited from each parent.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

ACKNOWLEDGEMENT

Declared none.

REFERENCES

- [1] Hussain R, Bittler AH. The prevalence and demographic characteristics of consanguineous marriages in Pakistan. *J Biosoc Sci* 1998; 30: 261-75.
- [2] Saad FA, Jauniaux E. Recurrent early pregnancy loss and consanguinity. *Reprod Biomed Online* 2002; 5: 167-70.
- [3] Bennett RL, Motulsky AG, Bittles A, *et al.* Genetic counseling and screening of consanguineous couples and their offspring: recommendations of the national society of genetic counselors. *J Genet Counsel* 2002; 11 (2): 97-119.
- [4] Fuster V, Colantonio SE. Socioeconomic, demographic, and geographic variables affecting the diverse degrees of consanguineous marriages in Spain. *Hum Biol* 2004; 76: 1-14.
- [5] Hussain R, Bittles AH. Sociodemographic correlates of consanguineous marriage in the Muslim population of India. *J Biosoc Sci* 2000; 32: 433-42.
- [6] Liascovich R, Rittler M, Castilla EE. Consanguinity in South America: demographic aspects. *Hum Hered* 2004; 51: 27-34.
- [7] Kerkeni E, Monastiri K, Saket B, Rudan D, Zgaga L, Ben Cheikh H. Association among education level, occupation status, and consanguinity in Tunisia and Croatia. *Croat Med J* 2006; 47(4): 656-61.
- [8] Bittles AH, Mason WM, Greene J, Rao N. Reproductive behavior and health in consanguineous marriages. *Science* 1991; 252: 789-94.
- [9] Kushki AM, Zeyghami B. The effect of consanguineous marriages on congenital Malformation. *J Res Med Sci* 2005; 10(5): 298-301.
- [10] Bromiker R, Baruch M. Association of parental consanguinity with congenital malformations among Arab newborns in Jerusalem. *Clin Genet* 2004; 66(1): 63-6.
- [11] Sawardekar KP. Genetic analysis of lethal congenital malformations causing perinatal mortality at Nizwa Hospital, Oman. *Clin Genet* 2004; 66: 239-43.
- [12] Bittles AH, Grant JC, Shami SA. Consanguinity as a determinant of reproductive behaviour and mortality in Pakistan. *Int J Epidemiol* 1992; 22: 463-67.
- [13] Grant JC, Bittles AH. The comparative role of consanguinity in infant and childhood mortality in Pakistan. *Ann Hum Genet* 1997; 61: 143-9.
- [14] Stoltenberg C, Magnus P, Skrondal A, Lie RT. Consanguinity and recurrence risk of stillbirth and infant death. *Am J Public Health* 1999; 89: 517-23.
- [15] Jorde LB. Consanguinity and prereproductive mortality in the Utah Mormon population. *Hum Hered* 2001; 52: 61-5.
- [16] Jaber L, Shohat M, Halpern GJ. Demographic characteristics of the Israeli Arab community in connection with consanguinity. *Isr J Med Sci* 1996; 32(12): 1286-9.
- [17] Gibbons A. The risks of inbreeding. *Science* 1993; 259: 1252.
- [18] Bittles AH. Consanguineous marriage and childhood health. *Dev Med Child Neurol* 2003; 45: 571-6.
- [19] World Health Organization: Primary health care approaches for the prevention and control of congenital and genetic disorders. WHO Meeting Report: Cairo Egypt 1999; pp. 6-8.
- [20] Zlotogora. What is the birth defect risk associated with consanguineous marriages. *Am J Med Genet* 2002; 109: 70-1.
- [21] Schull WJ, Neel JV. The effects of parental consanguinity and inbreeding in Hirado, Japan. V. Summary and interpretation. *Am J Hum Genet* 1972; 24: 425-53.
- [22] Khlal M, Khoury M. Inbreeding and diseases: demographic, genetic, and epidemiologic perspectives. *Epidemiol Rev* 1991; 13: 28-41.
- [23] Bittles AH, Neel JV. Consanguineous marriages in Turkey and its impact on fertility and mortality. *Nat Genet* 1994; 8: 117-21.
- [24] Rudan I, Smolej-Narancic N, Campbell H, *et al.* Inbreeding and the genetic complexity of human hypertension. *Genetics* 2003; 163: 1011-21.

- [25] Bener A, Hussain R, Teebi AS. Consanguineous marriages and their effects on common adult diseases: studies from an endogamous population. *Med Princ Pract* 2007; 16: 262-7.
- [26] Rudan I, Rudan D, Campbell H, *et al.* Inbreeding and risk of late onset complex disease. *J Med Genet* 2003; 40(12): 925-32.
- [27] Shami SA, Qaisar R, Bittles AH. Consanguinity and adult morbidity in Pakistan. *Lancet* 1991; 338: 954-5.
- [28] Ismail JTH, Jafar FH, Jafary F, White AM, Chaturvedi FN. Risk factors for non-fatal myocardial infarction. *Heart* 2004; 90: 259 - 63.
- [29] Simpson JL, Martin AO, Elias S, Sarto GE, Dunn JK. Cancers of the breast and female genital system. *Am J Obstet Gynecol* 1981; 141: 629-36.
- [30] Lebel RR, Gallagher WB. Wisconsin consanguinity studies. II: Familial adenocarcinomatosis. *Am J Med Genet* 1989; 33: 1-6.
- [31] Abaskuliev AA, Skoblo GV. Inbreeding, endogamy and exogamy among relatives of schizophrenia patients. *Genetika* 1975; 11: 145-8.
- [32] Vezina HE, Heyer I, Fortier G, Ouellette Y, Robitaille D, Gauvreau A. Disease in the saguenay region of Quebec. *Genet Epidemiol* 1999; 16: 412-25.
- [33] Rudan I, Campbell H. Late-onset Inbreeding Effects. *Coll Antropol* 2004; 28(2): 943-50.
- [34] Bittles AH. Empirical estimates of the global prevalence of consanguineous marriage in contemporary societies. Stanford, CA: Morrison Institute for Population and Resources Studies, Stanford University 1998.
- [35] Bittles AH. Consanguinity and its relevance to clinical genetics. *Clin Genet* 2001; 60: 89-98.
- [36] Jaber L, Shohat T, Rotter JI, Shohat M. Consanguinity and common adult diseases in Israeli Arab communities. *Am J Med Genet* 1997; 70: 346-48.
- [37] Stoltenberg C, Magnus P, Lie RT, Daltveit AK, Irgens LM. Birth defects and parental consanguinity in Norway. *Am J Epidemiol* 1997; 145: 439-48.
- [38] Bowirrat A, Friedland RP, Chapman J, Korczyn AD. The very high prevalence of Alzheimer's disease in an Arab population is not explained by ApoE ϵ 4-allele frequency. *Neurology* 2000; 55(5): 731-6.
- [39] Bowirrat A, Treves TA, Friedland RP, Korczyn AD. Prevalence of Alzheimer's Type Dementia in an elderly Arab population. *Eur J Neurol* 2001; 8(2): 119-23.
- [40] Farrer LA, Bowirrat A, Friedland RP, Waraska K, Korczyn AD, Baldwin CT. Identification of multiple loci for Alzheimer disease in a consanguineous Israeli-Arab Community. *Hum Mol Genet* 2003; 12: 415-22.
- [41] Bowirrat A, Cui J, Waraska K, *et al.* Association between angiotensin-converting enzyme (ACE) and alzheimer's disease (AD) among an elderly Arab population in Wadi Ara, Israel. *J Neuropsychiatr Dis Treat* 2005; 1(1): 73-6.
- [42] Charlesworth B, Charlesworth D. The genetic basis of inbreeding depression. *Genet Res* 1999; 74: 329-40.
- [43] Charlesworth BK, Hughes A. In: Singh RS, Krimbas CB (Eds): *Evolutionary genetics: From molecules to Morphology*. Cambridge UK: Cambridge University Press 1999; vol. 1: pp. 369-92.
- [44] Modell B, Darr A. Genetic counseling and customary consanguineous marriage. *Rev Genet* 2002; 3: 225-29.
- [45] Fay JCGJ, Wyckoffand CIWU. Positive and negative selection on the human genome. *Genetics* 2001; 158: 1227-34.
- [46] Carlborg O, Haley C. Epistasis: too often neglected in complex trait studies? *Nat Rev Genet* 2004; 5: 618-25.
- [47] Bittles AH. Endogamy, consanguinity and community disease profiles. *Commun Genet* 2005; 8: 17-20.
- [48] Bennett RL, Motulsky AG, Bittles A. Genetic counseling and screening of consanguineous couples and their offspring: recommendations of the national society of genetic counselors. *J Genet Counsel* 2002; 11(2): 97-119.
- [49] Smith CAB. Measures of homozygosity and inbreeding in populations. *Ann Hum Genet* 1974; 37: 377-91.
- [50] Bittles AH, Neel JV. The costs of human inbreeding and their implications for variations at the DNA level. *Nat Genet* 1994; 8: 117-21.
- [51] Jaber L, Halpern GJ, Shohat M. The Impact of Consanguinity Worldwide. *Community Genet* 1998; 1: 12-7.
- [52] Daniels D, Plomin R, McClearn G, Johnson RC. "Fitness" behaviors and anthropometric characters for offspring of first-cousin matings. *Behav Genet* 1982; 12(Supp 5): 527-34.
- [53] Chui DHK, Cunningham MJ, Luo H, Wolfe LC, Neufeld EJ, Steinberg MH. Screening and counseling for thalassemia. *Blood* 2006; 107: 1735-7.
- [54] Rund D, Rachmilewitz E. β -Thalassemia. *N Engl J Med* 2005; 353: 1135-46.
- [55] Cao A, Galanello R. Effect of Consanguinity on Screening for Thalassemia. *N Engl J Med*. 2002; 347: 1200-2.
- [56] Thornhill NW. *The Natural History Of Inbreeding And Outbreeding*. Chicago: The University of Chicago Press 1993.
- [57] Overall ADJ, Ahmad M, Nichols RA. The effect of reproductive compensation on recessive disorders within consanguineous human populations. *Heredity* 2002; 88: 474-9.
- [58] Bittles AH, Savithri HS, Murthy G, *et al.* In: Macbeth, Shetty HP: *Health and Ethnicity*. London: Taylor and Francis 2001.
- [59] Jaber L, Halpern GJ. Consanguinity among the Arab and Jewish population in Israel. *Pediatr Endocrinol Rev* 2006; 3: 437-46.
- [60] Boucher W. Calculation of the inbreeding coefficient. *J Math Biol* 1988; 26: 57-64.
- [61] Mueller RF, Young ID. *Elements of Medical Genetics*. 11th ed. Edinburgh: Churchill Livingstone 2001; vol. 100: p. 245.
- [62] Khan VS. The Pakistanis: Mirpuri villagers at home and in Bradford. In: Watson JL, Ed. *Between two cultures: migrants and minorities in Britain*. Oxford: Blackwell 1977.
- [63] Teebi AS, Marafie MJ. Uncle-niece/aunt-nephew marriages are not existing in Muslim Arabs. *Am J Med Genet* 1988; 30(4): 981-3.
- [64] Akrami SM, Osati Z. Is consanguineous marriages religiously encouraged? Islamic and Iranian considerations. *J Biosoc Sci* 2007; 39: 313-6.
- [65] Abukhaliz A. Gender boundaries and sexual categories in the Arab word. *Fem Issue* 1997; 15: 91-104.
- [66] Ali YA. *The meaning of the glorious Quran*. Cairo: Dar al-Kitab 1938; 2:187.
- [67] Al-Qaradawi Y. *The lawful and the prohibited in Islam*. Indianapolis: American Trust Publications 1960; pp. 148-236.
- [68] Al-Gazali LA, Bener Y, Abdulrazzaq R, Micallef A, Khayat, GT. Consanguineous Marriages in the United Arab Emirates. *J Biosoc Sci* 1997; 29: 491-7.
- [69] Radovanovic ZN, Behbehani SJ. Prevalence and social correlates of consanguinity in Kuwait. *Ann Saudi Med* 1999; 19(3): 206-10.
- [70] Klat M, Khudr A. Cousin marriages in Beirut, is the pattern changing. *J Biosoc Sci* 1984; 16: 369-73.
- [71] Granguist H. *Marriage conditions in a Palestinian village*. Parts I & III. Helsinki: Soderstrom 1931.
- [72] Resonfeld H. An analysis of marriage and marriage statistics for a muslim and Christian Arab village. *Int Arch Ethnogr* 1957; 68: 32.
- [73] Hussain R. Community perceptions of reasons for preference for consanguineous marriages in Pakistan. *J Biosoc Sci* 1999; 31: 449-61.
- [74] Devi RR, Rao A, Bittles AH. Inbreeding in the State of Karnataka, South India. *Hum Hered* 1982; 32: 8-10.
- [75] Mokhtar MM, Abdel-Fattah MM. Consanguinity and advanced maternal age as risk factors for reproductive losses in Alexandria, Egypt. *Eur J Epidemiol* 2001; 17(6): 559-65.
- [76] Modell B, Darr A. Genetic counselling and customary consanguineous marriage. *Nat Rev Genet* 2002; 3: 225-9.
- [77] Jimenez-Sanchez G, Childs B, Valle D. Human disease genes. *Nature* 2001; 409: 853-5.
- [78] Brown WM, Beck SR, Lange EM, *et al.* Framingham Heart Study: Age-stratified heritability estimation in the Framingham Heart Study families. *BMC Genet* 2003; 4 (Suppl 1): S32.
- [79] Lander ES, Botstein D. Homozygosity mapping: a way to map human recessive traits with the DNA of inbred children. *Science* 1987; 236: 1567-70.
- [80] Wright AF, Teague PW, Bruford E, Carothers A. Problems in dealing with linkage heterogeneity in autosomal recessive forms of retinitis pigmentosa. In: Edwards JH, Pawlowitzki IH, Thompson E, Eds. *Genetic mapping of disease genes*. UK: Academic Press 1997; pp. 255-72.
- [81] Broman KW, Weber JL. Long homozygous chromosomal segments in reference families from the Centre d'Étude du Polymorphisme Humain. *Am J Hum Genet* 1999; 65: 1493-500.

- [82] Woods CG, Cox J, Springell K, *et al.* Quantification of Homozygosity in Consanguineous Individuals with Autosomal Recessive Disease. *Am J Hum Genet* 2006; 78(5): 889-96.
- [83] Marazita ML, Ploughman LM, Rawlings B, Remington E, Arnos KS, Nance WE. Genetic epidemiological studies of early-onset deafness in the U.S. school-age population. *Am J Med Genet* 1993; 46: 486-91.
- [84] Denoyelle F, Weil D, Maw MA, *et al.* Prelingual deafness: high prevalence of a 30delG mutation in the connexin 26 gene. *Hum Mol Genet* 1997; 16: 2173-7.
- [85] Sathyanarayana TSR. Consanguinity: still a challenge. *Indian J Psychiatry* 2009; 51: (Suppl 1): 3-5.
- [86] Ober C. Inbreeding effects on fertility in human: evidence for reproductive compensation. *Am J Hum Gen* 1999; 64(Suppl 1): 225-31.
- [87] Baccetti B. Genetic sperm defects and consanguinity. *Hum Reprod* 2001; 16(Suppl 7): 1365-71.
- [88] Mehndiratta MM, Paul B, Mehndiratta P. Arranged marriage, consanguinity and epilepsy. *Neurol Asia* 2007; 12(1): 15-7.
- [89] Harper PS. *Pract. Gen. Counseling*, 5th ed. Oxford: Butterworth-Heinmann 1998.
- [90] Vogel F, Motulsky AG. *Book Review. Human genetics. Problems and approaches.* New York: Springer-Verlag 1986.
- [91] Harper P. *Practical Genetic Counseling.* London: Arnold. The Human Genetics Society of Australasia (HGSA) 2004.

Received: January 30, 2013

Revised: February 04, 2013

Accepted: February 04, 2013

© Abdalla and Zaher; Licensee *Bentham Open*.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>), which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.