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STUDYING THE EFFECT OF GENETIC SELECTION AND RANDOM DRIFT ON PREVALENCE OF GENETIC DISORDERS AMONG SAUDI POPULATION

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ABSTRACT

Consanguineous marriages have been practiced since the early existence of modern humans. Until now consanguinity is widely practiced in several global communities with variable rates depending on religion, culture, and geography. Arab populations have a long tradition of consanguinity due to socio cultural factors. Many Arab countries display some of the highest rates of consanguineous marriages in the world, and specifically first cousin marriages which may reach 25-30% of all marriages. In some countries like Qatar, Yemen, and UAE, consanguinity rates are increasing in the current generation. Research among Arabs and worldwide has indicated that consanguinity could have an effect on some reproductive health parameters such as postnatal mortality and rates of congenital malformations. The association of consanguinity with other reproductive health parameters, such as fertility and fetal wastage, is controversial. The main impact of consanguinity, however, is an increase in the rate of homozygotes for autosomal recessive genetic disorders. Worldwide, known dominant disorders are more numerous than known recessive disorders. However, data on genetic disorders in Arab populations as extracted from the Catalogue of Transmission Genetics in Arabs (CTGA) database indicate a relative abundance of recessive disorders in the region that is clearly associated with the practice of consanguinity.

KEYWORDS: Selection, random drift, consanguinity, genetic disorders, Saudi.

INTRODUCTION

Consanguinity, referring to a relationship between two people who share a common blood, biologically related individuals. In clinical genetics, a consanguineous marriage means union between couples who are related as second cousins or closer.[1,2] In population genetics, consanguinity may also refer to unions of individuals with at least one common ancestor such as those occurring within population isolates, small towns, and tribes; intra-community or endogamous marriages. The custom of endogamy among individuals belonging to the same tribe (hamula or kabeela) is and has been strongly favored among Arabs, with the consequence of unequal distribution of founder mutations among the population. A large number of studies into the effects of selection and random drift which increase the hypothesis of consanguinity and later on health and disease have not taken such discrepancies into consideration. Consanguinity in World Populations Consanguineous marriages have been practiced since the early existence of modern humans. At present, about 20% of world populations live in communities with a preference for consanguineous marriage.[2] Selection and Random drift rates vary from one population to another depending on religion, culture, and geography. Noticeably, many Arab countries display some of the highest rates of consanguineous marriages in the world ranging around 20-50% of all marriages, and specifically favoring first cousin marriages with average rates of about 20-30% (Ghazi O Tadmouri, 2009). One reason behind selection is many families found that consanguineous marriages are generally thought to be more stable than marriages between non-relatives, although there are no studies to compare divorce rates of consanguineous and non-consanguineous marriages among Arabs. It is generally believed that the husband's family would side with the consanguineous wife in marital disputes since she is considered part of the extended family. When there are children with disabilities, more family members share in

caring for these children. Unlike what is thought, consanguinity in the Arab World is not only confined to Muslim communities. Several other communities, including the Lebanese, Jordanian, and Palestinian Christian populations, have also practiced consanguinity, but to a lesser extent than Muslims.[4-7] Consanguinity rates show wide variations among Arab countries, as well as within the same country (Ghazi O Tadmouri, 2009). However, reports from Arab countries on consanguinity rates may sometimes include marriages between third cousins or far relatives within the consanguineous category. Although this discrepancy affects the total consanguinity rate, it does not markedly alter the average inbreeding coefficient. Therefore, for comparison of consanguinity rates among populations, two parameters are best used; the mean inbreeding coefficient (F) and marriages between first cousins. However, Arab societies have a long tradition of consanguinity, and the cumulative estimate of (F) may exceed the estimated value which is calculated for a single generation.[8] Secular changes in the consanguinity rates have been noticed in some Arab populations. In Jordan,[9] Lebanon,[5] Bahrain,[10] and among Palestinians,[11-13] the frequency of consanguineous marriage is decreasing. Several factors may be playing a role in decreasing the consanguinity rates in Arab countries. Amongst these factors are the increasing higher female education levels, the declining fertility resulting in lower numbers of suitable relatives to marry, more mobility from rural to urban settings, and the improving economic status of families. Moreover, genetic diseases may be feared more now that infectious diseases are on the decline as causes of severe morbidity and mortality. Generally, the highest rates of marriages to close relatives are consistently reported in the more traditional rural areas and among the poorest and least educated in society.[8] Reports from some Arab countries have shown that consanguinity rates are lower in urban when compared to rural settings. Urban to rural first cousin rates in Algeria were 10% and 15%,[14] in Egypt, 8.3% and 17.2%,[15] and in Jordan, 29.8% and 37.9%,[6] respectively. Likewise the mean inbreeding coefficient was lower in urban as compared to rural settings in Syria (0.0203 versus 0.0265).[16] In Jordan, it was evident that the higher the level of education of the female partner, the lower the consanguinity rate. Only 12% of university educated females would marry their first cousins, whereas 25% of university educated males tend to marry first cousins.[6] Similar trends of lower consanguinity rates among educated women, but not educated men, were noticed in Yemen[17] and Tunisia.[18] Consanguinity rates seem to be increasing at a higher pace in Qatar,[19] Yemen,[17] the United Arab Emirates (UAE),[20] and Tlemcen in Algeria.[14] In Morocco, a study indicated an increasing consanguinity rate from the previous (21.5%) to the present (25.4%) generation,[21] while another study indicated a decreasing consanguinity rate.[22] Consanguinity rates are not declining in some Arab countries because it is generally accepted that the social advantages of consanguinity outweigh the disadvantages,[23] and consanguinity is regarded as a deeply rooted cultural trend. It is believed that the practice of consanguinity has significant social and economic advantages. Consanguineous marriages among Arabs are respected because it is thought that they promote family stability, simplify financial premarital negotiations, offer a greater compatibility between the spouses and other family members, offer a lesser risk of hidden financial and health issues, and maintain the family land possessions.[3,24,25] On the other hand, social, religious, cultural, political and economic factors are all kind of selection factors effects on the randomization and play roles in favoring consanguineous marriages among the deferent generations. In this study, we are not just focusing on the consanguinity and inbreeding but more we are interested to know factors that increasing the hypothesis of consanguinity, and disease that rise due to misjudgment of the public awareness about random drift, which might be the major role high genetic disease frequencies. We also aim to improve public awareness about the concept of population random drift, which is almost not recognized and it is the cause of high genetic diseases with respect for premarital examination and inbreeding.

2. MATERIAL AND METHODS

2.1 Population characteristic

Saudi Individual and Families with history or with exist proband of one more of following common genetic disorders. This includes but not limited to Asthma, Down syndrome, blood genetic disorders, and psychiatric disorders.

2.2 Survey design

Questions were drawn from significant factors on heredity of genetic disease reported from previous studies, genetics knowledge. Data collection interests of all participants were considered and balanced throughout this process, taking into considerations revising the bioethics bylaw. Through pilot testing with cognitive interview techniques, we refined the wording of certain questions, and added or deleted questions to improve the length and overall flow of the survey.

Variables measured four broad domains: personal data (for example, ages, type of mirage, premarital examination); personal health (for example, family medical history, medical genetic status); familiarity with some genetic disorders, and we also personal interest for un-relative marriages.

2.3 Statistical analysis

We used descriptive statistics, which is the discipline of quantitatively describing the main features of a collection of information,[1] or the quantitative description itself. It is distinguished from inferential statistics (or inductive statistics), in that descriptive statistics aim to summarize a sample, rather than use the data to learn about the population that the sample of data is thought to represent. This generally means that descriptive statistics, unlike

inferential statistics, are not developed on the basis of probability theory.[2,3] Even when a data analysis draws its main conclusions using inferential statistics, descriptive statistics are generally also presented. It also provides simple summaries about the sample and about the observations that have been made. Such summaries may be either quantitative, summary statistics, or visual.[4]

3. RESULTS

3.1 Literature Review

Previous studies reported there are a high percentage of different genetic disorders in Saudi population. Regardless wither these studies considered the consanguinity factors, but it still significantly high. Table.3.1.

Table 3.1: Prevalence of different genetic diseases in Saudi Arabia.

Diseases	Number of research
Asthma	138
Blood genetic disorder	83
Down syndrome	23
Psychiatric disorder	182
Thalassemia	39
Diabetes	832
Obsessive–compulsive disorder	3
Parkinson's	26
gout	5
Acute lymphoblastic leukemia	40
Epidermolysis bullosa	4
Dermatitis	19
Epilepsy	82
Hypertension	399

3.2 Survey

Among 131 questioners were distributed to students inside the campus, 236 responses were obtained. Almost 58% of respond survey shows variant number of genetic disorders (Table 3.2). The variation of genetic (Table 3.3), show high prevalence come under blood genetic disorders 46.7% (sickle cell disease), 29.2 % diabetes, 11.7% Down syndrome, 10.2% Psychiatric disorder, and 13.1% reported as unknown disease. Culture affiliation parameters were considered for justification of selection and also can be considered as area of improvements (Table 3.4).

Table 3.2: Number of distributed and respond surveys.

Population size	Cases (n/%)	Control (n/%)	Total
Survey	32 (24.4)	99 (75.6)	131
Response	137 (58)	99 (42)	236

Table 3.3: Variation of disease distributed among reported cases.

Numbers (n=137)	n	(%)
Current / History of Asthma	11	8.0
Blood genetic disorder	64	46.7
Down syndrome	16	11.7
Psychiatric disorder	14	10.2
Thalassemia	0	0
Diabetes	40	29.2
Obsessive–compulsive disorder	2	1.4
Parkinson's	1	1
gout	4	2.9
Acute lymphoblastic leukemia	8	5.8
Epidermolysisbullosa	1	1
Dermatitis	5	3.6
Epilepsy	1	1
Hypertension	1	1
Unknown diseases	18	13.1

Table 3.4: Cultures affiliation factors.

Factors	Cases (N=15)		Controls (N=99)	
	Number	%	Number	%
Consanguine parents	8	53	56	56.6
Number of interest for un-relative marriages	11	73.3	74	74.7
Number of interest for foreign marriages	2	13.3	17	17.7
Familiarity with premarital examination	15	100	48	48.5

Table 3.5: Geographical and community stratification.

Regions	Cases		Controls	
	Number	(%)	Number	(%)
Western province	3	4.2	7	12.9
South Provinces	24	33.8	16	29.6
Qassem	1	1.4	7	12.9
Riyadh + central regions	9	12.7	13	24.1
Kharj	9	12.7	7	12.9
Eastern province	1	1.4	2	3.7
Haeil	3	4.2	2	3.7
Oman	1	1.4	---	0
Total	71	100	54	100

4. CONCLUSION

Consanguinity and Autosomal Recessive Disorders In mathematical terms, consanguinity does not alter the allele frequencies of common disorders, but increases the

probability of a mating between two individual heterozygotes for the same recessive mutant allele. In this regard, the risk for birth defects in the offspring of first-cousin marriage is expected to increase sharply compared to nonconsanguineous marriages particularly for rare autosomal recessive disease genes, because for common recessive conditions, there is a high chance that the abnormal gene may be carried by unrelated spouses and may be expressed in their progeny. In Arab populations and Diasporas, the deep-rooted norm of consanguineous marriage has been widely accused of being an important factor contributing to the preponderance of autosomal recessive genetic disorders.[35,47,72-76] In many parts of the Arab world, the society is still tribal. This has made the epidemiology of genetic disorders complicated, as many families and tribal groups are descended from a limited number of ancestors and some conditions are confined to specific villages, families, and tribal groups, leading to an unusual burden of genetic diseases in these communities.[77] Thus the extended family structure, commonly present in Arab societies and mostly associated with consanguinity, tends to display unique distribution patterns for genetic diseases that are not present in many other societies. There are disorders that are specifically prevalent among the Arabs, either uniformly or in certain locations, such as Bardet-Biedl syndrome, Meckel-Gruber syndrome, spinal muscular atrophy, osteopetrosis and renal tubular acidosis, Sanjad-Sakati syndrome, and congenital chloride diarrhea.[78,79] In an Arab society, mutation carriers mostly remain concentrated within the extended family and consanguineous marriages increase the probability of expression of autosomal recessive disorders when both mother and father are carriers of the mutation. Sometimes, autosomal recessive genes stay hidden within the family for generations and then show on the surface in a new consanguineous marriage within the family. An analysis of data in the Catalogue for Transmission Genetics in Arabs (CTGA), a database on genetic disorders in Arab populations maintained by the Centre for Arab Genomic Studies, indicates that in contrast to international databases, the overwhelming proportion of the disorders in the CTGA Database follow a recessive mode of inheritance (63%) compared to the smaller proportion of dominantly inherited traits (27%). A detailed study of countries for which surveys on the occurrence of genetic disorders have been completed (United Arab Emirates, Bahrain, and Oman) indicates that recessive disorders are more in number than the dominant ones.[80-82] As explained above, given the high rates of consanguinity in these countries, this pattern is not entirely surprising. In a study from Jordan, the consanguinity rate among parents of affected with autosomal recessive conditions was around 85%, while it was 25-30% among parents of affected with other genetic conditions such as X-linked recessive, chromosomal and autosomal dominant.[76]

5. LIMITATION AND CHALLENGED

In this research, we were several challenges such as lack of samples are analyzed, to make sure the results of research in genetics and disease and to know closely the transmission of genetic diseases work is unfortunately paper only specific, low-sources Difficult for Statistics from the Ministry of Health because of the lack of the ministry aware of the prevailing ignorance may affect the work of the ministry because of the lack of research in disease genetics may be a problem in the future, the emergence of new diseases and have the lives of the next generation, or have exacerbated the disease and increase the spread shall result generation properly take care of the injured neighbor's disease Legacy precipitated influenced by the economy and often fills hospitals patients non-susceptible to improved genetics Non-disclosure of the information may be embarrassing because of some because of the nature of man in the models questions. Some models let-up in search of answers to questions that has actually surroundings.

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