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Prevalence of Consanguineous Marriages in UAE Nationals and the Risk of Genetic Diseases

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Abstract

Introduction: *The occurrence of consanguineous marriages has been common in the Arab populations due to socio-cultural factors. Genetic diseases are rare in the overall population, but their frequency unusually increases as the prevalence of consanguineous marriages increases. The aim of our pilot study was to investigate the extent of consanguinity and its effects on non-communicable genetic diseases, in Emirati population.*

Methodology: *This research was based on a socio-economic survey (SES) conducted by a group of students of Dubai Pharmacy College for Girls in the year 2018. Subjects for this preliminary study were selected by using convenience sampling method from urban regions of United Arab Emirates local households. A questionnaire was designed for this purpose and data was collected during household visits.*

Results: *Our study showed that the incidence of consanguinity is relatively high with a rate of about 65% approximately and 33% of all these consanguineous marriages are of the first cousin and closer marriage type. Our results states that consanguineous marriages have a negative effect on reproductive health factors and in turn posing a risk for occurrence of noncommunicable genetic diseases, congenital malformations, and various chronic and complex multifactorial diseases in Emirati Arab population.*

Discussion: *Genetic counselling and premarital counselling must be accentuated to reduce the risk of genetic syndromes in the population.*

Keywords: *Consanguineous marriage, Autosomal recessive, carriers, inbreeding, noncommunicable genetic disorders*

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Introduction

Consanguineous marriage (CM) refers to a union between two biologically related individuals. In clinical genetics, it is defined as the marriage between two blood-related individuals who are second cousins or closer (inbreeding coefficient ~* 0.0156).[1] Genetically, consanguinity derives from the reduction in variation due to meiosis that occurs because of the smaller number of near ancestors. All humans share between 99.6% and 99.9% of their genome, consanguinity only affects a very small but significant part of the sequence. Consanguineous marriage (CM) is a universal practice; its prevalence has been chosen to keep cultural values intact, preserve family wealth, maintain geographic proximity, keep tradition, strengthen family ties, and maintain family structure. Their prevalence is common in North African, Middle Eastern, and West Asian countries. The prevalence of CM does not exceed 0.5%, in Western and European countries whereas, in Arab Gulf countries,, the prevalence of CM ranges between 40% and 60%.[3,4,5,6,7,8] It has been noted that high prevalence of genetic disorders in Arab populations' is related to the dominance of consanguineous marriages.

Mutations in DNA causes genetic disorders. These diagnostic changes can be single gene mutation, several-gene mutations, chromosomal mutations or copy number changes in gene or chromosomes.[9] Miscarriage, child death and frequent abortion are more prevalent in consanguineous marriage.[10] This is because certain genetic disorders are inherited from the parents either as autosomal dominant/recessive, X-linked dominant/recessive and single-gene disorders.[11]

Autosomal dominant disorder is transmitted to the offspring if only one parent is affected such as Huntington's Disease (HD).

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Autosomal recessive diseases are transmitted, when both parents are either affected or carriers for diseases such as thalassemia.[12] Previous studies indicated that the most common inheritance pattern of consanguinity is the autosomal recessive disorder (78.8%) and multifactorial disorders (69.8%).[10]

It has been noted that high prevalence of autosomal recessive genetic diseases in Arab populations' is related to the dominance of consanguineous marriages. The frequency of autosomal recessive genetic disorders increases with the increase in maternal age such as Down Syndrome, dominant mutations related to advanced paternal age leads to increase in malformations, large family sizes, increases the risk of affected children with autosomal recessive disorders; and inadequate genetic counselling facilities directed towards prevention of genetic disorders before and during pregnancy.[10,12]

Offspring of parents associated with consanguineous mating are also at a higher risk of noncommunicable genetic disorders (NGDs) such as cardiovascular disease, blood disorders, cancers, schizophrenia, and diabetes.[13,14]

High incidence rates of NGDs affect public health and the healthcare system by decreasing productivity because of the disease. Studies have shown that people with genetic, chromosomal, or congenital diseases use more than one-third of the resources of the healthcare system.[15,16,17,18,19] This indicates the need for encouraging preventive health risks. Identification of carriers in various genes leading to NGDs may help to reduce their occurrence in future generations.

The present study was undertaken to determine the prevalence of CM and explore the role of CMs as a risk factor in the occurrence of NGDs in a selected sample of the Emirati Arab population. This can also provide decision makers with reliable knowledge for planning awareness programs related to public health to reduce the burden of genetic diseases.

Subjects and methods

Study population and sample

The cross-sectional study data was collected from July 2018, to January 2019.

Sampling Method

- Subjects for this preliminary study were selected by using convenience sampling method from urban regions of United Arab Emirates local households.
- A sample(N) of 400 married Emirati (national) females aged 18 years and over were approached to participate in the study.
- Out of 400 females 381 agreed to participate in the study.

Inclusion Criteria for Sampling

- Married females above the age group 18 years of age.
- Subjects who are willing to participate in the study.
- Subjects who are available at the time of data collection.

A questionnaire was designed for this purpose and data was collected during household visits. Written informed consents were obtained for participants after explaining to them the nature and purpose of the study.

The questionnaire had 2 parts:

PART – I:

Consist of demographic variables such as name, age, education, occupation and place of residence.

PART – II:

- The mother in each household was asked about the relationship to her husband, with a choice of one of three answers: first-degree cousin (including all four types), more distant relationship, or no relationship.
- The history of all cases of genetic diseases, including other malformations and complex diseases, in children was also recorded.

Information on consanguinity was obtained through the household visits and personal interviews. Relationships were categorized as: consanguineous and non-consanguineous marriages. Consanguineous marriage: This group included either: a. Marriages between First cousins or closer. These include double-first cousins (in which all grandparents are shared) and first cousins in which the couple are parallel or cross cousins of either paternal or maternal origin; b. Distant relative marriages, in which the couple were relatives but not with first-degree relations, for example they were first cousin once removed, second cousin, second cousin once removed.

Validity and Reliability

The questions were shared with two professors from Dubai Pharmacy College for Girls belonging to Genetics department who finally approved the questionnaire.

Cronbach's Alpha used to calculate reliability, which should range from 0 (no reliability) to 1 (perfect reliability). SPSS (v26) software has, and it equals 0.857, which is at a good level (0.800++), therefore, we conclude that the questionnaire is reliable.

Ethical approval:

Initially, the research proposal got ethical approval from the ethical research committee from Dubai Pharmacy College for Girls (DPC-REC) NO: REC/G/2018/7

Analysis:

SPSS software package (SPSS, Chicago, IL, USA) version 24 was used.

Statistical Methods:

Chi-square test to compare proportions of cases in first-cousin consanguineous and non-consanguineous groups. Statistically significant results were assumed when the p value was <0.05.

Results

Table 1. *Prevalence of consanguineous marriage in Emirati Population*

Total No. of Participants	Consanguineous	Non-Consanguineous
381	343 (64%)	138 (36%)
	FC	DR
	126 (52%	117 (48%)

FC- First cousin marriages DR- Distant Relative marriage

Table 1 (Figure 1) shows that out of 381 marriages, 243 (64%) were consanguineous and 138 (36%) were non-consanguineous. Out of these consanguineous mating 126 (52%) were first-cousin marriages, and 117 (48%) were distant relation marriages. It was found that among the first cousin marriages the son/daughter of father's brothers getting married was high (50.3%) when compared to other types.

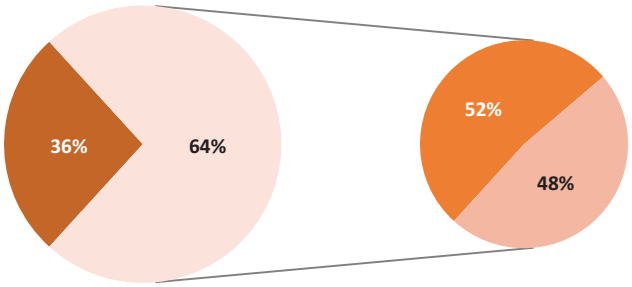

Figure 1: *Prevalence of consanguineous marriage in Emirati Population*

Table 2. *Distribution of disorder types among offspring from consanguineous and non-consanguineous marriages*

Type of Disorder	No. of affected children = % (n)	Consanguineous		Non-consanguineous	*p*
		FC	DR		
Respiratory	25% (98)	6.30%	9.20%	10.30%	0.43
Mental	4% (16)	2.30%	0.50%	1.30%	0.65
Physical	11% (42)	3.70%	2.60%	4.70%	0.36
Visual	7% (28)	2.90%	1.80%	2.60%	0.92
Hearing	2% (9)	1.30%	0%	1%	0.62
Other Hereditary diseases	49% (185)	16.40%	16%	16.30%	0.23
Total	100% (378)				

Of the 1524 total children from the sample, 378 children were found to have one or more disorders which form 24.8% of total children. The total number of affected children were separated into those from consanguineous and those from non-consanguineous marriages, presented in table 2.

Out of these 63% of affected children were product of consanguineous marriages. NGDs were more frequent in consanguineous marriages suggesting that there is significant association between consanguinity and non-communicable genetic disorders (Table 2).

Table 3. *Comparison of disorder types among offspring of different gender from consanguineous and non-consanguineous marriages*

Gender of affected children in consanguineous	Respiratory	Mental	Physical	Visual	Hearing	Other hereditary diseases	Affected children
Males %	38.9	63.6	58.3	50	0	36.6	41.6
Females %	61.1	36.4	41.7	50	100	63.4	58.4
Gender of affected children in Non consanguineous	Respiratory	Mental	Physical	Visual	Hearing	Other hereditary diseases	Affected children
Males %	48.7	80	38.9	10	25	46.8	44.2
females %	51.3	20	61.1	90	75	53.2	55.8

Table 3 reports types of disorders among offspring based on gender from consanguineous and non-consanguineous marriages. Female children were more affected in consanguineous mating, while males are more affected in non-consanguineous mating.

Table 4 reports the Cause of the disorder in offspring. 93% of affected children reported that they were diagnosed either after illness or after birth as congenital defects in consanguineous marriages. Illness was recorded in 108 cases (45%) and in 117 cases (48%) there was a congenital cause. Only 15 cases (6.2%) reported that they were diagnosed "at birth".

Table 5 observes different types of genetic disorders in affected children in the study group. It is found that there was a significant increase in chromosomal, multifactorial, and single gene disorders in children born to consanguineous parents. The occurrence of chromosomal disorders was highest (73%) in children born to consanguineous parents.

In Table 6 (Figure 2), single gene disorders were again classified based on mode of inheritance as either autosomal dominant, autosomal recessive, and X-linked recessive disorders. The data suggests an increase in autosomal dominant, Autosomal recessive and X-linked recessive disorders seen in offspring of consanguineous mating when compared to non-consanguineous mating. More children were affected with single gene disorders in consanguineous mating (74%) when compared to non-consanguineous marriages. Out of them 53 (71.6%) of children from consanguineous marriages had autosomal recessive disorders, compared to 19 children only affected in (57.6%) non-consanguineous mating.

Table 4. *Cause of the disorder in offspring*

Cause of disorder in consanguineous mating	Respiratory	Mental	Physical	Visual	Hearing	Other hereditary diseases	Total N%
Illness	49.2	18.2	20.8	55.5	40	48.8	45
Congenital	45.8	72.7	70.8	33.3	60	45.5	48.8
At birth	5	9.1	8.4	11.1	0	5.7	6.2
Cause of disorder in Non consanguineous mating	Respiratory	Mental	Physical	Visual	Hearing	Other hereditary diseases	Total N%
Illness	59	60	16.7	70	75	54.8	52.9
Congenital	33.3	0	72.2	10	0	38.7	37
At birth	7.7	40	11.1	20	25	6.5	10.1

Table 5. *Types of Genetic disorders in affected Children in the study group*

	Consanguineous		Non-Consanguineous		
Genetic disorders in affected Children	N	%	N	%	*p*
Chromosomal	11	73.40%	4	26.60%	0.04
Multifactorial	46	54.10%	39	45.90%	0.02
Single gene disorders	74	69.20%	33	30.80%	0.05

Table 6. Comparison of consanguinity in relation to different modes of inheritance of single gene disorders in the sample

	Consanguineous		Non-Consanguineous		
Single gene disorders in affected Children	N	%	N	%	*p*
Autosomal Dominant	14	18.90%	4	12.10%	0.37
Autosomal Recessive	53	71.60%	19	57.60%	0.12
X-linked Recessive	7	9.50%	10	30.30%	0.007

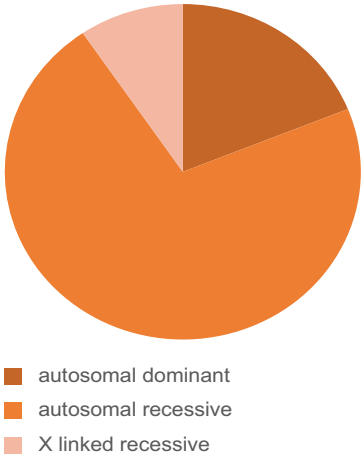

Figure 2: *Modes of inheritance of single gene disorders seen in consanguineous mating.*

Table 7. *Prevalence of common diseases among offspring in consanguineous and non-consanguineous mating.*

Offspring Diseases	*C= 139	**NC= 82	%
Acrodermatitis enteropathica	1	0	0.45
Albino	1	0	0.47
Allergy	2	1	1.40
Anemia	20	8	13.02
Anemia + DM	1	0	0.47
Asthma	25	17	19.53
Autism	1	1	0.93
Bartter syndrome	1	0	0.47
Behcet's disease	0	1	0.47
Cancer	0	1	0.47
Cardiac infection	1	1	0.93
Cerebral palsy (CP)	1	0	0.47
Cirrhosis	1	0	0.47
Colorectal cancer	0	1	0.47
Congenital Bicuspid aorta	0	1	0.47
Congenital dys erythropoietic anemia	1	0	0.47
Congenital malformation	1	0	0.47
Crohn's disease	0	1	0.47
Dawn syndrome	11	4	6.98
DM	19	18	17.21
DM/Hypothyroidism	0	1	0.47
Dyskeratosis congenita	0	1	0.47

Table 7. *Cont'd*

Offspring Diseases	*C= 139	**NC= 82	%
Dyslexia	1	0	0.47
Eczema	1	0	0.47
Epidermolysis Ballosa	1	0	0.47
Epilepsy	3	0	1.40
Eye disorder-color blindness	3	4	3.26
FlatFoot	0	1	0.47
Folic anemia, Thalassemia	0	1	0.47
G6Pd Deficiency	0	1	0.47
G6PD Deficiency	4	3	3.26
Glaucoma	1	0	0.47
Growth retardation disease	1	0	0.47
Haemolytic anemia	1	1	0.93
HTN	1	1	0.93
hypercholesterolemia	1	0	0.47
Hypothyroidism	2	1	1.40
Hypothyroidism/G6PD Deficiency	1	0	0.47
Ichthyosis	1	0	0.47
Idiopathic Scoliosis	1	0	0.47
Leg varicose veins	0	1	0.47
Mental Retardation	0	1	0.47
Migraine	1	0	0.47
Niemann-pick	1	0	0.47
Noonan syndrome	1	0	0.47
OCD	1	0	0.47
Osteoporosis	2	1	1.40
PCOS	2	0	0.93
Psoriasis	0	1	0.47
Pyelonephritis	1	0	0.47
Retinal detachment	0	1	0.47
Sickle cell anemia	5	2	3.26
Spinal muscular atrophy	1	0	0.47
Spinal obstruction	1	0	0.47
Spino-Cerebral ataxia	1	0	0.47
Thalassemia	11	3	6.51
Thrombocytopenia	0	1	0.47
Tyrosinemia	0	1	0.47
Vitiligo	1	0	0.47

*C: Consanguineous
**NC: Non-Consanguineous

Disorders seen in consanguineous and non-consanguineous unions are reported in table 7. Most common reported disorders are Asthma, Diabetes Mellitus, Anemia, Down Syndrome, and Thalassemia. Most of them are autosomal recessive disorders.

Discussion

Consanguinity is practiced for centuries and attracts considerable attention as a causative reason in the occurrence of genetic disorders. Our data suggest an increased incidence of single gene (autosomal recessive), chromosomal and multifactorial disorders in consanguineous mating. The association between consanguinity and genetic defects is well demonstrated in previous studies performed in different societies. Inbreeding has an effect on the rates of reproductive loss, congenital malformations and genetic diseases, mainly autosomal recessive.[3,4,5,6,7,8] In our study, Parental consanguinity was reported in 71.6% of patients with autosomal recessive disorders compared to 57.6% in non-consanguineous parental mating. In Jordan, *Hamamy et al. 2005.*[20] *(*Department of Genetic Medicine and Development, Geneva University Hospital, Switzerland) stated that 85% of the parents were consanguineous in affected children with autosomal recessive diseases. Moreover, in India *Sharma et al,*[7] has shown a high percentage of consanguineous marriage in parents of patients with autosomal recessive disorders. A study done in the UAE also showed a high frequency of rare recessive disorders in this population.[21] which indicates that long term inbreeding in this population may not have resulted in elimination of recessive genes, which is supported by our study. Overall, there were some limitations to our study which includes the need for a larger sample size to be obtained to extrapolate results to all population of citizens in the UAE. Reporting bias was an issue as some households didn't report their children's diseases, therefore access to patient's health records is needed. Since there is lack of prior research studies on the topic, only one was done in UAE in 1997, therefore we used an exploratory research design rather than explanatory design. Lack of funding has limited our choices of measures to collect data, such as access to patient records. As well as including a specific question about the number of children for each parent, in retrospect, could have helped us report the number of genetic mutations or diseases within each family. The questionnaire as a tool of gathering information in this research was difficult to verify independently; therefore, we expect rise of biases that may include selective memory or exaggeration. Measuring accurate incidence of genetic diseases needs larger sample size and close follow up and monitoring of mother and child since birth.

We recommend using the science of genetics and genomics in applications to provide optimal health to individuals of a community. National registries should be adapted to (human genome data) provide several avenues for studying the genetic basis of single gene and complex diseases by containing information on human mutation and polymorphism database. National wide Campaigns to be done on a routine basis to increase awareness of risk factors leading to genetic disorders, and prevention strategies. Birth cohort studies to be done to track incidence of genetic diseases or any possible mutations that may lead to onset of diseases in future to obtain complex data for further use in omics. And finally use the data from such research to translate basic research into clinical application).

Conclusion

The prevalence and status of consanguineous marriage is a matter of conjecture. A rapid decline in its prevalence is questionable in the meantime in Arab countries. Extensive community education programs are needed to reduce the burden on health care systems, and to complement the existing diagnostic, counseling, and treatment facilities. The government should implement strict laws for premarital testing. As the possibility of controlling consanguineous unions is high, the study gives clear indications for prevention. The health authorities, health care providers, genetic counselors and academicians should consider the negative impact of consanguineous marriage in terms of increased genetic risks to the offspring's, as opposed to the potential social, cultural and economic benefits while educating the society at large. It is important that primary health care providers, specifically in highly consanguineous communities, have clear evidence-based guidelines in counseling a consanguineous couple to minimize their risks for having affected offspring.

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Conflict of interest statement:

The authors have no conflict of interest to declare.

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