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Original Article

Genetic diseases and associated risk factors in some Libyan districts: A cross sectional study

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ABSTRACT

Genetic disorders are caused by defects in the genetic material ranging from point mutations to chromosomal deletions. Manifesting of recessive defects requires the mutation inheritance from both parents, whereas dominant disorders require the mutation inheritance from one parent. This study aimed to investigate the rate of genetic disorders among Libyan participants with genetic disorders, to investigate their most causative risk factors and the level of awareness of these diseases. This cross sectional study was carried out through a questionnaire with a set of questions about genetic diseases distributed both on paper and electronically. 256 participants have generic disorders from different regions of Libya were involved. The participant's answers were collected from July 2021 to February 2022. The findings showed that the most prevalent genetic diseases were blood disorders 13.7%, CI=13.3-15.4), Down syndrome (13.3%, CI=9.5-17.4), autoimmune diseases (12.1%, CI=8.2-16.0), hereditary cancer (9.0%, CI=5.1-12.9) and congenital malformations (7.4%, CI= 4.1-10.9). The results showed that consanguineous marriage was a risk factor associated with the incidence of genetic diseases (P= 0.000, CI= 3.34-3.48) and there was a high rate of second-degree consanguineous marriage for the parents of participant patients (55.0%, n=141). Moreover, there was a family history of genetic disease (53.5%). The findings showed a lack of awareness of genetic diseases and their nature among the participants' families. Data from this survey should be taken into account by the health authorities to outline a policy to prevent these genetic disorders in the country.

Keywords: Genetic Diseases, Genetic material, Mutations, Risk Factors, Libya

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Introduction

Human genetic disease is any of the diseases and disorders that are caused by mutations in a single gene, by mutations in multiple genes, by abnormalities in chromosomes, or by a combination of gene mutations and environmental factors (multifactorial disorders)(1). The mutations can be inherited from both parents which are called autosomal recessive or from one parent (autosomal dominant), in addition, some other mutations are linked to chromosome X (2).

Approximately 10,000 genetic diseases have been identified; they constitute almost 80 of all rare diseases affecting 6-8% of all world populations. About 1 in 50 individuals are affected by single gene mutation; whereas, 1 in 263 individuals are affected by chromosomal abnormalities and about 5.3% of newborns will have genetic disorders. It is estimated that autosomal recessive disorders are the most frequent because of a high proportion of consanguineous marriages (3). Moreover, genetic alteration could contribute to the development of many diseases such as cancer, diabetes, and others, which appear with existing other factors including environment (for example lifestyle) (4).

Genetic diseases constitute a significant problem globally and the knowledge of the prevalence of these diseases would help to manage, establish and organize cure services for these diseases. It is observed that up to 71% of hospitalized children are with genetic diseases, which cause death in about 20-30% of them (3).

In Libya, There is a lack of information about the prevalent types of genetic diseases and their prevalence rates; there are few studies on the prevalence of the genetic diseases, their causes and their seriousness. According to the Centre for Arab Genomic Studies, there is 38 pathogenic entities have been identified in Libya that represent the cause of the most prevalent genetic disorders in the country (5). In a study to estimate the incidence of Down Syndrome in children at the genetic clinic at Al-jamahiriya maternity hospital, Benghazi from 1994 to 2003, the incidence rate of Down Syndrome was 1.9 patient per1000 live births, which was higher than the international incidence rate (1-1.2 patient per 1000 live births)(6). The global prevalence of Down syndrome in total population is 1 in 700, with little variation from country to country. In the United States, it is 8.27 per 10,000 people (7). Another study with similar findings about Down syndrome among live births in the Jamahiriya Hospital in Benghazi in 1985, showed that one affected child in every 516 live births (1.9/1000)(8). According to the available data from previous studies, the prevalence of sickle cell trait and sickle cell disease in Libya was found about 4.2% and 1.2%, respectively; the prevalence rate of sickle cell disease was 1.2% in the southern region and 0.005% in the eastern region (9). Another study included 210 participants from the Marzouk region found that 112 (53.33%) participants were carriers of the sickle cell disease (HbAS) and 23 (11%) of the participants were affected by the disease; the percentage of the carriers of the trait and infected people with the disease in this region is high (10).

In the Benghazi region, a 3-year study about the prevalence of genetic neuromuscular diseases found that the prevalence rates per 100,000 population were 6 for Duchenne dystrophy, 3.7 for limb-girdle dystrophy, 0.8 for facioscapulohumeral dystrophy, 0.6 for opthalmoplegia-plus and 7.9 for HMSN (6.4 and 1.5 for Types I and II, respectively) (11). Another 4-year-search in Benghazi city conducted to assess the epidemiology of hereditary motor neuropathies (HMN) showed that the average annual incidence of HMN was 0.3/100,000 total population in Benghazi (12).
In Libya, data about the types of prevalent genetic disorders and their risk factors, awareness of patients and their families about the nature of these diseases in addition to the availability of appropriate treatments and services required for people with these diseases is scarce.

Methods

Study subjects

A cross-sectional survey included 256 genetic disease patients from different regions of Libya using printed and electronic questionnaires from February to November 2021. All participants and children's parents gave their approval to participate in this survey.

The questionnaire included 25 questions categorized into three sections; the first section was about patients' information, the second was about their parents and risk factors and the last section was about the participants' awareness about the genetic disorders as illustrated in figure 1.

Questionnaire for the participants

Part one: About patient

- **Sex :** M ☐ F ☐
- **Age:** 1-10 ☐ 11-20 ☐ 21-30 ☐ 31-40 ☐ over 40 ☐
- **Residence:** The eastern region ☐ The western region ☐ The middle region ☐ The southern region ☐
- **The type of the genetic disease:** Down syndrome ☐ Blood disorder* ☐ Autoimmune disease* ☐ Hereditary cancer ☐ Cystic fibrosis ☐ Congenital anomalies ☐ Motor disability ☐ Spinal Muscular Atrophy ☐ Diabetes ☐ blindness ☐ Hypertension ☐ cleft lip ☐ Autism ☐ Others* ☐

  *Secify ……...

  ……..
- **Age at disease onset:** From birth ☐ After birth ☐
- **Education:** Illiterate ☐ Primary ☐ Secondary ☐ High ☐
- **Other chronic disease:** Yes* ☐ No ☐

  *Specify ……..
- **Medical report of the genetic disease:** Yes ☐ No ☐
- **Follow up with geneticist:** Yes ☐ No ☐
- **Order of the patient in the family: First** ☐ Second ☐ Third ☐ Fourth ☐

Part two: About parents and Risk factors

- **Mother age at patient delivery** ……..
- **Medications during pregnancy:** Yes ☐ No ☐
- **Kinship relation of the parents:** Cousins ☐ Distant kinship ☐ **No** kinship ☐
- **Is there any landfill, chemical or radioactive pollutants near residence:** Yes ☐ No ☐
- **Is there another members with genetic disease in the family** Yes* ☐ No ☐ *if yes: how many …… type of disease ……
- **Is there a family history of any genetic disease:** Yes* ☐ No ☐ *if yes: what is the most inherited disease in the family ……..

Figure1: the study questionnaire

Statistical analysis

The data were analyzed using SPSS software (version 19). The prevalence mean and standard deviation were calculated for patients' age and their mothers' age, where $P < 0.05$ was considered statistically significant in all tests and a 95% confidence interval (CI) was used to identify the risk factors associated with genetic disorders.

Results

256 patients with genetic disorders participated in this study, 138 patients of them were male (53.9%) and 118 were female (46.1%). Their mean age was 21.69 with a standard division of 16.75, there were no significant differences among patients' ages ($P = 0.510$), the majority 49.6% (127/256) of the participants were among the age group 0-15 years. The distribution of participants according to the regions of the country was 52.7% (135/256) from the middle (central) region, 34% (87/256) from the western region, 7% (18/256) from the southern region, and 6.3% (16/256) from the eastern region.

Among all participants, the most prevalent genetic disorders were blood disorders 13.7% (35/256), Down syndrome 13.3% (34/256), autoimmune diseases 12.11% (31/256), hereditary cancer 9.0% (23/256), congenital anomalies 7.4% (19/256), motor disability 6.3% (16/256), Spinal Muscular Atrophy 5.5% (14/256), Diabetes 5.1% (13/256). The rates of the other genetic diseases were lower as illustrated in Table 1.

Table 1. Genetic diseases frequencies among the study participants

Genetic disease	Frequency	Percentage %
Blood disorders*	35	13.7
Down syndrome	34	13.3
Autoimmune diseases	31	12.1
Hereditary cancer	23	9.0
Congenital anomalies	19	7.4
Motor disability	16	6.3
Spinal Muscular Atrophy	14	5.5
Diabetes	13	5.1
blindness	10	3.9
Hypertension	8	3.1
cleft lip	8	3.1
Cystic fibrosis	7	2.7
Autism	7	2.7
Multiple disabilities	6	2.3
Deaf and dumb	6	2.3
Epilepsy	5	2.0
Mental disability	4	1.5
multiple sclerosis	3	1.2
Ichthyosis	3	1.2
Parkinson's diseases	2	0.8
Huntington syndrome	1	0.4
Nyctalopia	1	0.4

*Blood disorders include hemophilia, thalassemia, sickle cell anemia, G6PD deficiency, Aplastic anemia.

*autoimmune diseases include Coeliac disease, Crohn's disease, Asthma, Eczema.

The mothers' mean age was 30.10 years with a standard deviation of 7.33 years. The results showed no significant statistical differences between mothers' age and genetic disorders occurrence (P= 0.831, CI=0.80-1.00) (Table 2). The majority of mothers (78.5%, n=201) did not take any unsafe medicines during the pregnancy of their patient child.

Table 2. Participants mothers' ages

Age group	frequency	percentage %	*P* value	95% CI
15-25	67	26.2	0.831	0.80-1.00
26-36	130	50.8		
37-47	59	23.0		

The results showed that a high rate of second-cousin consanguineous marriage between the patients' parents (second degree relative) (55.0, n=141) (*P*=0.000, CI= 3.34-3.48) and the results revealed an association between second-cousin consanguineous marriage and an increased risk of genetic disorders among the study participants.

Table 3: Consanguineous marriages among patients, parents

Degree of Kinship	frequency	Percentage %	P value	95% CI
First cousin	5	2.0	0.000	3.34-3.48
Second cousin	141	55.0		
Not related	110	43.0		

Also, we found a significant statistical relationship (*P*=0.000, CI= 1.71-1.97) between family history and genetic diseases (53.5%, n=137). (Table 4)

Table 4: family history and genetic disorders

Family history	Frequency	Percentage %	P value	95% CI
Yes	137	53.5	0.000	1.71-1.97
No	28	10.9		
Unknown	91	35.6		

Moreover, the results showed that in 111 (43.4%) families there were no other patients in the family, while in the other 145 families there were one or more patients with the same diseases in the same family with a percentage (Table 5).

Table 5: the percentage of other patients in the same family

Number of patients in family	frequency	Percentage %
No	111	43.4
One	84	32.8
Two	39	15.2
Three	9	3.5
Four	7	2.7
Five	6	2.4

Disscusion

Rates of genetic disorders vary significantly from country to country depending on many factors such as social factors, overall lifestyle, genetic and environmental factors. However, in developed countries, patient registries are established and assisted in assessing the burden of genetic diseases and contributed to introducing appropriate services to the patients.

In Libya, however, there is a lack of information about the prevalent genetic disorders; the epidemiological studies about these diseases; also, there are no studies on the risk factors for these diseases.

Libya is an Arab country and one of the eastern societies that are characterized by some societal characteristics, for example, the large size of families, pregnancy at advanced ages, and a high rate of endogamy, which is estimated at about 25-60% (13). In a previous study about consanguineous marriage in Libya, the rate was around 48.4% (14).These characteristics could increase the prevalence of genetic disorders especially autosomal recessive disorders.

Recent reports by the Center for Arab Genomic Studies demonstrated that genetic diseases have a high prevalence rate in many Arabic countries like Saudi Arabia, Bahrain, United Arab Emirates, with a high rate of endogamy among these populations, and there is high prevalence rate in genetic diseases in these countries including Libya (15).

There are few studies on the prevalence of some inherited diseases and their risk factors in different regions of the country. However, a study conducted in Benghazi from 2004 to 2005 showed that the prevalence rate of congenital anomalies was 5.8 per 1,000 live births, most of these congenital anomalies were due to chromosomal disorders 2.4/1000, and the main risk factor was endogamy (Consanguinity). (16) These findings are similar to the study conducted about parental consanguinity in the Tunisian population 17). Another study about the impact of consanguineous marriages on the occurrence of some specific autosomal recessive disorders in Tunisia in 2016 revealed that the consanguinity was observed in 65% of the patients with autosomal recessive disorders (18).

In our study, the most common risk factor associated with genetic diseases among the participants is consanguinity marriage (second cousin), which is about (55% (P= 0.00, CI= 3.34-3.48); in addition to the family history, which was almost 53.5% (P=0.00, CI= 1.71-1.97).

Our finding showed that blood disorders were the dominant genetic disorder among the study participants; this was similar to the findings of the Marzouk area study. (10) These were similar to the findings of the study of the prevalence of genetic neuromuscular diseases in the Benghazi region, which reported that large family size and a high rate of consanguineous marriages contribute to the high frequency of familial disorders (11).
Our study revealed a lack of knowledge among participants about genetic diseases and their risk factors. Therefore, awareness campaigns should be directed to the affected families.

The present study has several limitations; first, the sample size was small and selected in a non-randomized way. Second, it is difficult to access all regions of the country due to frequent closings because of the political unrest in the country. Third, lack of specialized diagnostic centers and health care resources for genetic disorders in the country. Fourth, the study cannot be compared to international similar studies because the results obtained do not represent the whole of the Libyan population.

CONCLUSION

Our initial findings provided insights into the most common genetic disorders among Libyans and estimated some risk factors for these disorders. Further larger studies are needed in future to study these genetic disorders. Data from this survey should be taken into account by the health authorities to outline a policy to prevent these genetic disorders in the country.
Recommendations

The authors suggest establishing a national registry for genetic disorders and larger studies to investigate these disorders further. Also, developing strategies to reduce and prevent the occurrence of these disorders, by establishing genetic clinics for screening, examination, and follow-up services.

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Conflict of interest
All authors declare that they have no conflicts of interest.

Informed consent
Informed consent was obtained from all individual participants included in the study.

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