Original Article

Relative frequency of inherited retinal disorders in Khuzestan province, southern Iran

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ABSTRACT

Inherited retinal disorders (IRDs) are a broad range of diseases characterized by progressive visual loss due to improper development, dysfunction, or premature death of the retinal photoreceptors. In this cross-sectional study, we tried to determine the epidemiology of IRDs in Khuzestan province, southwest of Iran. In a population-based, cross-sectional study conducted from March 2018 to February 2021 in Khuzestan province. The sample size was 136 patients with a definitive diagnosis of Inherited retinal disorders. Detailed medical history was taken, visual acuity was determined and extensive eye examinations were performed. The distribution of different causes of IRD in patients was determined. From March 2018 to February 2021, 136 patients with a definite diagnosis of IRD were identified in Khuzestan province. 62 patients (45.6%) were female and 74 patients (54.4%) were male. The highest number of patients were in the age group over 15 years. The most common IRDs in Khuzestan province were retinitis pigmentosa (RP) so that 126 patients (92.6%) had RP. Parents of 113 patients (83.1%) had consanguineous marriage and were related, but only 16.9% of patients' parents were not relatives. There was a statistically significant relationship between patients' parents' consanguineous marriage and RP (P-value < 0/05). Concerning the high prevalence of consanguineous marriage in parents of IRDs patients in Khuzestan Province and the high prevalence of consanguineous marriage in Khuzestan Province, health policymakers should consider training and genetic counseling for families and perform the required pre-marital screening, especially if consanguineous marriages are ongoing.

Keywords: Inherited retinal disorders, Retinitis pigmentosa, Consanguineous marriage, Khuzestan province

Introduction

Inherited retinal disorders (IRDs) are common genetic diseases and untreatable rare ocular degenerations, associated with progressive visual disorders which cause visual loss due to improper development, dysfunction, or premature death of the retinal photoreceptors [1]. They are a group of clinically heterogeneous diseases with a prevalence of 1 in 2000 individuals which often lead to a progressive loss of vision that may result in blindness [2]. There are more than 4 million IRDs patients around the world [3]. There are 20 type IRDs phenotypes with different prevalence, including rod-dominated dystrophies, cone-dominated dystrophies, generalized retinal degenerations, and vitreoretinopathies [3, 4]. The prevalence of retinitis pigmentosa (RP), the most common type of IRDs, is estimated at 1 in 4,000 [3]. IRDs follow Mendelian inheritance patterns and mutations in Up to 270 genes associated with incidence them [5]. The forms of hereditary transmission IRDs can range from autosomal dominant and recessive to X-linked [1], but rarely can be digenic, mitochondrial, or have another pattern [6]. The first IRD described was RP by Donders in 1857, Since then these diseases have remained untreated, and nothing to do for these devastating diseases [7]. Population-based studies and registration of inherited diseases have the potential to identify disease prevalence along with genetic inheritance patterns, disease-causing genes, and mutations as well as clinical outcomes and to set a framework for applying possible therapeutic approaches [8]. The complete risk factors contributing to IRDs in the Iranian population have not been systematically defined

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due to a lack of information about the distribution of them in the community and a lack of an accurate disease registration system. The proven role of genetic transmission of these diseases has been confirmed in various studies and the role of consanguineous marriage (CM) as the main route of transmission of genetic diseases was investigated in studies on IRDs [7, 9]. CM is a widely accepted social custom among Iranian families and a leading cause of birth defects [10]. Children born from CM may be at increased risk for genetic disorders including IRDs [11].

This population-based study aimed to register IRDs patients and to determine the relative frequency of inherited retinal dystrophies in Khuzestan province and study the relationship between CM age and IRDs in patients with related parents.

Materials and Methods

The present study is a cross-sectional study based on population was designed to evaluate the epidemiological assessment and record information of patients with IRDs in Khuzestan province from March 2018 to February 2021. To determine the frequency and incidence of IRDs in the Khuzestan province population based on patient demographics (age, gender, education) Percentage of CM in patients' parents as a risk factor for transmission of hereditary diseases.

This study was performed in four referral eye centers including the Ophthalmology Clinic of Imam Khomeini Hospital located in the Ahwaz city, Patients in private ophthalmology Clinic, Patients supported by welfare and rehabilitation centers, and patients of Khuzestan RP Association. 136 patients with a definitive and suspected diagnosis of IRDs were included in the study.

All patients were referred to the ophthalmology center of Imam Khomeini Hospital in Ahvaz and underwent direct examination by retinal professors according to a pre-determined protocol. After introducing the disease and complications to the patients, with the full consent of the patients, the information of the study was collected. Then, detailed optometric examinations, Macular Optical Coherence Tomography and Fundus Photography, Fluorescein angiography if necessary, perimeter and ERG were performed for all patients free of charge. 5 cc of blood samples were taken from all patients for genetic testing in subsequent studies and were frozen at Temperature 18 degrees below zero. During the two years that the study was conducted, the study team frequently visited data collection centers to monitor the diagnostic process and prevent patients from getting lost as much as possible.

Results and Discussion

From March 2018 to February 2021, 136 patients with a definite diagnosis of IRD were identified in Khuzestan province. Demographic characteristics are presented in **Table 1**.

Table 1. Demographic characteristics of inherited retinal disorders patients

Variable		Number	Percent
Gender	Female	62	**45.6**
	Male	74	**54.5**
Age	<5	1	**0.7**
	5-15	16	**11.8**
	>15	119	**87.5**
Marital status	Single	62	**45.6**
	Married	74	**54.4**
Education	Under Diploma	77	**56.6**
	Diploma	23	**16.9**
	University education	36	**26.5**
Age of onset of symptoms	<5	52	**38.2**
	5-15	49	**36.0**
	>15	35	**25.7**

Nystagmus was observed in 22 patients (16%). Also, color vision blindness was observed in 87 patients (64%), night blindness in 105 patients (77%), and visual field defects in 72 patients (52%).

One of the important results is the high rate of CM among the patients' parents **(Table 2)**.

Table 2. Marriage status of inherited retinal disorders patients' parents.

marriage Consanguineous		
Yes		No
113 (83%)		23 (17%)
Kinship ratio		
First degree	Second degree	
99 (72.8%)	14 (10%)	

The relationship between the CM of the patients' parents and their final diagnosis was investigated by the chi-square test. The rate of CM in the parents of RP patients was statistically significant (P-value = o.012) **(Table 3)**.

Table 3. The relationship between the consanguineous marriage (CM) of the patients' parents and different types of inherited retinal disorders

Final diagnosis	Parental CM		P-value
	Yes	No	
Macular dystrophy	9	1	**0.072**
Retinitis Pigmentosa	119	7	**0.012**

The vision of all patients was relatively low **(Table 4)**.

Table 4. Patient's vision

	UCVA				BCVA				Near VA			
	OD		OS		OD		OS		OD		OS	
No Light-Perception	21	15/4	23	16/9	21	15/4	23	16/9	21	15/4	23	**16/9**

Hand- motion	30	22/2	35	25/7	27	19/9	30	22/2	28	20/6	36	**26/5**
1-3 m	25	18/3	19	14/0	21	15/4	17	12/5	4	2/9	5	**3/7**
3-6 m	12	8/8	17	12/5	12	8/8	15	11/0	2	1/5	1	**0/7**
1/10-3/10	25	18/4	26	19/2	25	18/4	24	17/6	21	15/4	23	**16/9**
4/10-7/10	16	11/8	12	8/8	16	11/8	13	9/6	22	16/3	14	**10/3**
8/10-10/10	7	5/1	4	2/9	14	10/3	14	10/2	38	27/9	34	**25/0**

UCVA: uncorrected visual acuity, BCVA: best-corrected visual acuity, Near VA: Near visual acuity, OD: right eye, OS: left eye.

Myopia was common in patients of this study **(Table 5)**.

Table 5. Manifest refraction in both eyes

Manifest refraction		Number	Percent
Right eye	Emmetropia	46	**33/8**
	Hyperopia	21	**15/5**
	Myopia	64	**47/0**
	High Myopia	5	**3/7**
Left eye	Emmetropia	42	**30/9**
	Hyperopia	23	**16/9**
	Myopia	66	**48/5**
	High Myopia	5	**3/7**

Diseases of hereditary origin are usually incurable, and IRDs are also incurable as a group of inherited diseases [12]. IRDs eventually lead to incurable low vision and blindness; Not only the patient but also the patient's family suffers from the end of life and puts a great economic and social burden on society [13]. This study was performed on 136 patients with IRDs that were identified in Khuzestan province, to investigate the distribution of different types of these visual disorders of hereditary origin. 54% of patients were male, in most studies that examined the effect of sex on IRDs, such as usually study of Motta FL (2018) in Brazil Gender was equal in both groups [14]. 87.5% of patients were over 15 years old. In 38.2% of cases, the age of diagnosis was less than 5 years. The results showed that the most common IRDs in Khuzestan province was RP and in the Motta FL study, RP was the most common IRDs with a prevalence of 35%, causing irreversible visual impairment [14]. The results of the present study showed that 50.7% of IRDs patients have moderate or severe myopia. In Lee SH study in South Korea, 77.5% of RP patients had myopia [15] that is higher than our study, thus, it can be concluded that myopia in RP patients is common. IRDs patients' parents in 83.1% had CM. CM has been traditionally practiced in Iran as a consequence of socio-cultural factors [16]. It is estimated that nearly 40% of Iranian marriages are between related individuals, of which 21% are first cousins and 19% are second cousins [17]. Khuzestan province has a higher prevalence of CM due to its ethnic structure [18]. This overt relationship is especially evident in RP due to their higher prevalence. As this disease is among the most frequent ocular disorders in our country, CM should be considered within health care screening programs. In Kumaramanickavel G, a study in south India, CM was significantly associated with genetic ocular diseases in childhood [19]. Retinal degenerative diseases are still recognized as untreated diseases, but in recent years, gene therapy methods have been suggested in some studies that have provided hope for access to treatment for these diseases [20].

Our study limitations were the small sample size to evaluate different types of IRD except for RP and lake of genetic tests. The important strengths of the present study were being the first registration and clinical description of IRDs patients in Khuzestan province and data collection using in next steps including genetic tests to identify the causative gene and genetic mutation in these people, genetic counseling to patients and patients' families and calculating the risk of disease before marriage will be possible.

Conclusion

Concerning the high prevalence of CM in parents of IRDs patients in Khuzestan Province and the high prevalence of CM in Khuzestan Province, health policymakers should consider training and genetic counseling for families and perform the required pre-marital screening, especially if CM is ongoing. The registration of these diseases will pave the way for future fundamental research on these blind diseases.

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Conflict of interest: None

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Ethics statement: This study was approved by Ahvaz Jundishapur University of Medical Sciences Ethics Committee (approval number: IORC-9805) and conducted by the tenets of the Declaration of Helsinki. The study was explained to all patients and a written consent form was obtained from them.

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