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Epidemiological Study of The Mortality of Patients with Progeria during the Years 2013 To 2022 in Iran

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In Brief

Hutchinson-Gilford progeria syndrome (HGPS) is a genetic disorder that is autosomal dominant and characterized by clinical features and different phenotypes of physiological premature aging. This genetic disorder is caused by mutations affecting the LMNA gene (1).

The reported incidence rate is approximately 1 in 4 to 8 million people. Progeria's prevalence is largely considered a sporadic disease (2) due to its absence of sexual, regional, or ethnic bias (3). The average age of death for patients with HGPS is around 14.6 years (4, 5). At birth and early infancy, patients with this disorder typically appear normal. During the first year of life, there is a significant delay in growth. Common symptoms of this disease include delayed growth and delayed loss of baby teeth, abnormal skin pigmentation with aged-appearing skin, osteoporosis leading to increased risk of fractures, severe premature arteriosclerosis, hearing loss, failure to gain weight and growth at the expected rate for age, lack of sexual maturation, and craniofacial disproportion with a small, pinched jaw and narrow facial features. About the size of the head, the narrow way and the rigid structures of the larynx, high blood pressure, and the presence of stiff joints were also mentioned (1, 4, 6).

Due to the unavailability of a suitable diagnostic kit for Hutchinson-progeroid syndrome, the infant's medical history is the primary factor in scientific determination, along with its physical manifestations. At present, there is no known effective treatment for HGPS. The clinical management of HGPS has largely relied on treating symptoms and preventing secondary complications, which are mostly palliative in nature. For example, anticongestive therapy is used to treat congestive heart failure (7). Physiotherapy, body bracing, or even hip reconstructive surgery are also used to manage hip dislocation problems (8, 3). The main factor affecting the mortality of patients with HGPS is cardiovascular disease. Death from complications of severe atherosclerosis, heart disease (myocardial infarction or heart failure), or cerebrovascular disease (stroke) usually occurs between the ages of 6 and 20 (6).

The aim of epidemiological investigation of the mortality of patients with progeria in Iran was achieved through the conduct of very few studies regarding this disease for the first time.This descriptive-cross-sectional study was conducted with the aim of epidemiological investigation of the mortality of patients with progeria during the years 2013 to 2021 in Iran. The target population includes information on

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↑What is "already known" in this topic:
Progeria is a rare genetic disorder causing premature aging symptoms. Average age of death is 14.6 years, usually from cardiovascular issues. Incidence is around 1 in 4-8 million people. No curative treatment exists currently.

→What this article adds:
First epidemiological study of progeria mortality in Iran. Based on 74 deaths from 2013-2022. Calculated mortality rate of 0.46 per million. Significant link found between age and mortality risk. Provides baseline data to inform health system planning for this rare disease.

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74 patients with progeria in Iran during the study period, whose main cause of death was recorded as the disease. The system of registration and classification of causes of death in Iran was used to extract the data related to this research. The registered deceased was identified according to the international ICD-10 (International Classification of Diseases) coding system with the specific code E34.8, which is defined as other endocrine disorders. Age, gender, nationality, and place of residence (urban, rural, and unspecified) are all variables that were examined in this research. The results were analyzed using SPSS software version 26. Descriptive statistics methods were used to express the frequency distribution of death rate and Fisher's exact test was used to show the relationship between the frequency of progeria cases and qualitative variables. The specific mortality rate was calculated as well.

According to the 2015 census data (last census), the specific death rate per one million population was calculated at 0.46. The total number of progeria deaths during the years 2013 to 2022 was 74 cases. In the examination of the codes related to other causes of death of progeria sufferers in the secondary data based on the international coding system of ICD-10, according to the order of increased activity of the pineal gland (with code E34.8), cardiac arrest (with code I46) is one of the most causes of death in These patients are mentioned. Table 1 displays the demographic data of the deceased based on their year of death. In this study, age included three groups: less than five years, 5-60 years, and more than 60 years, where the highest percentage of deaths occurred in the age of less than five years and more than 60 years. The percentage of cases involving men is 47%, and the percentage of cases involving women is 53%. The distribution of the residence status variable in the study was almost identical, with 52% of the cases being urban and 48% being rural. Another point is that out of all the death cases investigated, 2 were non-Iranian and 72 were Iranian.

The data in Figure 1 shows that the trend of deaths in different months of the year is the same and no different trends are observed in any of the months of the year. A Fisher's test has shown a significant relationship between the occurrence of death due to progeria and age variables (P 0.048). The mortality rate due to progeria was not linked to other variables, such as place of residence or gender, according to the results of this study.

This study is the first epidemiology study conducted based on registered death data in the country, and for this reason, it can provide valuable information for the health system. The mortality rate for this research is 0.46 per million people. The significant difference observed between the year of death in different age groups is one of the results of the present study, in the age group under 5 years and people over 60 years of age, the most cases of death were observed. Among the age group under 5 years, the most cases were observed in people under one year. It is such

Table 1. Frequency distribution and relative frequency of the number of deaths during the years 2013 to 2020 according to the demographic data of the deceased

Variable levels	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	Total	*P*-value
Age												
<5	2(66.6)	2(25)	2(66.7)	1(14.3)	2(16.7)	5(55.6)	1(11.1)	3(23.11)	5(55.6)	0(0)	23	0.048
5-60	1(33.3)	1(12.5)	0(0)	3(42.9)	1(8.3)	1(11.3)	3(33.3)	7(53.8)	0(0)	0(0)	17	
>60	0(0)	5(62.5)	1(33.3)	3(42.9)	9(75)	2(33.3)	5(55.6)	3(23.1)	4(44.4)	1(100)	34	
Gender												
Female	1(33.3)	5(62.5)	2(66.7)	5(71.4)	6(50)	5(55.6)	4(44.4)	7(53.8)	4(44.4)	0(0)	39	0.964
male	2(66.7)	3(37.5)	1(33.3)	3(28.6)	6(50)	4(44.4)	5(55.6)	6(46.2)	5(55.6)	1(100)	35	
Residence												
urban	1(33.3)	6(75)	2(66.7)	2(28.6)	6(50)	5(55.6)	4(44.4)	8(61.5)	4(44.4)	1(100)	39	0.826
rural	2(667)	2(25)	1(33.3)	4(57.1)	6(50)	4(44.4)	5(55.6)	5(38.5)	5(55.6)	0(0)	34	
unknown	0(0)	0(0)	0(0)	1(14.3)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1	

Statistical test: Fisher Exact Test, $P<0.05$ was considered significant.

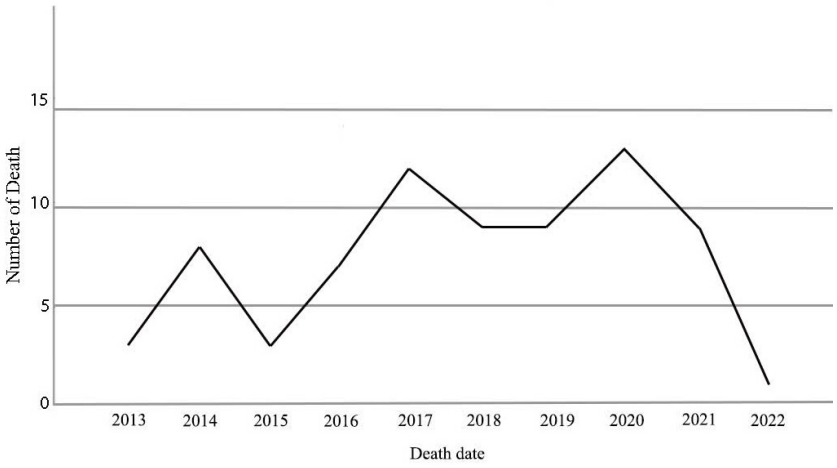

Figure 1. Temporal Pattern of Progeria Deaths in Iran, 2013-2022

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that 95% of people under 5 years old are under one year old, which may be due to their susceptibility and weaker immune system at this age. The results of this study show that other variables (place of residence, gender) are not related to the death rate due to progeria. The data in Figure 1 shows that the trend of deaths in different months of the year is the same and no different trends are observed in any of the months of the year. One of the strengths of this study is that the data of this study is based on the population. The data registration of the country's death system has been done according to the International Standard 10 ICD.

Limitations

A major limitation is the potential for incomplete case identification and coding inaccuracies for this very rare disease within Iran's mortality registration system. As progeria is extremely rare, some deaths may have been misclassified or missed entirely, leading to an underestimation of mortality, especially in areas with less clinical expertise in diagnosing this condition. The accuracy of properly coding progeria cases with the ICD-10 code E34.8 is a key caveat impacting the findings.

Authors' Contributions

Conceptualization: Ensieh Tavana, Masoumeh Andish, Samaneh Eslami, Monavar Afzalaghaee, and Ehsan Mosa Farkhani. Methodology: Samaneh Eslami, Amin Moradi, Iman Mosaei and Ehsan Mosa Farkhani. Writing the original draft: Ensieh Tavana, Masoumeh Andish, Samaneh Eslami, and Amin Moradi. Review & editing: Ensieh Tavana, Masoumeh Andish and Ehsan Mosa Farkhani.

Ethical Considerations

The study protocol was approved by the ethics research committee at Mashhad University of Medical Sciences (IR.MUMS.FHMPM.REC.1402.109).

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Conflict of Interests

The authors declare that they have no competing interests.

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