

Incidence of Phenylketonuria in Lorestan Province, West of Iran (2006- 2016)

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Abstract

Background: Phenylketonuria (PKU), is one of the most common metabolic diseases that resulted in mental retardation. The study aimed to investigate the incidence of phenylketonuria in Lorestan province, Iran.

Materials and Methods: The study was an observational-descriptive study which included all identified cases of patients from April 2006 to February 2016. The required data were collected from patients' records. The Entered variables in data survey checklist included gender, date of birth, County Residence, parental education, parental occupation, parental kinship, conducting genetic consultation and screening. Recorded data were analyzed in Stata-12 software after completion.

Results: Newborns were identified with Phenylketonuria during the years 2006 to 2016 and incidence rate calculated 1.91 per 10,000 live births. The highest incidence rate of disease was 3.86 per 10,000 live births in 2014. Delfan (Nurabad) County and Borujer County had maximum and minimum rate of incidence with 5.94 per 10,000 and 0.64 per 10,000, respectively. Among 74 patients, 42 (56%), were female and there was patients' parental kinship in 82% of parents that about 92 percent of suffering children parents had done genetic consultation.

Conclusion: The incidence of phenylketonuria in the Lorestan province is more than other provinces. Given that most cases of patients resulted from cousin marriages, paying attention to the screening tests prior to marriage, particularly in familiar marriage is essential.

Key Words: Incidence rate, Children, Iran, Phenylketonuria.

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1- INTRODUCTION

Genetic and congenital abnormalities are the most important cause of death and newborns' malformation in first month of life (1, 2). Approximately 7.6 million newborns are born with severe genetic and congenital abnormalities in the world every year. Most of metabolic disease symptoms appear early days, but sometimes the symptoms are slight and invisible (3, 4). Due to the contagion of the abnormalities in Iran, lack of diagnosing the disease and starting well-timed treatment in the first year of birth, cause to reduce children Intelligence Quotient (IQ). Also chronic cerebral lesions, mental retardation, muscle paralysis, liver problems and heart disease, are of other complications which impose heavy financial charge on families and government (1, 2).

Phenylketonuria (PKU), is among diseases which cause mental retardation in newborns. The disease is metabolism error that is inherited as autosomal recessive and is the most common genetic disorder in amino acids metabolism (5). The disease caused by hepatic enzyme deficiency, phenylalanine hydroxylase, effective enzyme in hydroxylation of phenylalanine to tyrosine (6). Due to the enzyme deficiency, phenylalanine accumulates in individual's fluids of body and causes precipitation in different areas such as brain tissue (7). The mechanism of the mental damage which is created by increasing phenylalanine is still unknown, but phenylalanine is considered as toxic factor to brain cells (8).

The child with this disease seems normal in early days of birth, but mental retardation progress gradually and reveal over several months (5). Phenylketonuria in child causes brain injuries and its IQ score will be decreases every 4 months and until the end of the first year, their IQ scores will decrease 50 points (7).

Phenylketonuria screening programs was started in 2006 in Iran (5). Phenylketonuria contagion is different among different races and geographical areas. Maximum rate of the disease has been reported among Irish and minimum rate in Japan. The disease is very rare in African Americans (9). Frequency of PKU in Caucasians is estimated 1 per 10,000 people and is changeable among other populations and races (10).

Incidence of the disease had been is 1: 11144, 1: 12037, 1: 12000 and 1: 20000, in China, Portugal, England and Brazil, respectively (11). The highest incidence of PKU has been reported from countries such as Iran and other neighboring countries. The incidence rate in Turkey is estimated 1 per 4,000 and in Iran 1 per 3,627 live births (12). PKU inheritance pattern of autosomal recessive is affected by relative marriage. Relative marriage is common in Iran, especially in some regions of country (5). The high level of familiar marriage in these areas could be the most important reason for the high prevalence of phenylketonuria in these areas (13).

In recent years, several studies have been conducted on patients with phenylketonuria (14, 15). According to the results of various studies, the incidence rate in Tehran was 1.1 per 10,000 (16), in Fars 1.6 per 10,000 (14), and in South Khorasan 0.98 per 10,000 (5). Lorestan is one of Western Province of Iran (**Figure.1**).

Lorestan is mountainous and is surrounded by Zagros Mountains except of several limited plains (2). Because the study of the incidence of the phenylketonuria in Lorestan had not ever conducted, this study is aimed to investigate the phenylketonuria during 2006-2016 in Lorestan province.

2- MATERIALS AND METHODS

2-1. Study design and population

The study is an observational-descriptive study. Statistical society includes all identified patients of 384,993 live births in Lorestan Province from April 2006 to February 2016.

2-2. Measuring tools

Required information was extracted from the records of patients and in case of the absence of the required information, data was obtained using phone call. The variables extracted from checklist including gender, year and month of birth, place of residence, parental education, parental occupation, parental familiar relationship, genetic counseling and genetic screening.

2-3. Ethical consideration

In order to moral considerations, the data included anonymous and obtained data were analyzed as a group.

2-4. Inclusion and exclusion criteria

Babies during 2006 to 2016 who were born alive and had positive High Performance Liquid chromatography (HPLC), included in the study. Babies with negative HPLC excluded from study.

2-5. Laboratory measurements

For screening phenylketonuria, 5 drops of blood were taken from newborn heel by the lancet in the closest health center. Blood samples collected on Whatman 903 (W-903) filter paper, using colorimetric method and using ELISA method was screened.

If the Phenylalanine levels were higher than 3.9 mg per deciliter, the sample was considered suspicious. Next, the suspicious samples referred to Tehran in order to control High Performance Liquid chromatography. Samples maintained at a temperature of 25-20 ° C and were placed in wells before the test. If HPLC was

positive, the patient considered as definite case of phenylketonuria in newborns (17).

2-7. Data Analyses

Recorded data were entered into Stata-12 software after completion and were analyzed statistically. Descriptive statistics were used to determine the demographic characteristics of the patients.

3- RESULTS

Lorestan includes eleven counties (Shahrestans): Aligudarz County, Azna County, Borujerd County, Delfan County, Dorud County, Doureh County, Khorramabad County, Kuhdasht County, Selseleh County, Poldokhtar County, and as of 2013 Rumeshgan County (**Figures. 1, 2**).

Demographic data analysis showed that 42 patients (56%), were female and 32 patients (44%), were male that 60 % of them were residents of urban areas. There was parental kinship in 82% of patients. There was parental kinship in 82% of patients.

In terms of educational level, most of the suffering children parents (35.8 %) had diploma, and the majority of their fathers (87.8 %), were self-employed and all of their mothers (100%), were housewives (**Table.1**).

The results showed that 82 % of parents of children had familiar relationship with each other (**Figure.3**).

The results showed that about 92 % of parents had done genetic counseling. About 70 % of them did not do screening and only 30 % of children were screened (**Figure.4**).

The highest incidence rate was 3.86 per 10,000 live births in 2014 (**Figure.5**).



Fig1: Consort diagram



Fig.2: The counties of Lorestan province

Table-1: Demographic data of patients with phenylketonuria in Lorestan Province (2006-2016)

Variables	Frequency (%)	Variables	Frequency (%)
Gender		Place Of Residence	
Female	42 (56%)	Urban	45 (61%)
Male	32 (44%)	Rural	29 (39%)
Father's Education		Mother's Education	
Illiterate	9 (12.16)	Illiterate	15(20.27)
Elementary	15 (20.27)	Elementary	24 (32.43)
Junior School	20 (27.04)	Junior School	8 (10.81)
High School	24 (32.43)	High School	24 (32.43)
Collegiate	6 (8.10)	Collegiate	3 (4.06)
Father's Occupation		Mother's Occupation	
Self-Employed	65 (87.83)	Housewife	74(100)
Governmental	9 (12.17)	Employee	(0) 0

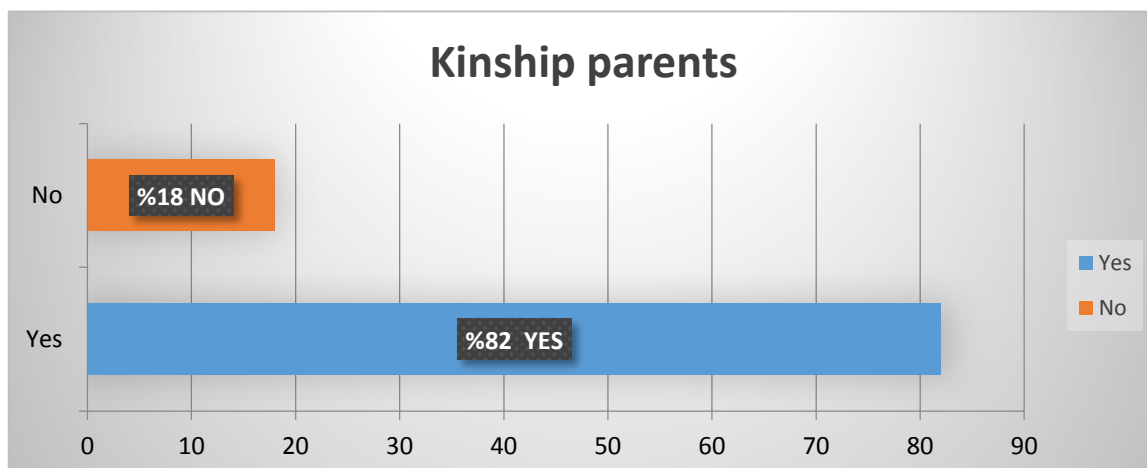


Fig.3: Screening percentage in patients with phenylketonuria

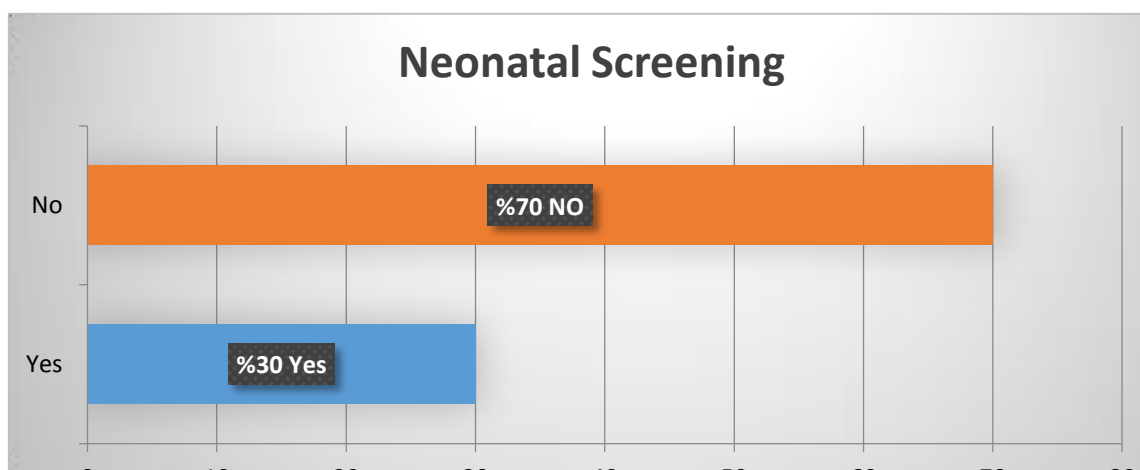


Fig.4: Parental kinship in children with phenylketonuria

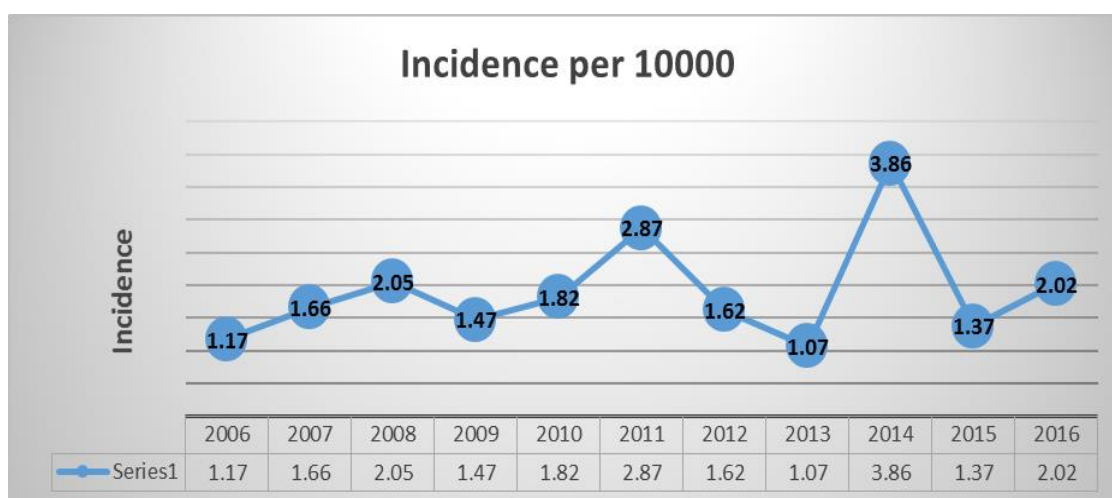


Fig.5: Incidence rate of phenylketonuria in Lorestan Province (2006-2016)

Delfan (Nurabad) County with 22 (29.72%) patients, and Aleshtar County with 2 (2.99%) patients, had maximum and

minimum number of individuals who were suffering by phenylketonuria, respectively (**Figure.6**).

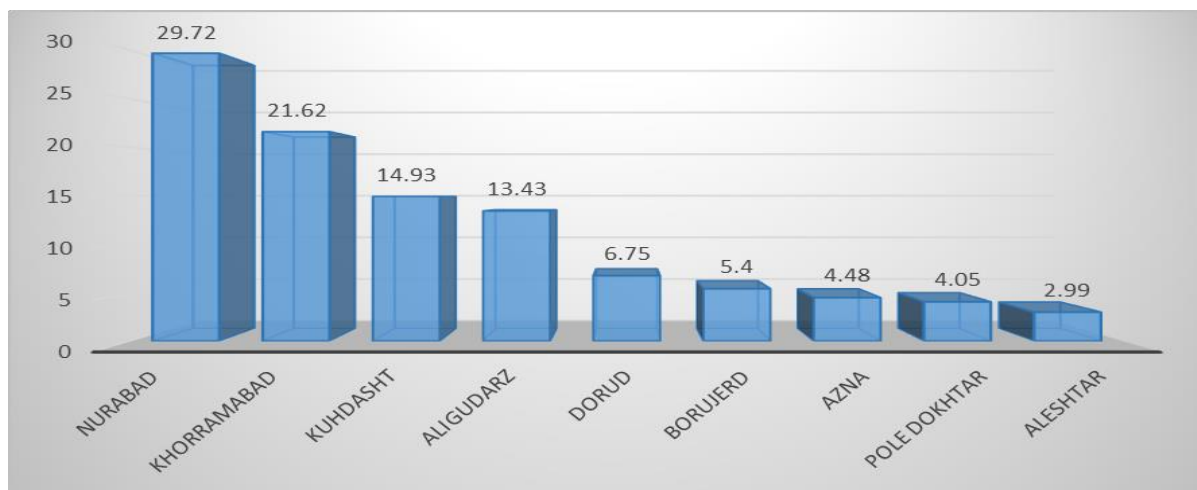


Fig.6: Frequency of phenylketonuria based on cities in Lorestan Province during 2006-2016

The maximum incidence rate was for Delfan (Nurabad) County with 5.94 per 10,000 live births, and minimum incidence

rate was for Borujerd County with 0.64 per 10,000, respectively (**Figure.7**).

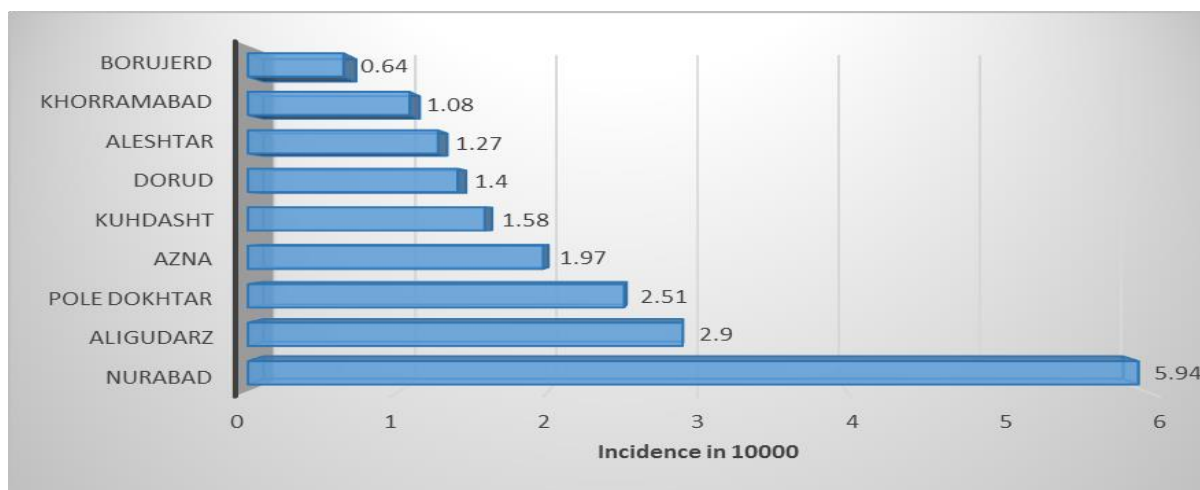


Fig.7: Incidence rate of phenylketonuria based on residence in Lorestan Province during 2006-2016

4- DISCUSSION

Given that total number of live births was 384,993 during April 2006 to February 2016, and 74 newborns were identified with phenylketonuria (incidence

1.91 per 10,000 live births), that the highest incidence rate of phenylketonuria was related the year 2014 with incidence rate of 3.86 per 10,000 live births. Delfan (Nurabad) County with incidence rate of 5.94 per 10,000 and Borujerd County with

0.64 per 10,000 had maximum and minimum incidence rate, respectively. Among 74 patients, 42 (56%), were female. There was parental kinship in 82% of patients' parents that about 92% of children parents had done genetic consultation, but 72% had not done screening. The prevalence of this disease is 1 per 10 thousand. While per every 10 thousand births in the world, one newborn has a metabolic disease such as phenylketonuria. According to experts in Iran, the prevalence of this disease is more than global level and its reason is familiar marriage. The incidence of this disease in Greece, Bulgaria, Poland, Germany, Spain and Italy had been reported 1 per 10000, 1 per 18000, 1 per 7000, 1 per 7400, 1 per 14000 and 1 per 11500, respectively (18).

Conducted overall incidence of the disease in Iran based on newborns screening program from 1997 has estimated 1 per 8,000 people and incidence range is changeable based on different areas of Iran from 1 person for 3,000 till 1 person for 60,000 (19). The results of our study showed that the incidence of disease has been 1.9 per 10,000 during the years which is higher than the calculated amount in study of Karamifar et al., in Fars with incidence rate of 1 per 10,000 (20), study of Saadati Nasab et al. in 2014 in South Khorasan, with incidence rate of 0.98 per 10,000 (5), the study of Habib et al., in Fars with incidence rate of 1.6 per 10,000 (15), and the study of Kabiri in Tehran with 1.15 per 10,000 (21).

Delfan (Nurabad) County has the highest incidence rate of 5.94 per 10,000 that emphasizes on necessity of more screening and genetic consultation in this town till reducing incidence growth. So, according to the results of our study, it can be said that the incidence of phenylketonuria in Lorestan province is higher than the average level of country. The results of our study showed that 82% of newborns parents had parental kinship. In study of

Shiva et al., 77.5% of patients have had parental kinship (22). Perhaps high tendency to cousin marriages can be considered as one of the reasons that the incidence rate of PKU in this province is almost twice of other studies in other provinces. All disorders leading to PKU are recessive autosomal. The hereditary pattern is affected by relative marriages and increases the chances of incidence up to 2 times. Considering that relative marriages are common particularly in some areas of Iran, so the disease incidence is affected by the process (5).

The results of our study showed that among 74 patients, 42 persons (56%), were female; while in study of Badiiee et al. (19), and Karamifar et al. (20), frequency of PKU in males were more than females, that is not matched to result of our study.

The results of our study showed that there was disease background in other members of family 6.35% of patients. Family background was reported 12% in the study of badiiee et al. (19), 10% in the study of Karamifar et al. (20), and 12% in conducted study in Mexico, and 9.5% in the study of Mirbolook et al. (23). Therefore frequency of PUK in a family necessitates more awareness to families.

The results of our study showed that near 70% of the patients had not done screening, so there is necessity of paying attention to the screening program, along with genetic consultation for patients and individuals who have patient in their family till to prevent the occurrence of the disease in families.

4-1. Limitations of the study

Possible for diagnosis and treatment a number of patients are referred to neighboring provinces and notify them altogether.

5- CONCLUSION

The high incidence of Phenylketonuria disease in Delfan (Nurabad) County

requires to paying attention to genetic screening and counseling programs before marriage. Phenylketonuria disease can cause death, mental retardation, and irreparable complications in newborns and hence the delay in starting the treatment causes irreversible brain injuries, it emphasize the importance of paying attention to the "disease". Also, results showed that the incidence of phenylketonuria in the Lorestan province is more than other provinces.

6- CONFLICT OF INTEREST: None.

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