Phenylketonuria

Among

Palestinian Children

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ABSTRACT

Phenylketonuria Among Palestinian Children

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PKU is an inborn error in the metabolism of phenylalanine to tyrosine due to the absence or markedly reduced activity of phenylalanine hydroxylase in the liver.

The discovery and elucidation of PKU is a medical advance because it changes the lives of patients from one of disability to one of ability.

This study was conducted to estimate the prevalence of PKU in the West Bank, and to identify certain factors such as late detection and treatment of PKU children and their effect on the physical and mental health of PKU children.

The study questionnaires were based on certain data related to demographic characteristics of PKU children, the health services provided for them, and the complications associated with PKU. These being growth retardation, mental retardation, seizures, itching skin, discoloration of hair, eyes and skin color, and psychological problems (over activity, depression, headache).

The sample of "52" PKU subjects (N=52) (Total population) was selected from five districts in the W.B

Data was collected using the questionnaire form. Physical measurement tools for measuring head circumference, weight and height according to the growth percentile. One or more of the

following tests were performed (Wechsler scale, Binnet scale Violent scale), to measure mental development and intelligent quotation according to each individual's age and level of response.

The incidence of PKU on the West Bank in Palestine for the year 1997 was 2.35 per 10,000 live births as notified to the Preventive Medicine Department. The prevalence in the period that the data was collected (November, 1997 - February, 1998) was 3 per 100,000. The prevalence and incidence of PKU may be much higher than those that were notified in our community, as some cases were missed and not notified to the PMD due to low coverage of the screening program for PKU. The coverage rate was 70% in 1997, but in previous years it was very low - below 50%.

Importance of routine newborn screening can be clearly seen in early detection of positive cases, and prevention of physical and mental retardation, if positive cases were given a low phenylalanine diet early after birth. Out of 41 subjects whose IQ were tested, 17 subjects were mentally retarded. From those who were mentally retarded, only one subject was under five years of age.

There was a significant relationship between early detection of the positive PKU cases and prevention of mental retardation using Chi square (P value = .0048). From those who were detected before one month of age, none were mentally retarded. Also those who started taking the low Phenylalanine diet early after birth, before one month of age, did not develop mental retardation (P value = .008). The subjects who were not treated or treated with the special diet after one month of age (50%) of them developed mental retardation.

Other complications such as psychological problems, dilution of the skin, hair and eye color, itching skin and seizures happened more frequently in subjects who were treated late or deprived of treatment. The highest frequency of these complications was psychological problems, approximately 66% of cases suffer from psychological problems.

Growth retardation was investigated in 35% of subjects of whom 56% were not treated with special low Phenylalanine diet, the other 44% of subjects were treated with low Phenylalanine diet but

suffer from growth retardation since time of birth. Sometimes over restriction of the diet and poor dietary management can lead to growth retardation.

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CHAPTER I

INTRODUCTION

The subject of Phenylketonuria (PKU) is relatively recent for the Palestinian population.

PKU, a form of hyperphenylalaninemia (HPA), was seen as an "epitome of human biochemical genetics " in the early 1980s. While PKU implies HPA, not all HPA is PKU (primary deficiency of Phenylalanine Hydroxylase (PAH) activity). Genetic locus heterogeneity is the explanation (Scriver & Clow, 1980). (See Appendix 1).

PKU is an inborn error of metabolism characterized by an increased concentration of phenylalanine and its by-products (notably phenylpyruvate, phenylacetate, phenylactate, and phenylacetylglutamine) in urine, and severe mental retardation. This high serum phenylalanine level is due to the absence, or markedly reduced activity, of phenylalanine hydroxylase in the liver. Two conditions are necessary to cause clinical manifestations in PKU: mutation and exposure to L-phenylalanine. Early recognition of signs and treating symptoms can prevent the onset of complications.

Two variants PKU have been noted which are clinically indistinguishable in the untreated state: classical and atypical PKU. The hydroxylation of phenylalanine to tyrosine requires two enzymes: phenylalanine hydroxylase and dihydropteridine reductase. Two co-factors, tetrahydrobiopterin (BH4) and reduced pyridine nucleotide (NADH+H+) are required. (see Appendix 1).

Before the introduction of the newborn screening program, most PKU cases among Palestinian children were not discovered early, which resulted in mental retardation or microcephaly, congenital heart disease, intrauterine growth retardation, and other defects that

Table 1 Percentages of Newborns Screened for PKU in the West Bank from the Year 1989 - 1997.

Year	Coverage
1989	25.00%
1990	25.05%
1991	27.00%
1992	31.00%
1993	35.00%
1994	50.00%
1995	60.00%
1996	No screening
1997	70.00%

Statement of the problem

PKU children in the WB suffer from different problems and complications which require further study for appropriate action to be taken. Moreover, nobody can identify the prevalence of this disease in our community due to lack of studies related to PKU in the WB, and low coverage of the routine newborn screening program.

Moreover, PKU cases have been adversely affected due to termination of treatment and blood testing for phenylalanine for at least two years because of the changes in direction of the health authority from Israel to Palestine. This may lead to development of unpleasant complications among PKU patients or latent discovery of new cases.

Justification and Significance

This study was designed to investigate the size of the problem of PKU in the West Bank, that resulted from a variety of mutations in the gene for the hepatic enzyme phenylalanine hydroxylase, which may affect the offspring and lead to harmful effects of high maternal HPA.

Screening phenotypically normal siblings and other close relatives of PKU patients can help detect persons who have HPA. This is important in order to offer them premarital genetic counseling or further prenatal diagnosis to control the spread of the disease in society. In addition to this, complications of HPA in the fetus of affected mothers can be minimized or modified by a Phenylalanine-restricted diet that controls the phenylalanine level, especially if diet is started early, before conception, or during the first trimester of pregnancy. It is also common to find that PKU disseminates in societies were there is poor awareness of the health problems, deficiency of primary health care, or where consanguineous mating is prevalent, as among Palestinians - especially those living in rural areas.

Purpose of the Study

Long term goal

The aim of this research is to identify the needs and problems of PKU children living in the WB, and to stimulate awareness amongst health managers and community personnel to support PKU families for future care.

Specific Objectives

1. To ascertain the prevalence of PKU, through newborn screening in the West Bank.
2. To increase awareness amongst health managers and personnel about the importance of initiating a health education program for PKU families, for genetic counseling, diet restriction, as well as social and psychological understanding of the disease.
3. To sensitize the Palestinian Public about the disease and its socio-economic implications.

Research Questions

This study concentrated on the following questions:

1. Is PKU considered a problem in the Palestinian population which needs prompt action for helping those suffering from PKU?
2. What is the Prevalence rate of PKU in the WB?
3. What are the factors that lead to the development of complications in PKU among affected Palestinian children?
4. What kind of health services are available for PKU children in the WB?

Out come of the Study

The study concentrated on these items:

1. Finding out the prevalence of PKU cases among the Palestinian population through studying PKU cases on the West Bank, Palestine.
2. Questionnaires related to enhancement of quality of life for PKU cases were answered and analyzed.