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CLINICAL RESEARCH / KLİNİK ARAŞTIRMA

Newborn Metabolic and Endocrine Disease Screening Program: Example of Giresun Province Between 2015 and 2020

Yenidoğan Metabolik ve Endokrin Hastalık Tarama Programı: 2015-2020 Yılları Arası Giresun İli Örneği

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Abstract

Objective: In this study, we aimed to evaluate the cases diagnosed within the scope of the newborn metabolic and endocrine disease screening program carried out by the provincial health directorates between 2015 and 2020 in Giresun province.

Methods: In our study, the results obtained from the newborn metabolic and endocrine disease screening program between 2015 and 2020 were evaluated. Diagnoses/records between September 20th, 2021 and October 10th, 2021 were reviewed retrospectively. A total of 114 cases were identified in the 6-year period diagnosed with phenylketonuria, congenital hypothyroidism, cystic fibrosis, and biotidine deficiency.

Results: 43.9% (n=50) of the diagnosed newborns were girls and 56.1% (n=64) were boys. There was no significant difference in terms of gender distribution among those diagnosed (p>0.05). In 2015, 4 newborns were diagnosed with hyperphenylalanemia, and no newborn was diagnosed with phenylketonuria. Eleven newborns were diagnosed with congenital hypothyroidism. In 2016, 7 newborns were diagnosed with hyperphenylalanemia, one neonatal phenylketonuria, one neonatal cystic fibrosis, one neonatal biotidinase deficiency. In 2020, 4 newborns were diagnosed with hyperphenylalanemia, and no newborn was diagnosed with phenylketonuria. Four newborns were diagnosed with congenital hypothyroidism, and one newborn were diagnosed with biotidine deficiency.

Conclusion: Among the cases diagnosed within the scope of newborn metabolic and endocrine disease screening program, frequency of congenital hypothyroidism was found to be high in 2015, 2017, and 2019. It is recommended that the families of the diagnosed newborns be contacted and the current development and health status of the children be evaluated.

Keywords: Newborn, metabolic and endocrine screening, phenylketonuria, congenital hypothyroidism

Öz

Amaç: Bu çalışmada Giresun ilinde 2015-2020 yılları arasında İl Sağlık Müdürlüğü tarafından yürütülen yenidoğan metabolik ve endokrin hastalık tarama programı kapsamında tanı konulan olguların değerlendirilmesi amaçlanmıştır.

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Öz

Yöntem: Çalışmamızda 2015-2020 yılları arasında yenidoğan metabolik ve endokrin hastalık tarama programında elde edilen sonuçlar değerlendirilmiştir. 20.09.2021-10.10.2021 tarihleri arasındaki tanılar/kayıtlar retrospektif olarak incelenmiştir. Fenilketonüri, konjenital hipotiroidi, kistik fibrozis ve biyotidinaz eksikliğine ilişkin tanı alan, 6 yıllık süreçte, toplam 114 olgu tespit edilmiştir.

Bulgular: Tanı alan yenidoğanların %43,9'u (n=50) kız, % 56,1'i (n=64) erkektir. Tanı alanlar arasında cinsiyet dağılımı açısında anlamlı farklılık belirlenmemiştir (p>0,05). 2015 yılında 4 yenidoğan hiperfenilalaninemi tanısı almış olup, fenilketonüri tanısı alan yenidoğan yoktur. Onbir yenidoğan konjenital hipotiroidi tanısı almıştır. 2016 yılında 7 yenidoğan hiperfenilalaninemi tanısı, 1 yenidoğan fenilketonüri, 1 yenidoğan kistik fibrozis, 1 yenidoğan biyotidinaz eksikliği tanısı almıştır. 2020 yılında 4 yenidoğan hiperfenilalaninemi tanısı almıştır, fenilketonüri tanısı alan yenidoğan bulunmamaktadır. Dört yenidoğan konjenital hipotiroidi tanısı, 1 yenidoğan biyotidinaz eksikliği tanısı almıştır.

Sonuç: Yenidoğan metabolik ve endokrin hastalık tarama programı kapsamında tanı konulan olgulardan konjenital hipotiroidinin 2015, 2017 ve 2019 yıllarında yüksek olduğu belirlenmiştir. Tanı konulan olguların aileleri ile iletişim kurulup çocukların mevcut gelişim ve sağlık durumlarının değerlendirilmesi önerilmektedir.

Anahtar Kelimeler: Yenidoğan, metabolik ve endokrin tarama, fenilketonüri, konjenital hipotiroidi

Introduction

There are many diseases and disorders that can lead to significant morbidity or mortality in newborns if left untreated. Usually, early intervention is most effective or is only effective when started early in infancy. Successful treatment can have enormous benefits for the child, family, and society. The purpose of newborn screening (NBS) is to detect, as early as possible, a range of conditions that, if left undetected, will adversely affect the child's quality of life. NBS programs are secondary prevention interventions that are widely recognized in the world in the field of public health[1,2]. Early diagnosis and intervention during the neonatal period and infancy can prevent disability and death and enable children to reach their full potential. Certain metabolic, genetic and hormonal disorders are screened by scanning using a few drops of blood from the heels of newborns[3]. With the neonatal screening program to test treatable diseases in newborns in the United States, success has been achieved in the field of public health by reducing neonatal and childhood morbidity and mortality[4].

Within the scope of the NBS program, by screening newborns for phenylketonuria, congenital hypothyroidism, biotinidase deficiency, and cystic fibrosis (CF), the prevention of mental retardation, brain damage and irreversible harms, prevention of economic burden to society, and raising public awareness about reducing consanguineous marriages are aimed[3-5].

Phenylketonuria is the most common disorder caused by an inborn error in amino acid metabolism. It is caused by mutations in the phenylalanine *hydroxylase* gene. Phenotypes can range from a very mild increase in blood phenylalanine concentrations to a severe classical phenotype with marked hyperphenylalaninemia; this results in profound and irreversible intellectual disability if left untreated. Starting a phenylalanine-restricted diet immediately after birth prevents neuropsychological complications[6,7]. Congenital hypothyroidism is a clinical condition characterized by thyroid hormone insufficiency, which is mostly caused by a problem related to the lack of thyroid gland development or a thyroid hormone biosynthesis disorder[3,8]. Thyroid hormone is needed for normal brain development. Children born with congenital hypothyroidism face brain damage and mental retardation. Since the 1980's, it has been detected in newborns in the early period with NBS programs. Easy, inexpensive and effective treatment can be provided in children who are detected early. The incidence is approximately 1/4000. It has been determined that it is seen approximately two times more frequently among women than among men[3,9,10]. CF is an incurable chronic disease that causes serious damage to the respiratory and digestive tracts. It is reported that more than 100,000 people worldwide suffer from this disease[11]. In many countries, CF is involved in neonatal screening (NBS) programs. In infants with a positive screening test, the diagnosis of CF should be confirmed with a sweat test showing a sweat chloride concentration above 60 mmol/L[12]. Symptoms such as frequently recurring lung infections, growth development retardation in infancy, foul smelling oily stool, obstructive jaundice, anemia, edema, purulent sputum production, and clubbing in the fingers are observed. With treatment, the quality of life increases and the survival time is prolonged[3]. Biotinidase deficiency is an autosomal recessive inherited disease and can be detected in the early period with NBS programs. Growth development retardation, hypotonia, alopecia, skin rash, and neurological

symptoms can be seen. If left untreated, seizures, spastic paresis, and hearing loss may occur in young children[13-15].

In this study, we aimed to investigate the incidence of phenylketonuria, CF, congenital hypothyroidism, and biotidinase deficiency diseases obtained by a NBS test in Giresun province.

Materials and Methods

The research was carried out in Giresun province in the Black Sea Region of Turkey. The principles of the Helsinki Declaration were followed in the study, and the necessary permissions were obtained from the Ethics Committee of Giresun Provincial Health Directorate (no: E-41544352-799, date: 21.09.2021). The records of the Provincial Health Directorate were analyzed retrospectively. The cases are detected by the evaluation of heel blood samples taken from newborns in all health units throughout the province within the scope of the national NBS program in national laboratories. The results are transmitted to the provinces via the web application of the NBS program, and babies with suspicious results are referred to the relevant clinics[3]. In our study, the results obtained in the newborn metabolic and endocrine disease screening program between 2015 and 2020 were evaluated. Diagnoses/records between September 20th, 2021 and October 10th, 2021 were reviewed retrospectively, and 114 diagnosed cases were identified.

Statistical Analysis

The data were evaluated using the IBM SPSS 21 statistical analysis package program for Windows. Counts, percentage distributions, and chi-square tests were applied during data analysis.

Results

In Giresun, 114 of the babies screened between 2015 and 2020 within the scope of the Newborn Metabolic and Endocrine Disease Screening program were diagnosed with phenylketonuria, congenital hypothyroidism, CF, and biotinidase deficiency diseases or their subgroups.

43.9% (n=50) of the diagnosed newborns were girls and 56.1% (n=64) were boys. There was no significant difference in terms of gender distribution among those diagnosed newborns (p>0.05). The mean age at which the mothers gave birth was 28.5±5.6. 40.7% (48) of the families live in the city center, 54.2% (66) live in the district and village. The average birth weight of babies is 3,135±606 606 grams. 11.9% (14) of the babies were born under 1,500 g, and 6 babies (5.1%) were born with 4,000 g or above birth weight.

In 2015, there were a total of 4,588 births. Four newborns were diagnosed with hyperphenylalanemia, and no newborn was diagnosed with phenylketonuria. Eleven newborns were diagnosed with congenital hypothyroidism. There was no significant difference in the incidence of congenital hypothyroidism between girls and boys (p>0.05). In 2015, no cases of CF or biotidine deficiency were detected in Giresun province.

There were 4,425 births in 2016. Seven newborns were diagnosed with hyperphenylalanemia, one neonatal phenylketonuria, one neonatal CF, and one neonatal biotidinase deficiency. There were 4,428 births in 2017. Seven newborns were diagnosed with hyperphenylalanemia, 11 newborns were diagnosed with congenital hypothyroidism, and one newborn with CF. No newborn was diagnosed with congenital phenylketonuria and biotidine deficiency in 2017.

In 2018, there were 4,403 births. Seven newborns were diagnosed with hyperphenylalanemia and one newborn were diagnosed with biotidinase deficiency. Fourteen of the newborns were diagnosed with partial biotidinase deficiency. No newborn was diagnosed with congenital hypothyroidism or phenylketonuria in 2018.

In 2019, 4,237 deliveries were made and 5 newborns were diagnosed with hyperphenylalanemia. There is no newborn diagnosed with phenylketonuria. Eight newborns were diagnosed with congenital hypothyroidism and one newborn with biotidinase deficiency. Six of the newborns were diagnosed with partial biotidine deficiency.

There were 4,002 births in 2020. Four newborns were diagnosed with hyperphenylalanemia, and no newborn was diagnosed with phenylketonuria. Four newborns were diagnosed with congenital hypothyroidism, one newborn was diagnosed with biotidinase deficiency, and 19 newborns were diagnosed with partial biotidinase deficiency (Table 1).

Discussion

Neonatal metabolic and endocrine disease screening is an application that determines individuals at risk within the framework of social screening principles that ensure early diagnosis and timely treatment of treatable diseases[16].

In our study, 4 of the babies screened in 2015 were diagnosed with neonatal hyperphenylalanemia, and no baby was diagnosed with phenylketonuria. In 2016, 1 newborn

were diagnosed with phenylketonuria. The frequency of phenylketonuria was determined as 1/4425. The frequency of phenylketonuria in 2016 was similar to the Turkey average. Seven newborns in 2017, 7 newborns in 2018, 5 newborns in 2019, 4 newborns in 2020 were diagnosed with hyperphenylalanemia, and there were no newborns diagnosed with phenylketonuria. In the study of Dervişoğlu et al.[17], in which they evaluated babies screened within the scope of newborn metabolic and endocrine disease screening program in stanbul in 2018, the incidence of infants with phenylketonuriawas was determined as 1/6153. In the study by Karamifar et al.[18] in Fars (South Iran), the frequency of phenylketonuria was determined as 1/10000. It can be seen that the frequency of cases in these studies is lower than in our study. In addition, it is seen that the number of newborns diagnosed with hyperphenylalanemia by years is high in our study. The fact that mental retardation, brain damage, and neurological damage seen in phenylketonuria cases can be prevented with treatment starting in the early stages of life shows the importance of NBS programs[19-21].

Table 1. Newborn metabolic and endocrine disease screening results between 2015 and 2020

Years	Diagnosis	Cases	Frequency
2015	Phenylketonuria	0	-
	Congenital hypothyroidism	11	11:4588
	Cystic fibrosis	0	-
	Biotidinase deficiency	0	-
2016	Phenylketonuria	1	1:4425
	Congenital hypothyroidism	0	-
	Cystic fibrosis	1	1:4425
	Biotidinase deficiency	1	1:4425
2017	Phenylketonuria	0	-
	Congenital hypothyroidism	11	11:4428
	Cystic fibrosis	1	1:4428
	Biotidinase deficiency	0	-
2018	Phenylketonuria	0	-
	Congenital hypothyroidism	0	-
	Cystic fibrosis	0	-
	Biotidinase deficiency	1	1:4403
2019	Phenylketonuria	0	-
	Congenital hypothyroidism	8	8:4237
	Cystic fibrosis	0	-
	Biotidinase deficiency	1	1:4237
2020	Phenylketonuria	0	-
	Congenital hypothyroidism	4	4:4002
	Cystic fibrosis	0	-
	Biotidinase deficiency	1	1:4002

In our study, the frequency of congenital hypothyroidism was determined as 0.002 (11/4588) in 2015, 0.002 (11/4428) in 2017, 0.002 (8/4237) in 2019, and 0.001 (4/4002) in 2020. It is observed that the frequency tends to decrease over the years. The increase in the frequency of prenatal pregnancy follow-up in our country recently and the encouragement of the use of iodine supplementation during pregnancy may be among the reasons for the decrease in congenital hypothyroidism. In the study of Simsek et al.[22] in the Western Black Sea Region of Turkey, the incidence was determined as 1/2326 between the years 2000 and 2002.

In our study, one (1/4425) CF case in 2016 and one (1/4428) CF case in 2017 were determined. Studies on the frequency of CFin our country are limited. It is expressed as 1/3000 in the literature[23]. The prevalence of CF was found to be 1/6029 in a study conducted by Dankert-Roelse et al.[24] in the Netherlands. In another related study by Soltysova et al.[25] in newborns in Slovakia, the incidence of CF was determined as 1/6000-7000. It can be observed that the frequency of CF in these studies is lower than the results in our study. The reasons for these differences may include genetic factors, consanguineous marriages, and other related cultural and sociodemographic characteristics.

In our study, it was determined that there was one (1/4425) case of biotidine deficiency in 2016, one (1/4403) in 2018, one (1/4237) in 2019, and one (1/4002) in 2020 in Giresun province. In our country, Aytaç et al.[26] evaluated the results of the newborn metabolic and endocrine disease screening program in Adana province in 2010 and 2011, and it was determined that biotidine deficiency was seen in one in 8120 births in 2010 and one in 14,261 births in 2011. Compared to our current study, it is seen that the frequency is lower in this study. Studies on the frequency of cases are limited in the literature. Biotidinase deficiency is an autosomal recessive inherited disease. By disrupting the biotin cycle, signs and symptoms such as metabolic acidosis, hearing and vision disorders, alopecia, and neurological symptoms are observed[27].

Study Limitations

One of the limitations of the study is the inability to access information about the process applied after diagnosis for the diagnosed cases revealed in the analyzed data. It will be useful to equip the newborn endocrine and metabolic

disease screening system with the necessary steps to be followed after diagnosis.

Conclusion

Neonatal metabolic and endocrine screening programs are widely known secondary prevention interventions for public health worldwide. Thus, it is aimed to provide early diagnosis and treatment to prevent complications, permanent sequelae, and premature death and to increase the quality of life. In our study, it was determined that phenylketonuria, congenital hypothyroidism, CF, and biotidine deficiency cases were detected with the screening program, and the cases were referred to the relevant units. Studies on the epidemiology of metabolic and endocrine diseases in our country are limited. In this context, obtaining comprehensive sociodemographic data on the family and pregnancy history of the cases and conducting follow-up studies on the participation of patients in treatment and medical practices after diagnosis will be helpful.

Ethics

Ethics Committee Approval: The principles of the Helsinki Declaration were followed in the study, and the necessary permissions were obtained from the Ethics Committee of Giresun Provincial Health Directorate (no: E-41544352-799, date: 21.09.2021).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: E.E.K., M.B., Ü.Ö., S.T., Design: E.E.K., M.B., Ü.Ö., S.T., Data Collection or Processing: E.E.K., M.B., Ü.Ö., S.T., Analysis or Interpretation: E.E.K., M.B., S.T., Literature Search: E.E.K., M.B., S.T., Writing: E.E.K., M.B., S.T.

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