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Research Article

Families of Children Followed with the Diagnosis and Pre-diagnosis of Neurometabolic Disease Comparison of Depression and Anxiety Levels

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Received: September 03, 2020; **Published:** October 09, 2020

Abstract

The diagnosis of neurometabolic diseases, one of the chronic diseases of childhood, is often difficult. Sometimes, there are difficulties in reaching the tests required for diagnosis, which causes some patients to be delayed in diagnosis. Various psychological disorders may develop in the parents of children with this disease, which may have significant morbidity and mortality in the patient until the specific diagnosis is reached and even after the diagnosis. In our study, in the parents of children who were followed up with the diagnosis and pre-diagnosis of neurometabolic disease; Considering the sociodemographic features; It was aimed to compare depression and anxiety levels.

Dr. Behcet Uz Pediatrics and Surgery Training and Research Hospital pediatric neurology and pediatric metabolism units (60 patients) who were diagnosed with neurometabolic disease and followed up with a pre-diagnosis (60 controls) were taken to cross-sectional research. In the first part, the questionnaire consisting of questions including sociodemographic features, depression and anxiety levels were applied in the second part.

It was determined that the pre-diagnosed group lived in a higher rate of good home environment, while the diagnosed group lived in a higher rate of medium and poor home environment. While the low and high socioeconomic status was higher in the diagnosed group, most of the pre-diagnosed group had a medium socioeconomic status. Depression analysis of the pre-diagnosed mothers and fathers was higher. It was observed that there was mild depression in the diagnosed group, and moderate depression in the pre-diagnosed group. In diagnosed cases, state and trait anxiety were found at a higher rate than the pre-diagnosed group.

We think that the families of the patients who are followed up with a diagnosis or pre-diagnosis of neurometabolic disease should be followed up with a multidisciplinary approach and continued monitoring with psychiatric support.

Keywords: *Neurometabolic Disease; Disabled Child; Depression; Anxiety Level; Family*

Introduction

An important part of childhood neurometabolic diseases (NMH), as a result of defects in various intracellular biochemical pathways; deficiency in energy production is characterized by damage to brain tissue due to the accumulation of complex molecules and toxic metabolites in primary and/or secondary pathways [1]. In other words, they are pathological tables that develop as a result of the abnormal progression of processes related to the synthesis, catabolism or transport of protein, carbohydrate and fatty acids. Neurometabolic diseases are very rare when considered individually, but when considered together, their incidence is quite frequent. It is inevitable that these diseases, most of which are inherited as autosomal recessive, are seen more frequently in our country where the marriage of relatives is high. Diagnosis of neurometabolic diseases is often difficult. Considering the large number of metabolic pathways and their interrelations, extensive information is needed for the diagnosis of NMD. While the diagnosis can be established even with the first step tests, more advanced tests are often needed. This situation leads to prolonged diagnosis process.

As a general definition, chronic disease is defined as "the situation that shows deviation or distortion from the normal, can leave permanent insufficiency, irreversible, result from pathological changes, requires special training for the rehabilitation of the patient, and requires long-term care, surveillance and supervision" [2]. Childhood diseases are also defined as chronic health problems if they affect the normal activities of the child for the last year or more, require a lot of time in the hospital and at home, and have high medical expenses [3]. Childhood chronic diseases have important effects on the life of the patient and the whole family [4]. On average, 10 - 20% of children in the general population have chronic diseases [5].

Chronic diseases affecting approximately 10% of children are an important source of stress for both the child and their family [6]. It is observed that some psychological disorders develop after a while in the parents of children who have progressive diseases such as NMD and who may have significant morbidity and mortality in the patient.

In this study, parents of children with diagnosis of neurometabolic disease and followed up with a pre-diagnosis of neurometabolic disease; taking into account the variables related to the disease and sociodemographic characteristics; depression and anxiety symptom levels were compared.

Materials and Methods

Patient selection

University of Health Sciences Dr. Behçet Uz Children's Diseases and Surgery Training and Research Hospital, the families of children who were followed up with the diagnosis of neurometabolic disease in the pediatric neurology and pediatric metabolism departments included the study group. The informed consent form was obtained from the families who agreed to participate in the study. The families of the patients who were followed up with a pre-diagnosis of neurometabolic disease (not diagnosed yet) were defined as the control group. The study protocol was approved by the Institutional Ethics Committee XXXXXX with the decision of Ethical Committee dated 16.02.2006 and numbered 1693. The universe where the study conducted has been included in the research as the study criteria were evaluated. A total of 120 people, 60 patients and 60 controls, were interviewed for the survey study. A case-control and cross-sectional study was conducted.

The patients who were diagnosed/prediagnosed with NMD, who were followed-up and treated for at least one year in our child pediatric neurology and metabolism outpatient clinics between December 2016 and May 2017, constituted the research group. Considering

the follow-up periods of the cases followed up at the stage of diagnosis and prediagnosis, the study was completed by reaching 87% of all cases.

Test materials

The first part of the questionnaire consists of 12 questions with sociodemographic characteristics prepared by the researchers, and the second part consists of Beck Depression scale and STAI Form TX I and II.

The data obtained with the information gathering form were evaluated in computer environment and frequency tables were made, and the extent to which the independent variables affect the dependent variables were analyzed by Epi Info Version 3.3.2 package program analysis methods.

Beck depression inventory

In this study, 21-item Beck Depression Inventory (BDI) form was used to measure the presence of depression in patient families. The adaptation, validity and reliability study of Beck Depression Scale to Turkish for primary care Akturk., *et al* [7]. It was made in 2005 by Each title contains a four-digit rating from 0 to 3; BDI score is obtained by adding the highest scores in each title [8].

Situation and continuous anxiety scale

It was developed in 1970 by Spielberger., *et al*. [17] it was translated into Turkish by Öner and Le Compte [18] and used to investigate anxiety levels by adapting it. It measures state and trait anxiety levels. State Anxiety (A - State); is the subjective fear that an individual feels due to the stressful (pressed) situation he/she is in. Trait Anxiety (A- Trait); it is the tendency of the individual to experience anxiety. This can also be called the tendency to perceive the situations in which the person is usually stressed or to interpret it as stress. It is observed that individuals with such anxiety level are easily hurt and pessimistic. These individuals experience state anxiety more frequently and intensely than others. The inventory has two separate scales with 20 items each.

State Anxiety Scale; determines how the individual feels at a certain moment and under certain conditions. Trait Anxiety Scale; It usually determines how the individual feels himself, regardless of the situation and circumstances. Two scales are printed on two separate pages, Form TX-1 and TX-2.

To make it easier for individuals to answer scale questions in a friendly and vulnerable manner, testers did not use the word anxiety in the title of the inventory; They called the "Self (Self) Evaluation Questionnaire" in the inventory. Therefore, care was taken not to use the word anxiety during application.

State and trait anxiety scale scoring

If more than three statements are not answered, the filled form is considered invalid and not scored. Answer options collected in four classes: On the state anxiety scale, 1: none, 2: a little, 3: very and 4: completely; Options on the trait anxiety scale are 1: almost never, 2: sometimes, 3: much time and 4: almost always.

Interpretation of Points

The scores obtained from both scales theoretically range from 20 to 80. Big score indicates high anxiety level, small score indicates low anxiety level [9].

Statistical analysis

The data obtained as a result of the research were reviewed and appropriate statistical analyzes were done using the SPSS 22.0 statistical package program. Frequency tables, cross tables, Pearson chi-square, Exact Chi-square, and "Chi-squared Automatic Interaction Detector" (CHAID) analysis tests were used to evaluate the data. Inter-group T-Test analysis for scale scores was performed under the control of importance.

Statistical significance level "p" was given together with the relevant tests, when $p < 0.05$. It was considered statistically significant.

In categorical data, it was summarized as arithmetric mean and plus-minus standard deviation in scale scores in numbers and percentages.

Results

Eighty five (70.8%) of the research group were mothers and 35 (29.2%) were fathers. There was no significant difference between the diagnosed and pre-diagnosed groups of the study group in terms of parental distribution ($p = 0.841$). The demographic characteristics of the research group are shown in table 1.

Filling out the form	Number	%
Mother Father	85 35	70.8 29.2
Age range		
Infant Older age	69 51	57.5 42.5
Gender		
Female Male	64 56	53.3 46.7
Consanguineous marriage		
Available Absent	81 39	67.5 32.5
Sibling		
Absent Available	63 57	52.5 47.5
Neurometabolic disease in the sibling		
Absent Available	118 2	98.3 1.7
A history of death in sibling		
Absent Available	109 11	90.8 9.2
Time of birth time		
Miad Prematurity	109 11	90.8 9.2
Birth way		

NSV C/S	107 13	89.2 10.8
Birth asphyxia		
Absent Available	108 12	90 10
Home environment		
Good Medium Poor	61 43 16	50.8 35.8 13.3
Socioeconomical condition		
Low income Medium income High İncome	33 75 12	27.5 62.5 10
Monitoring in another hospital		
Absent Available	106 14	88.3 11.7

Table 1: *Demographic features of the research group.*

It was determined that infant rate was higher in the pre-diagnosed group and the rate of older children was higher in the diagnosed group ($p = 0.02$).

No significant gender difference was found between the diagnosed and pre-diagnosed groups of the study group ($p = 0.272$).

There was a significant difference between the diagnosed and pre-diagnosed groups of the study group in terms of relationship between the mother and father, and there was a higher rate of relationship in the diagnosed group ($p < 0.001$).

No significant difference was found between the diagnosed and pre-diagnosed groups of the study group in terms of the presence of siblings diagnosed with neurometabolic disease ($p = 0.154$).

A significant difference was found between the diagnosed and pre-diagnosed groups of the study group in terms of the history of sibling death ($p = 0.004$). In the diagnosed cases, the sibling death history was higher.

There was no significant difference between the diagnosed and pre-diagnosed groups of the study group in terms of birth time ($p = 0.114$). The presence of difficult birth was higher in the diagnosed group. ($p = 0.019$).

A significant difference was found between the diagnosed and pre-diagnosed groups of the research group in terms of their home environment ($p < 0.01$). It was determined that the pre-diagnosed group lived in a higher rate of good home environment, and the diagnosed group lived in a higher rate of medium and poor home environment.

A significant difference was found between the diagnosed and pre-diagnosed groups of the study group in terms of socioeconomic status ($p < 0.01$). While low and high socioeconomic status was higher in the diagnosed group, it was observed that 80% of the pre-diagnosed group had a medium socioeconomic status. While there was a higher rate of follow-up in another hospital in the diagnosed group, it was not in the pre-diagnosed group.

In the research group, which were used to evaluate the depression status with Beck depression scale, and to evaluate the anxiety state, STAI Form TX I and II, were used to evaluate instantaneous (state) anxiety and trait anxiety (Table 2).

	Diagnosed		Prediagnosed	
	Average	SDS	Average	SDS
Beck Depression Inventory	12,2667	5,66843	17,0167	5,53415
STAI Form TX I	38,5500	9,78831	19,5667	5,44111
STAI Form TX II	40,6333	8,16144	21,0833	6,79803

Table 2: *Comparison of the groups' beck depression inventory (BDI), state/trait anxiety inventory averages.*

A significant difference was found between the diagnosed and pre-diagnosed groups of the study group in terms of Beck depression scale analysis ($p < 0.01$). According to Beck depression scale scoring, 10-18 points were interpreted as mild depression symptoms. It was observed that there was mild depression in the diagnosed group, and moderate depression in the pre-diagnosed group.

A significant difference was found between the diagnosed and pre-diagnosed groups of the study group in terms of STAI Form TX I analysis ($p < 0.01$). In cases diagnosed, state anxiety was found to be higher than the pre-diagnosed group.

A significant difference was found between the diagnosed and pre-diagnosed groups of the study group in terms of STAI Form TX II analysis ($p < 0.01$). In the diagnosed cases, the trait anxiety was found to be higher than the pre-diagnosed group.

In the evaluation of Beck depression scale in the study group, there was no significant difference between the parents in the diagnosed and pre-diagnosed groups in terms of scale mean score ($p = 0.425$, $p = 0.374$). In the Beck depression scale evaluation among the diagnosed and pre-diagnosed groups, the depression analysis of the mothers and fathers was found to be higher ($p = 0.012$, $p = 0.016$) in the pre-diagnosed group ($p = 0.012$, $p = 0.016$).

In the evaluation of STAI Form TX I scale in the study group, there was no significant difference between the parents in terms of scale mean score ($p = 0.103$). No significant difference was found between the mothers and fathers in the prediagnosed group in terms of scale mean score ($p = 0.154$). There was a significant difference between the groups in the state anxiety scale assessment of the mothers within the diagnosed and pre-diagnosed group ($p = 0.025$). State anxiety analysis of diagnosed mothers was found to be higher. There was a significant difference between the groups in the state anxiety scale evaluation of fathers within the diagnosed and pre-diagnosed group ($p = 0.034$). Instant anxiety analysis of diagnosed fathers was higher.

In the evaluation of STAI Form TX II scale in the study group, no significant difference was found between the mothers and fathers in terms of scale mean score ($p = 0.458$). No significant difference was found between the mothers and fathers in the prediagnosed group in terms of scale mean score ($p = 0.364$). There was a significant difference between the groups in the continuous anxiety scale evaluation of the mothers in the diagnosed and pre-diagnosed group ($p < 0.01$). Trait anxiety analysis of diagnosed mothers was found at a higher level. There was a significant difference between the groups in the continuous anxiety scale evaluation of fathers within the diagnosed and pre-diagnosed group ($p < 0.01$). Trait anxiety analysis of diagnosed fathers was higher.

Discussion and Conclusion

In the researches, if the parents' anxiety and depression levels are high or low; It was emphasized that various factors such as the severity, duration and whether it is fatal for a child are important [10]. In our study, we compared that families will live in the pre-diagnosed stage and whether the presence of an unknown condition will increase depression and anxiety more, or that families who have been diagnosed and continue their lives in this way have higher levels of depression and anxiety.

When we look at the sociodemographic characteristics of the patients who were diagnosed with a disease from the neurometabolic disease group and who were at the pre-diagnosis stage, there was no significant difference in terms of parental distribution, gender of the patient, sibling status, and birth time. It was determined that infant rate was higher in the pre-diagnosed group and the rate of older children was higher in the diagnosed group. This result may be related to the fact that the examinations performed while making the diagnosis of NMD take a certain period of time and that a prompt examination is requested. In diagnosed groups, consanguineous marriage and sibling death history were found to be higher. This situation was evaluated in accordance with our classical knowledge.

The presence of difficult birth was higher in the diagnosed group. This result can be attributed to children with NMD having difficulty performing normal labor because they are hypotonic. It was determined that the pre-diagnosed group lived in a higher rate of good home, and the diagnosed group lived in a higher rate of medium and poor home environment. While the low and high socioeconomic status was higher in the diagnosed group, 80% of the predignosed group was found to have a medium socioeconomic status. This made us think that NMD is more common in people with low socioeconomic status, and that a higher rate of diagnosis were made because families with high socioeconomic status can access more tests. While there was a higher rate of follow-up in another hospital in the diagnosed group, it was not in the pre-diagnosed group. Perhaps patients with follow-ups from other hospitals had increased chances of getting a diagnosis because they could be examined further.

In the study conducted by Toros., *et al.* [10] on the levels of depression and anxiety in the families of patients with chronic disease, the scale of depression and anxiety was found higher in mothers than in fathers, but no difference was found in our study. Although this situation expects high levels of depression and anxiety in the mother as the person who cares more for the sick child in our society, we can think that this is due to the fact that the child with the chronic disease affects all the members of the house and the regular follow-up and treatment is carried out by the parents.

In the study by Damiani [19], it is stated that the current adversity may cause changes in the roles within the family, the family members have to switch to roles that are not suitable for them, and this situation may cause problems in family functions. In our study, the high levels of depression and anxiety without any significant difference between the mothers and fathers of especially diagnosed cases may be an indicator of this. Of mothers who have disabled children; It is stated that she is the person who tries hard to solve the psychological, social and economic problems and they are lonely in this situation while trying to organize the daily life of the disabled child [20-23]. According to our clinical experience, it was seen that in the follow-up and treatment controls, the mother and father brought their children to the outpatient clinic, and in our study, it was seen that the person who struggled to solve the psychological, social and economic problems was not separated and assumed together as a mother and father. Perhaps, only in this way can the diagnosis process of the patients be started.

In the study conducted by Law., *et al.* it was found that the problems of the child, which provides biological and sociological continuity in the concept of family, which is the main element of the society, negatively reflect to the child, family and society [11]. Mc Manus., *et al*. [12] also concluded that physically and psycho-social health is negatively affected in families and caregivers who have to take care of children with disabilities all day and for many years. In our study, we found a high predisposition to depression in the group that was at the prediagnosed stage. We found that cases diagnosed in terms of instantaneous and constant anxiety had higher anxiety in both mothers and fathers than mothers and fathers of the predignosed group. Our study was determined in accordance with the analyzes of Law and McManus., *et al*. According to these results, it can be thought that current uncertainty increases anxiety.

In a study evaluating parents in a chronic disease; 50% depressive symptoms, 31% anxiety symptoms detected [24]. In some studies; increased depression and anxiety level in parents with children with a chronic disease are compatible with the results of our study [25-28]. In the previous study conducted by Çakaloz., *et al*. [13], the presence of an increased level of depression and anxiety in parents with a child with a chronic disease is consistent with the results of our study too.

In the study by Pless., *et al*. [29]; it is stated that the risk of developing psychological or social problems in children with chronic diseases is 1.3 - 3 times higher than in healthy children. We can say that our study is similar to Pless's study, which evaluates the effect of psycosocial problems on the family in the foreground, as we evaluate the levels of depression and anxiety due to the difficulties faced by parents in the stage of diagnosis of NMD. Even social problems are the reason for the high level of depression and anxiety in families of both pre-diagnosed and diagnosed cases.

In the study of Ross., *et al*. [14], a child with a disability states that it can be perceived as a big disappointment in the family and can be a source of intense anxiety. The results of our study are also related to this situation. The family of a child with a suspicion of neurometabolic disease is wondering when the type of this will be determined, but they can be psychologically affected while waiting for the results, since more accurate information about prognosis and treatment can be given after diagnosis. While waiting for the result of a test, a new test is requested when the elapsed time is over and the waiting process is started again. Therefore, it can increase the anxiety and depression level of the family, both from the long waiting period, as well as intervening infection, new detected/progressive findings, etc.

Many professionals investigated the social and psychological impact of children with disabilities on the family and emphasized that families should learn to deal with the disabled child. In addition, the inability of families to spare enough time for themselves and other children causes weakness in family relationships. In a study by Slack., *et al*. [15] he emphasized coping with living with a chronically ill child and stated the effect of family relationships on the quality of life. On the basis of our study, the existing depression and anxiety states of the families were identified and suggestions were planned to make improvements in this regard.

In their study, Blacher., *et al*. [16] stated that with the increase of the severity of the disability, the child's dependence on family members, especially the mother, and in parallel, the level of anxiety experienced by the mother also increased. Similarly, in our study, STAI state and trait anxiety scale scores were found to be higher in patients with diagnosed cases, and the anxiety level of the families was higher due to the fact that the prognosis of the diagnosed patients were more certain and their dependence on the family was known.

In the light of all this information, the effect of a chronic disease, which is a progressive process that requires follow-up and treatment in a long process such as NMH, will continue increasingly over time. The families of the patients who are followed up and treated in terms of neurometabolic disease will also be followed as multidisciplinary, performing psychiatric evaluations at certain intervals, receiving support will lead to significant improvements in the quality of life of the families.

In a study it was suggested that the clinician should not only be interested in the physical condition of the child, but also the evaluation of the mental state of both the child and other family members [17]. Similarly, the same study emphasizes that the child is social-psychological-biological as a whole and should be evaluated together with the family. Since the mothers of children with chronic diseases are considered to be at risk for psychopathology, it is recommended to provide appropriate psychological support to the family. It shows that a multidisciplinary treatment approach may be required to provide assistance when needed, as shown in our results.

Due to the nature of the study, the fact that the data is based on personal declaration and includes a certain risk of deviation from the facts constitute the limitations of the study. In order to ensure the correctness of personal statements, the participation of the mothers and fathers was voluntary and the collecting of the identity information of the participants was avoided.

As a result, it was determined that the risk of depression was higher in the families of the patients with NMD prediagnosis, and the state and trait anxiety were higher in the diagnosed families. In addition, depression and anxiety scales scores were higher than normal in both groups. The families of all cases followed with a diagnosis or pre-diagnosis of neurometabolic disease must be followed with a multidisciplinary approach, and their follow-up with psychological and psychiatric support should be continued with both individual and group evaluations. In this way, the improvement of the psychopathology of all families will be maintained and the state of well-being will

be maintained. We think that more research is needed to examine the causes of the difficulties that a chronic disease such as neurometabolic disease causes in the families of children.

Conflict of Interest

There is no conflict of interest in our study.

Funding Support

There is no sources finansial assistance in our study.

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Volume 9 Issue 11 October 2020