

DEPRESSION AND ANXIETY IN PARENTS OF CHILDREN WHO ARE CANDIDATES FOR LIVER TRANSPLANTATION

Yasin SAHIN¹, Osman VIRIT² and Bahadır DEMIR²

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ABSTRACT - Background - The primary stress factor for families in the pre-transplant period is reported as the waiting time for suitable organs, leading to anxiety, despair, and distress. **Objective** - We investigated the psychosocial factors, anxiety and depression, in the parents of children who are candidates for liver transplantation. **Methods** - Thirty-five pediatric liver transplantation candidates and their 38 parents, from February to August 2014, were included. Participants were evaluated using the Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A), and Clinical Global Impression Scale (CGI). **Results** - We found that a significant number of parents (n=25, 65.7%) were diagnosed with clinical psychiatric disease: 18.4% (n=7) with depression and 47.3% (n=18) with anxiety disorders. There was a significant difference in the examination scores of parents between genders ($P<0.05$). There was also a significant difference in CGI and HAM-D scores of parents relative to the history and presence of liver disease ($P<0.05$). **Conclusion** - The rate of these disorders was high in relation to the prevalence of depression and anxiety disorders in the community reported in the literature. Therefore, it is necessary to evaluate psychosocial factors of parents of all transplant candidate children as a part of routine care so that the high-risk to family members and to enable early intervention.

HEADINGS - Organ transplantation. Emotions. Family. Psychosocial impact. Pediatrics.

INTRODUCTION

The first liver transplantation was performed in a 2-year-old patient with biliary atresia by Thomas Starzl in 1963⁽²⁷⁾. In recent years, survival rates and times have improved dramatically with the development of safer and more efficient immunosuppressive agents. Liver transplantation in selected patients who have acute and chronic liver failure is currently being implemented as a standard method of treatment. It is not indicated in cases such as non-resectable extrahepatic malignant tumors, uncontrolled sepsis, or terminal liver failure, which have poor outcome expectancy and quality of life, in particular during and after transplantation⁽²⁶⁾.

The main indications for liver transplantation in the pediatric population are, 1) extrahepatic cholestasis: biliary atresia; 2) intrahepatic cholestasis: sclerosing cholangitis, Alagille syndrome, non-syndromic intrahepatic bile duct paucity and progressive familial intrahepatic cholestasis; 3) metabolic diseases: Wilson's disease, alpha-1 antitrypsin deficiency, Crigler-Najjar

syndrome, bile acid metabolism disorder, tyrosinemia, disorders of the urea cycle, organic acidemia, acid lipase deficiency, disorders in metabolism of carbohydrates and oxaluria type-1; 4) Acute liver failure; and 5) others: primary liver tumor and cystic fibrosis⁽²⁶⁾.

If a patient is a suitable candidate for liver transplantation, he is first added to the organ waiting list. Unfortunately, the number of patients on this waiting list is greater than the number of organs obtained in each year. The mortality rate of children in United Network for Organ Sharing waiting list is approximately 17%⁽¹⁰⁾.

Significant psychological difficulties and confusion have been reported in both the parents and children during the pre-transplant period⁽²⁸⁾. The course of disease in children is influenced by the mood disorders of caregivers, poor child care, and poor nutritional and emotional support. Therefore, the psychiatric conditions should be detected early in families and caregivers to enable intervention. However, very few studies have examined the psychological state of parents prior to liver transplantation^(11,14,18,20,25,28,33).

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¹Department of Pediatric Gastroenterology-Hepatology and Nutrition, Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, Turkey; ² Department of Psychiatry, Faculty of Medicine, Gaziantep University, Istanbul, Turkey.

Correspondence: Yasin Sahin, MD, Department of Pediatric Gastroenterology-Hepatology and Nutrition, Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, Turkey. E-mail: ysahin977@gmail.com

In this study, we aimed to investigate the psychosocial factors, anxiety and depression, in the parents of children who were candidates for liver transplantation. To our knowledge, this is the first study that will be conducted in the parents of children who are candidates for liver transplantation in Turkey.

METHODS

The parents of children who are candidates for liver transplantation, followed up and treated in Pediatric Gastroenterology Clinics between February–August 2014, were studied. Parents who have any mental retardation or psychotic disorders were excluded from the study. Ethics committee approval was not received. But the study was performed in accordance with the principles of the Helsinki Declaration as revised in 2013. Written informed consent was obtained from participants before the study. Fifty-two patients were followed up as candidates for liver transplantation. The parents of 35 patients agreed to participate in this study and the parents of 17 patients refused to participate.

Scoring systems are used to evaluate the need for transplantation due to chronic liver disease with objective criteria. These are the Model For End Stage Liver Disease (MELD) and Pediatric End Stage Liver Disease (PELD) scores. The MELD scoring system has been used in patients who have chronic liver disease and liver transplantation candidates over the age of 12 since 2002. Patients' creatinine level, prothrombin time, and bilirubin level are used in the MELD score. The MELD score is a measure of the risk of death within 3 months. A higher MELD score relates to a higher expected mortality⁽¹²⁾. The PELD score is used for patients under the age of 12. Unlike the MELD score, parameters which are very important for pediatric nutrition on growth and development are also used. Additional PELD points are added to the patient's PELD score if liver tumors, hepatopulmonary syndrome, or metabolic disorders are present⁽²⁶⁾.

The parents were assessed by using The Sociodemographic Data Form. The parents were evaluated with the Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V) by a resident in the Department of Psychiatry. Symptom levels were assessed using the Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A), and Clinical Global Impression Scale (CGI).

The Socio-demographic Data Form is used to evaluate patients' socio-demographic characteristics, disease history and current status, their diagnosis and treatment, comorbid status, and family history. The findings of their children have also been added to this form.

The HAM-D is a scale containing 17 items that is used to measure the level and severity of depression symptoms, applied by a clinical investigator. It is a widely used scale developed by Hamilton and transformed into the present status by restructuring. The reliability and validity of the Turkish version was conducted by Akdemir et al.⁽¹²⁾. Depression is rated as: 0–7 points = “no depression”, 8–12 points = “mild depression”, 13–17 points = “moderate depression”,

18–29 points = “major depression”, and 30–52 points = “more severe than major depression”.

The HAM-A was developed by Hamilton and is a scale used to determine the level, distribution, and severity of anxiety symptoms in individuals. It consists of 14 items. The presence and severity of items is evaluated by an interviewer. Total scores are obtained by giving a value of 0–4 for each question. Total scores are calculated, 0–5 points “no anxiety”, 6–14 points “mild anxiety” (mild to moderate) or above 15 points indicates “severe anxiety”. The reliability and validity of the Turkish version was conducted by Yazici et al.⁽³¹⁾.

The CGI is a scale used to evaluate the level, symptoms, severity and improvement of any disease. The physician evaluates the items using a 7-point scale. This is described as 1 (not ill) to 7 (very severe patients) for severity of the disease and from 1 (very much improved) to 7 (very deteriorated) for the recovery of disease, based on the overall experience associated with the disease⁽¹⁵⁾. The item of illness severity was used in our study.

Statistical analysis

The Kolmogorov–Smirnov test was used to check the normal distribution of continuous variables. The Mann–Whitney U test was used for statistical analysis of two independent groups that had variables that were not normally distributed. Frequency, percentage, and mean \pm standard deviation (SD) were used as descriptive statistics. Statistical Package for the Social Sciences for Windows, version 22.0 (SPSS software, SPSS Inc, Chicago, Illinois, USA) was used for statistical analyses and $P < 0.05$ indicated statistical significance.

RESULTS

Fifty-two patients were followed up as candidates for liver transplantation in the Department of Pediatric Gastroenterology-Hepatology and Nutrition. The parents of 35 patients agreed to participate in this study and the parents of 17 patients refused to participate. There were 19 girls (54.3%) and 16 boys (45.7%) in our study, with a mean age of 9.1 ± 5.2 years. Before the study, oral and written informed consent was received from the parents. The demographic characteristics of our patients who are candidates for liver transplantation are shown in Table 1.

TABLE 1. The demographic features of children who are liver transplant candidates

Diseases	Number (n)	Percentage (%)
Biliary atresia	7	20
Wilson's disease	13	37.1
Cryptogenic liver cirrhosis	2	5.7
Primary biliary cirrhosis	1	2.8
Cryptogenic chronic liver failure	4	11.4
PFIC*	4	11.4
Cholestatic hepatitis	3	8.6
Budd-Chiari Syndrome + liver cirrhosis	1	2.9

* Progressive familial intrahepatic cholestasis.

One of our patients with biliary atresia died approximately 3 months after the study began. The diagnosis of 3 siblings of patients who participated in the study was Wilson's disease. The other 2 siblings of patients were diagnosed with cholestatic hepatitis. Both parents of five pediatric patients participated in the study. Only the mothers of siblings participated in the study. A total of 35 pediatric patients with liver transplantation candidates and their 38 parents have agreed to participate in our study.

The demographic features of the parents of children who are liver transplant candidates are shown in Table 2. Psychiatric evaluation scores, diagnosis, and recommended treatment for parents are shown in Table 3. There was no significant difference in the examination scores of parents relative to the gender of children ($P>0.05$). However, there was a significant difference in the examination scores of parents between gender ($P<0.05$; Table 4). There was also a significant difference in CGI and HAM-D scores of parents relative to the history and presence of liver disease ($P<0.05$; Table 5).

TABLE 2. The demographic features of the parents of children who are liver transplant candidate

	Number	Percentage (%)
Gender		
Mother	22	57.9
Stepmother	1	2.6
Father	15	39.5
Educational status		
Illiterate	5	13.1
Primary school	27	71.1
Secondary school	3	7.9
High school	2	5.3
University	1	2.6
Legal domicile		
Country	27	71.1
Town	4	10.5
Village	7	18.4
Psychiatric background		
Not available	36	94.7
Available	2	5.3
Psychiatric family history		
Not available	34	89.5
Available	4	10.5
Presence of donor		
Not available	36	94.7
Available	2	5.3
Family history of liver disease		
Not available	28	73.7
Available	10	26.3
Psychiatric complaint		
Not available	27	71.1
Available	11	28.9

TABLE 3. The psychiatric examination results of the parents

Psychiatric evaluation	Score (mean \pm SD)	Min-max
CGI	3.1 \pm 1.6	(1-5)
HAM-D	12.1 \pm 7.2	(2-22)
HAM-A	5.8 \pm 5.6	(0-23)
	Number (n)	Percentage (%)
Diagnosis		
No pathology	13	34.2
Anxiety disorder	18	47.4
Depression	7	18.4
Treatment		
Medication	19	50
Cognitive therapy	3	7.9
No medication	16	42.1

CGI: Clinical Global Impression Scale; HAM-D: Hamilton Depression Rating Scale; HAM-A: Hamilton Anxiety Rating Scale.

TABLE 4. The examination scores of parents according to gender

	Gender	Number	Score (mean \pm SD)	P
CGI	female	23	3.7 \pm 1.4	0.01
	male	15	2.2 \pm 1.4	
HAM-A	female	23	14.6 \pm 6.8	0.02
	male	15	8.2 \pm 6.1	
HAM-D	female	23	7.5 \pm 6.4	0.04
	male	15	3.2 \pm 2.6	

CGI: Clinical Global Impression Scale; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale.

TABLE 5. The examination scores of parents according to the history and presence of liver disease

	History	Number	Score (mean \pm SD)	P
CGI	no	28	2.8 \pm 1.6	0.047
	yes	10	4.0 \pm 1.4	
HAM-A	no	28	10.8 \pm 7.1	0.056
	yes	10	15.9 \pm 6.1	
HAM-D	no	28	4.3 \pm 4.1	0.011
	yes	10	10.2 \pm 7.1	

CGI: Clinical Global Impression Scale; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale.

There was no significant difference in the examination scores of parents in terms of the parental psychiatric evaluations, the number of children in a family, the MELD and PELD scores of patients, number of hospitalizations and days in hospital, the family's place of residence, or family history of psychiatric disease ($P>0.05$).

DISCUSSION

Children with chronic liver disease should be directed to transplantation without complications and any complications should not affect the quality of life and development of patients and their families. It may be difficult to determine the best time for a liver transplant because children with chronic liver disease may develop cirrhosis and portal hypertension, which may have compensated liver function for a long time⁽⁸⁾. Patients on the waiting list are classified according to the severity of disease and blood group; therefore, organ sharing is made according to medical urgency rather than waiting time.

Although transplantation provides solutions for mortality, this process includes many stress factors, such as uncertain waiting time for the family, comprehensive financial support, and isolation from the social environment during hospitalization⁽⁵⁾. If there is no donor from relatives or a donor organ is expected from deceased donors, the families of these patients are exposed to significant stress. The greater the urgency for transplantation, the greater the risk of losing their children to the families; therefore, these parents have more anxious⁽⁹⁾.

Children with chronic illnesses have a greater life expectancy at present. Curative treatment is not possible in most chronic diseases; therefore, it is necessary to support children's physical, cognitive, and psychosocial traits to minimize the complications of the disease⁽⁴⁾.

A significant number of parents ($n=25$, 65.7%) were diagnosed with clinical psychiatric disease in our study. Of these, 18.4% ($n=7$) were diagnosed as depression and 47.3% ($n=18$) were diagnosed with anxiety disorders. We found that 16 parents had received psychiatric treatment at the time of the evaluation. In this study, a control group (parents of a healthy child) was not used. Our study is cross-sectional, so it is appropriate to compare our results with sectional or annual prevalence results in epidemiological studies.

It has been reported in the literature that the prevalence of depression is 5%–10% for adults^(2,5). Dogan O has detected that the prevalence of depression is 18.8%, while Rezaki found that it is 11.6%, in studies conducted in Turkey^(6,22). The risk of depression is higher in women than in men; the lifetime probability of developing depression is 10%–25% for women, while this rate is 5%–12% in men^(16,21,29,30).

Anxiety disorders are the most commonly seen psychiatric disorders. The lifetime prevalence of anxiety disorders has been reported as 28.8%⁽¹⁷⁾. Although anxiety disorders are claimed to be more common in women than men in general, there has also been a study reporting no difference between the genders⁽¹³⁾. Considering the above data on the prevalence of depression and anxiety disorders in the general population, the rate of these disorders seems to be higher than average in our study.

Almost everyone will encounter the death of a loved one, but the death of a child is rare, particularly in developed countries. The impact of losing a child is devastating and can last for decades, resulting in intense grief and poor psychological and physical health⁽²³⁾. One of the most important cause of depression for parents is the death of child⁽³²⁾. It is a significant stress factor to have a child with a fatal liver disease that needs transplantation. There were parents who are faced with the risk of losing a child in our study. Moreover, fatal liver disease has a chronic progression. In this study, we clearly saw clinical outcomes.

The chronic diseases also severely affect the health of all family members. Therefore, these parents are faced with many challenges and often this will result in increased stress⁽²⁴⁾.

Tarbell and Kosmach have investigated quality of life and stress in the parents of children who have had liver and intestinal transplantations before and after transplantation. Forty one mothers and 20 fathers were included in the study. The Brief Symptom Inventory was used and increased psychological symptoms were reported in 31 parents. They found that there was more stress in fathers than mothers⁽²⁸⁾.

In contrast to this, it has been reported in another study that there was no difference in the prevalence of depression and anxiety between the normal population and parents of children with solid organ transplantation (heart, liver, and kidney)⁽³³⁾.

The expected survival rate is 86.8% in children with a PELD score between –11 and 6, 76.3% in children with a PELD score between 7–17, and 65% in children with scores above 17 on the waiting list⁽⁴⁾. Therefore, if liver transplantation is not performed in patients with a PELD score over 17, 1/3 of them will decrease in one year. The PELD score is a scoring system that determines the priority and urgency of the transplantation requirement⁽¹⁹⁾. One of our patients died approximately 3 months after the study began. While her PELD score was 12 at the beginning of the study, this increased to 18 before she died. The psychiatric examination scores of the patient's mother were 4, 14, and 2 on the CGI, HAM-A, and HAM-D, respectively. Therefore, moderate anxiety was present in the mother.

Another important finding of our study was that depression, anxiety, and level of disease severity was higher in mothers. These findings are paralleled in the community where higher levels of depression and anxiety are present in women. Similar results have been reported in many studies^(16,21,29,30). In a study in which mothers were evaluated before a liver transplant, desperation was found to be associated with stress in the family. Stress and uncertainty decreased with an improvement in finding a remedy in time⁽¹⁸⁾.

There are many stress factors for parents in addition to the risk of losing a child. Children with a chronic illness have complex needs (physical, developmental, behavioral and emotional); therefore, their needs should be coordinated by primary health care to reduce family stress⁽¹¹⁾. The family environment is significantly reflected in children's behavior and the parents' stress of having healthy and ill children. A positive family environment, where family members support each other, is characterized by high compliance⁽¹¹⁾.

Improving the parents' spiritual state is important as it indirectly affects the health of the child, in addition to their own health⁽⁷⁾. It has been reported that a poor parental psychological and social condition is associated with increased mortality, risk of late rejection, and hospitalization time⁽¹⁾. Determining parental distress, understanding their level of stress, and identifying the factors that are associated with increased stress is vital so that an effective intervention can be made. Early recognition of psychosocial risk factors in families and early intervention can prevent or reduce psychological distress. This will be essential to obtain better results for children and families⁽²⁸⁾.

In another study, 34 mothers and 22 fathers were evaluated psychologically before transplant. They found that it was less stressful for mothers who received social support but this did not affect the stress levels of the fathers. In the same study, it was reported that there was less distress in fathers who frequently used problem solving, cognitive evaluation, and emotional expression. More distress was found in mothers who had children waiting for transplant compared with mothers with healthy children in this study. Significant levels of distress were clinically identified in 21% of both parents⁽²⁵⁾.

Limitations of our study

The first limitation was the small number of cases in this study, because some parents refused to participate. Ethics Committee approval was not received. But the study was performed in accordance with the principles of the Helsinki Declaration as revised in 2013. Secondly, we could

not evaluate the parents during the post-transplant period, because liver transplantation was not performed in our center during the period of our study.

It is important that health teams always act with family and include them in the decision-making process. The American Academy of Pediatrics suggests family-centered care and that the opinion of parents should be taken into account in all decisions regarding the care of their children⁽³⁴⁾.

Consequently, it is necessary to evaluate the psychosocial traits of parents of all children with chronic disease and transplant candidates as a part of routine care so that high-risk family members can be recognized and to enable early intervention. In this way, the mental health of family members improves at an early stage, which will positively affect the child's health.

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Authors' contributions

Sahin Y and Virit O: conception and study design, data collection, analysis and/or interpretation of data, final approval of manuscript, writing of the manuscript or review of its content. Demir B: data collection, analysis and interpretation of data; approval of the final version of the manuscript.

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RESUMO - Contexto - O fator primário de estresse para famílias no período pré-transplante é relatado como o tempo de espera por órgãos adequados, levando à ansiedade, desespero e angústia. **Objetivo** - Investigamos os fatores psicossociais, ansiedade e depressão, em pais de crianças que são candidatas a transplante hepático. **Métodos** - Foram incluídos trinta e cinco candidatos a transplante de fígado pediátrico e seus 38 genitores, entre fevereiro e agosto de 2014. Os participantes foram avaliados usando a escala de avaliação de depressão Hamilton (HAM-D), escala de avaliação de ansiedade Hamilton (HAM-A) e escala clínica de impressão Global (CGI). **Resultados** - Um número significativo de pais (n=25, 65,7%) foram diagnosticados com doença clínica psiquiátrica: 18,4% (n=7) com depressão e 47,3% (n=18) com transtornos de ansiedade. Houve uma diferença significativa nas pontuações exame dos pais entre os sexos ($P<0,05$). Também houve uma diferença significativa nos escores de CGI e HAM-D dos pais em relação a história e a presença de doença hepática ($P<0,05$). **Conclusão** - A taxa destes transtornos foi elevada em relação a prevalência de depressão e transtornos de ansiedade na comunidade relatados na literatura. Portanto, é necessário avaliar fatores psicossociais dos pais de todas as crianças candidatas a transplante como parte dos cuidados de rotina e para o alto risco para os membros da família e assim permitir uma intervenção precoce.

DESCRITORES - Transplante de órgãos. Emoções. Família. Impacto psicossocial. Pediatria.

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