Original Article

The Patients' Experiences of Burden of Neurofibromatosis: A Qualitative Study

Samira Foji[1], Eesa Mohammadi[2], Akram Sanagoo[1], Leila Jouybari[3]

[1]School of Nursing and Midwifery, Golestan University of Medical Sciences, Gorgan, Iran, [2]Department of Nursing, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran, [3]Nursing Research Center, Golestan University of Medical Sciences, Gorgan, Iran

Abstract

Background: Neurofibromatosis Type 1 (NF1) is a common autosomal disorder; the criteria for the diagnosis of NF1 includes café au lait spots, freckling, and Neurofibromas (NF). Skin symptoms have a major impact on patients' Quality of Life (QOL) but little is known about the burden of the disease on patients. The aim of this study was to explore the experiences of patients with NF. **Materials and Methods:** Using purposive sampling, 20 participants were enrolled in this qualitative content analysis study. The study was carried out between 2019 and 2020. Unstructured interviews and field notes were used to gather data. Data collection was stopped when data saturation was achieved. **Results:** Data analysis revealed 14 subcategories and 4 categories including "failing and falling behind in life", "deprivation and restriction", "social isolation", and "ineffective adaptation to the disease", which indicate the perception of patients with NF. **Conclusions:** In addition to the physical burden due to physical complications and problems, NF imposes a high degree of psychological and social burden on patients causing mental conflicts, which in turn results in them failing and falling behind in life. These findings illustrate the need to develop strategies and use multidisciplinary approaches to support patients, and thus to reduce the burden of NF.

Keywords: *Global burden of disease, Iran, neurofibromatosis 1, qualitative research*

Introduction

Neurofibromatosis (NF) is a genetic disease of the central and peripheral nervous system that is inherited in an autosomal dominant manner. The more common type of the disease, NF type 1 (NF1) occurs at a prevalence of 1 in every 3,000 to 4,000 births.[1] Exact official statistics on the number of patients with NF in Iran have not been published as yet. Therefore, it is estimated that the number of patients with NF1 in Iran is the same as the global statistics, 1 in 3,000 people.[2,3] NF is considered as the most common nerve coetaneous disease syndrome. NF is a progressive, unpredictable disease with various symptoms. The severity of symptoms may range from mild aesthetic damage to life-threatening conditions.[4]

The most common clinical manifestations in these patients include hyperpigmented cutaneous lesions (Café au lait spots), cutaneous neurofibromas, lisch nodules, and learning difficulties. Optic gliomas and other gliomas, malignant tumors of the nerve sheath, and bone lesions are also seen less commonly.[5]

NF is considered as a chronic disease and, chronic and life-threatening diseases are stressful factors that affect a person's identity, psychosocial dimensions, emotional balance, self-satisfaction, sense of competence and efficiency, social interactions, and interpersonal relationships. People with chronic diseases must cope with existing challenges to achieve an acceptable level of health, and physical, mental, and social functioning.[6] Visible neurofibromas cause significant concern and low self-confidence, especially in young women.[7] Low self-confidence and other psychological problems can also be the result of learning disabilities during childhood and school failure.[8] Approximately, 20% of patients with skin diseases suffer from bad temper and 7% suffer from a depressed mood and have attempted suicide.[9] Mental disorders, anxiety and personality disorders, depression, and suicide attempts are also common in patients with NF.[10] Cognitive impairment may persist into adulthood and

How to cite this article: Foji S, Mohammadi E, Sanagoo A, Jouybari L. The patients' experiences of burden of neurofibromatosis: A qualitative study. Iran J Nurs Midwifery Res 2021;26:342-8.

Submitted: 26-Jul-2020. **Revised:** 11-Aug-2020. **Accepted:** 16-Mar-2021. **Published:** 20-Jul-2021.

Address for correspondence:
Dr. Leila Jouybari, Nursing Research Center, Goletsan University of Medical Sciences, Gorgan, Iran.
E-mail: jouybari@goums.ac.ir

Access this article online

Website: www.ijnmrjournal.net

DOI: 10.4103/ijnmr.IJNMR_178_20

Quick Response Code:

affect occupational performance, thus reducing the quality of life (QOL) of patients with NF, especially in severe cases.[11] Patients with NF are also at risk of various tumors and their life expectancy is reduced by 10 years compared to the general population.[12] Although skin lesions are the most significant manifestation of NF, there is a possibility of involvement of other organs and cancer.[13]

The concept of disease burden was first introduced by the World Health Organization (WHO) in 2010, and was used to determine the health status and public health priorities of a population. It was later changed to the burden of individual disease, which assesses disease-related psychological, socio-economic, and physical disability.[14] The Global Burden of Disease (GBD) study by Hay *et al*.[15] has shown that skin diseases are one of the main causes of non-fatal burden worldwide. The concept of burden plays a fundamental role in the evaluation of care, especially in skin diseases.[16] In a study regarding the perceived burden of different rare diseases (NF1, primary sclerosing cholangitis, pulmonary arterial hypertension, and Marfan syndrome), the main problems reported were psychological burden, constraints in professional, personal, and daily life, and stigmatization and lacking understanding.[17] They also experienced problems related to the healthcare system such as limited access to adequate care and lack of knowledge. Despite the differences in their diseases, they had many shared experiences, which may be the cause of their similar burden of disease. However, patients reported aspects that seemed to be specific to rare chronic diseases.[17] Most studies on NF have been limited and only deal with physiological aspects of the disease. Despite its significant impact on various aspects of patients' lives, few qualitative studies are available on NF and no specific study has been conducted in Iran in this regard.[18] Thus, the aim of the present study was to explore patients' perception of the burden of NF in their lives.

Materials and Methods

This qualitative content analysis study (as part of a larger project) was conducted between 2019 and 2020. In this study, in-depth interviews were used for data collection. Furthermore, data analysis was carried out using conventional content analysis method. The participants were selected and enrolled into the study using purposive sampling. Sampling was carried out in Golestan, Mazandaran, Tehran, and Khorasan Provinces of Iran. The participants included 8 men and 10 women with NF within the age range of 20 to 50 years. Single, married, and divorced, employed and unemployed individuals with a primary education level of master's degree were included in the study.

In this study, unstructured, face-to-face interviews were used to collect the data. The duration of the interviews ranged between 60 and 153 minutes (with an average of 78 minutes). It is worth noting that there was a complimentary 15 minute interview. In interviewing the caregivers, the open-ended question asked to the participants was "Please describe a regular day with NF". In addition, during interviews, some probing questions, like "What restrictions has this disease caused for you?", "What did you feel when that happened?", and "What do you do when you feel so?", were asked based on the participants' statements to deepen the interviews. The interviews were recorded with the permission of the participants. Data collection and analysis were performed simultaneously. Data gathering continued until data saturation (when no new data were collected). The inclusion criteria were age of over 18 years, diagnosis of NF and its approval by the Neurofibromatosis Association, awareness of their diagnosis, undergoing treatment for the disorder, disease duration of at least 6 months, and willingness to participate in the study. The first participant was introduced by the Neurofibromatosis Association. Purpose-based sampling was used to add the participants. Data saturation was reached after 16 interviews, but to be certain, 4 additional interviews were conducted. To ensure the rigor of findings, Lincoln and Guba's 4 criteria were used.[19,20] For the credibility of findings, long-term engagement, integration in research, and member check were implemented. In addition, the steps and process of the research were recorded and reported accurately, and step-by-step to the extent possible to ensure the dependability of the findings. For confirmability, the researcher tried to report the results based on the data from the interviews and quotes of the participants, and set aside his assumptions about the phenomenon and the results. In this study, in order to increase transferability, sampling was conducted with maximum variation in terms of sociodemographic characteristics so that the findings could be transferred to a larger population. In this study, 1492 initial codes were extracted from 20 interviews; after merging similar codes, 854 cods were obtained. The obtained codes were categorized into 14 subcategories and 4 main categories. The main categories were also grouped into more abstract concepts called themes [Table 1].

Ethical considerations

This study was approved (IR.GOUMS.REC.1398.231) by the Research Council of Golestan University of Medical Sciences, Iran. Prior to enrollment in the study, sufficient explanation was provided to the participants about the purpose and method of the study, and written informed consents were obtained from them. The participants were also assured of the confidentiality of the data and that they could leave the study whenever they wished.

Results

The results of the present study included 1492 initial extracted codes, and 14 subcategories and 4 categories, including "failing and falling behind in life", "deprivation and restriction", "social isolation", and "ineffective

Table 1: Themes and Subcategories Extracted from Content Analysis

Sub category	Main category
Deprivation of marriage and childbearing	Failing and falling behind in life
Employment failure	
Academic problems	
Restrictions on clothing	Deprivation and restriction
Restrictions on physical activity	
Refraining from others	Social isolation
Loneliness and social rejection	
Disturbed mental self-image	Ineffective adaptation to the disease
Feeling upset about lack of treatment for the disease	
Comparing yourself to others	
Complaining about the disease	
Inferiority complex	
Fear of the unpredictable nature of the disease	
Stigma	

adaptation to disease". The description and interpretation of the results are presented in the following sections using direct quotations from the participants.

Failing and falling behind in life

Problems with the nature and symptoms of the disease impose a high degree of stress on patients. Genetic transmission of the disease and aesthetic and cognitive problems resulting from the disease are factors of failing and falling behind in life. The main category of failing and falling behind in life includes the subcategories of "deprivation of marriage and childbearing," "employment failure," and "academic problems."

The first characteristic of failing and falling behind in life is deprivation of marriage and childbearing. Deprivation of marriage and childbearing is among the factors that double the burden of disease in patients with NF. Patients with NF are deprived of marriage due to fear of transmitting the disease to their child. Moreover, they lose any opportunity of marriage due to their skin condition (masses and spots). *"I would like to get married, but no one understands me. Boys look for beauty in girls and (patients) do not have it due to their masses or spots. I cannot get married due to my eyes or spots"* (P5, Female-21yr).

Another characteristic of failing and falling behind in life is employment failure. Chronic diseases can create some degree of employment limitation for people. Patients with NF reported that they experience employment failure in the form of not finding a job or being fired from a job due to physical limitations and complications, skeletal disorders resulting from the disease and facial changes, and the aesthetic impacts of the disease. *"I interviewed for a job, and the employer told me that he was hesitant because of my face and that he was afraid of losing his customers. I said: "I do not have leprosy; no one is treated like this, not even a person with leprosy. He said: "No, I want someone to attract my customers, not to make them run away"* (P10-Female-37yr). Educational problems are another characteristic of failing and falling behind in life. Most patients with NF experience some degree of learning disability. The existence of learning disorders and slow learning along with the disease manifestations of masses, spots, and skeletal disorders was a factor that caused school dropout or prolonged education period. *"I did not study past the second year of elementary school. I did not continue. I did not have the capacity anymore; whatever I read, nothing stuck in my mind. Now, I cannot learn much; I cannot remember anything at all. I cannot even learn anything new"* (P10-Female-37yr).

Deprivation and restriction

The nature of NF and the resulting social psychological burden create limitations for patients. The themes of "clothing limitations" and " physical limitation" indicate the characteristics of deprivation and restriction due to the disease.

The first characteristic of deprivation and restriction due to the disease was clothing deprivation. One of the challenges NF patients are faced with is the presence of neurofibroma masses and spots on the body and its effect on patients' body image, so that patients have to dress more than usual to cover lesions in visible areas of their body and cannot be well-dressed proportionate to their situation. *"I wish my body was smooth too. I want to wear revealing dresses; forget about revealing dresses, I just want to wear freer and comfortable clothes …"*

"I covered myself from the very beginning, I did not go to birthday parties, or if I did, I would not take off my clothes. Everyone would say: "Are you not comfortable? Why are you not taking off your clothes?" (P10-Female-37yr).

Another characteristic of deprivation and restriction due to the disease was physical limitation. Patients are restricted from engaging in physical activity due to skeletal disorders, organ deformities, and pain caused by mass growth in the nerve pathway. "… *I went to a confectionery workshop; we were applying paint onto sweets. Everyone's hands were quick. I had a mass in my hand and could not really apply paint onto the sweets quickly. Once I tried so hard to paint more sweets, I had hand pain for a few days. I cannot lift heavy objects because my neck and hands hurt. I cannot breathe.I cannot lift any heavy object. Physically, I get tired quickly*." (P2-Female-27yr).

Social isolation

Patients with NF are socially isolated for a variety of reasons. Complications such as facial changes due to visible spots and neurofibromas create an abnormal appearance in the patient that makes it difficult for the patient to communicate with others because they may experience rejection and inappropriate behaviors by relatives, such as

questioning and curiosity about the cause of the disease. Therefore, patients try to limit communication to prevent these behaviors, and if they communicate with others, they may experience loneliness and rejection. Social isolation included the two characteristics of staying away from the patient, loneliness, and social rejection.

The first characteristic of social isolation is staying away from others. The patient tries to avoid attending gatherings to avoid inappropriate reactions due to fear of the probable contagious disease despite the patient's explanation and the unpleasant manifestations of the disease. *"I do not have a relationship with any of their children. You know, I hate them all. It is just a greeting. When we were kids, we used to play. They would taunt me when we went to their houses. Sometimes, I remember what they used to say, I do not like to see them"* (P3-Female-38yr).

Loneliness and social rejection are other characteristics of social isolation. Staying away from the patients due to fear of their disease being contagious or their abnormal appearance led the patient to choose isolation and limit his/her communication with society. *"If cancer has spread, it immediately kills the person, but not this disease. Now I am isolated. They do not look at me. They do not communicate with me. They do not have contact with me both strangers and relatives."* (P18-Male-50yr).

Another participant stated: *"I was on the bus. I sat in the front row. A woman came with her child and sat next to me. Her child said: "Mommy, look at this girl. Why does she look like that?" The mother looked at me, and then, took her child's hand and moved to the back row of the bus. My heart was broken ... "* (P3-Female-38yr).

Ineffective adaptation to disease

In addition to the physical problems, such as difficult conditions resulting from changes in appearance, patients also face the psychological burden of the disease. Thus, they expressed different emotions such as impaired mental image, sadness about the lack of treatment for the disease, comparison of oneself to others, complaints about the disease, inferiority complex, fear of the unpredictable nature of the disease, and stigma.

Feeling upset about self-image is the first characteristic of ineffective adaptation to the disease. Patients form an impaired mental image of their body due to the destructive effects of the disease process. Embarrassment as a negative emotional experience increases the psychological burden of the disease. *"When I take a shower, or go to the bathroom, I am embarrassed; I feel embarrassed when I see myself in the mirror"* (P10-Female-37yr).

Feeling upset about lack of treatment for the disease is another characteristic of ineffective adaptation to the disease. The impact of the disease on various aspects of life and the subsequent mental preoccupation is a factor that leads to frustration and psychological burden of the disease. There is currently no definitive cure for NF. Lack of hope for treatment along with the disease-related problems and its unpredictable conditions have imposed additional pressure on patients. *"The fact that this disease is not treatable bothers me a lot. AIDS can be treated. Cancer can also be treated. Why should our disease not be treatable? Why should we be in torment? It is a torment; you cannot deny it"* (P11-Female-33yr).

Comparing yourself to others is another characteristic of ineffective adaptation to the disease. As a result of interaction in the society, patients feel that they are different from others. Feeling different and loneliness is a factor that causes mental conflict in patients. *"I saw other people being healthy, there was nothing on their bodies, but I am suffering from this disease; that is why I was upset"* (P14-Male-43yr).

"It is as if there is a difference between us and other people; as soon as they see us, they understand that we are different" (P12-Female-26yr).

Complaining about the disease is another characteristic of ineffective adaptation to the disease. Stress due to disease-resulted problems and considering themselves as victims reduced patients' tolerance and resilience in dealing with the disease, and led them to complain. *"... Why me! What sin have I committed? Many human beings have this disease like me"* (P7-Male-26yr).

"I was saying: "God, how could you bear to do this to me?!" I even got into a fight with him and cursed him. What sin have I committed against you? You made me like this, why did you not do this to them, why did you do this to me of all of my female cousins?" (P10-Female-37yr).

Inferiority complex is another characteristic of mental conflict with the disease. Negative adaptation to the disease causes loss of self-confidence. The patient feels deficient and experiences an inferiority complex in dealing with others. A patient expressed the psychological pressure of losing self-confidence as follows: *"I had an inferiority complex in society, which was due to the fact that I did not have self-esteem. I had completely lost my self-esteem due to the disease and I, let us say, experienced failure emotionally"* (P9-Male-34yr).

Another characteristic of ineffective adaptation to the disease is the fear of the unpredictable nature of the disease. Due to the nature of the disease, patients are always worried about the progression and exacerbation of symptoms and, as a result, are afraid of other limitations in their lives. These fears, anxiety, and psychological pressures sometimes engage the patients' mind so much that they cause them to commit suicide. *"I have fear and anxiety that this disease will get worse to the extent that I cannot go out. If I want to go out or I have to go out, I have to cover my face completely"* (P11-Female-33yr).

The last characteristic of ineffective adaptation to the disease is stigma. When they are present in the society and even in the family environment, patients with NF are faced with others' fears regarding contagion, annoying looks, taunts, and ridicule. These experiences suggest that patients with NF, despite being physically ill, have experienced neuroticism and psychologically and socially painful feelings such as stigma. These experiences can increase the psychological burden on them due to the nature of the disease and its symptoms. *"My brother quarrels with me. He makes fun of me. I have this disease. He calls me names, for example, he calls me spotty face. I went to the neighborhood hairdresser, but he did not cut my hair, he said: "I'm afraid the disease will spread to people who come here". They think that the disease is contagious because they do not know anything about it"* (P7-Male-26yr).

Discussion

The aim of the present study was to explain and explore the perceived pressures of patients living with NF. The results show the profound effect of the disease on various aspects of life, which were explained by the themes of "failing and falling behind in life", "deprivation and restriction", "social isolation", and "ineffective adaptation to the disease".

Most rare diseases are genetic, and often chronic, and are associated with physical and mental suffering and medical and social challenges.[21] The results of the present study showed that NF affected all the equations of life, and thus, patients' perception of this disease; perceived social deprivation and deprivation of marriage and childbearing are due to concerns about its genetic transmission to the next generation. Moreover, due to changes in their appearance, skeletal disorders, and learning disabilities, they are deprived of an appropriate job and faced with disease-induced stigma. Skin diseases, as one of the main causes of non-fatal burden worldwide, affect different aspects of the patients' lives.[15] Patients with ectopic dermatitis experience the burden of the disease due to its unpleasant symptoms and outcomes such as itching, pain, sleep disturbances, anxiety and depression, and low QOL and productivity.[22,23] Patients also face psychological, therapeutic, and social challenges due to lack of awareness of health care staff and the society about rare diseases.[24] Participants considered NF to be a life-limiting disease and different from normal life. Concerns about marriage and childbearing were reported by all participants. The results of a systematic review by Von Der Lippe *et al*.[25] on rare diseases such as scleroderma, hemophilia, phenylketonuria (PKU), and Wilson's disease also showed that patients have many limitations in social life such as attracting attention by others due to the apparent obviousness of the disease, physical limitation, and concerns about marriage and childbearing. In the present study, patients expressed dissatisfaction with the limitations caused by the disease and considered them to be a torment. Patients preferred overdressing or unconventional dressing in different situations due to restrictions in clothing because the presence of masses and spots on their skin causes inappropriate reactions in others such as questions and curiosity, taunts, or ridicule. These reactions also limit their presence in the society and communication with others. In addition to the facial manifestations of the disease, patients with NF also face several internal complications, such as skeletal disorders, which lead to limitations in daily life activities. These results were confirmed by previous studies. Rare diseases are associated with physical limitations, which affect various emotional, psychological, and social dimensions of the individual.[26-28]

Barlow *et al*.[29] stated that physical limitations in rare diseases can affect patients' employment and educational conditions. In addition to physical problems, patients with NF suffer from learning disabilities that affect their academic performance.[29] The results of the present study showed that patients with NF, in addition to physical problems, experience a large amount of psychological conflict with the disease. These problems cause limitations, unpredictable conditions, uncontrollable progression of the disease, anxiety, and fear of the future. Furthermore, disease-related aesthetic changes are factors that disrupt the patients' body image and make them feel embarrassed of their body. Moreover, considering their distinct conditions, patients compare themselves with others, feel deficient, form an inferiority complex, lose self-confidence, feel tormented, and complain about the stigma resulting from the disease. In a study on the psychological burden of NF on adult patients, Granström *et al*.[18] also showed that these patients had a more negative image of their body than other patients with skin problems. This finding has been confirmed in other studies on the QOL and psychological disorders of NF patients.[30,31] This means that patients' experience of and feeling about their bodies is one of the most important aspects that can help us to understand why people with facial deformity are psychologically stressed.[10] In NF patients, the visible symptoms are continuously progressive, unpredictable, and uncontrollable, which can explain the severity of the negative body image in NF patients.[18]

NF is associated with low self-esteem and poor QOL.[32] Most rare and chronic diseases are associated with high severity of physical symptoms, decreased life expectancy, anxiety and depression, and reduced QOL. The rare nature of the disease can lead to lack of contact with peers and feelings of isolation[33,34] and these pressures can be dangerous to a person's mental health. In a qualitative study, a high percentage of patients with rare diseases showed an increase in depression and anxiety symptoms.[35]

Another experience of NF patients was perceived stigma and discrimination due to visible (spot and skin mass)

and invisible symptoms (learning disorder). The results of the study by Shpigelman and HaGani also showed that even non-visible disability, such as psychiatric disabilities (mental diseases), may affect a person's feelings and thoughts due to the stigma associated with mental disabilities. These findings suggest that healthcare services should be modified to meet the psychological needs of people with different types of disabilities.[36] There were some limitations which can affect the transferability of the findings obtained in the present study. First, the participants of the present study were those introduced by the Iranian Neurofibromatosis Society. If the sample selected for the study included patients who were not members of the Iranian Neurofibromatosis Society, the analyses may have resulted in different findings in that the non-members might have had experiences different from those reported by the participants of the present study.

Conclusion

This study showed due to the distinctive living conditions of patients with NF, which result in failing and falling behind in life, they do not have the conditions to be present in society and experience social isolation. Moreover, physical problems caused by the disease restrict patients' activities and impose a heavy burden on them.

Participants' experiences suggest that people with rare disorders face challenges beyond physical problems. Many challenges can be alleviated by raising public awareness of rare genetic diseases, focusing on patients' mental health, and providing solutions for coping with the disease. These findings illustrate the need for further research on the psychological and social impact of living with a rare disease in order to improve the patients' physical and mental QOL.

Acknowledgements

This study is part of the PhD dissertation of the first author. The authors sincerely thank the board of the Iranian Neurofibromatosis Supportive Association and all the neurofibromatosis patients who shared their valuable experiences in this study.

Financial support and sponsorship

Golestan University of Medical Sciences

Conflicts of interest

Nothing to declare.

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