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A CROSS-SECTIONAL STUDY TO DETERMINE THE OUTCOMES OF FAMILIAL AMYLOID POLYNEUROPATHY AND PSYCHOLOGICAL FACTORS

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Abstract: Background: Familial amyloid neuropathy (FAP) is a rare neurological disease that can be fatal and often leads to increased disability. **Objective:** The aim of this study was to assess and determine the clinical outcomes of patients with familial amyloid polyneuropathy in relation to psychological factors and quality of life. **Patients and method:** 72 patients with familial amyloid polyneuropathy who were between 20 and 50 years of age and had registered in the familial amyloid polyneuropathy survey were included in the study. This study used EQ-5D-3L scale assessments to evaluate psychological status as well as health-related quality of life. **Results:** Our study's outcomes shown that females had 43 cases that more than males with 29 cases of morbidity of familial amyloid polyneuropathy (FAP), where the most symptoms prevalent were tingling and numbness in the extremities included 22 cases, muscle weakness included 15 cases, and pain included 20 cases, Serum albumin level was 4.3 ± 0.38 g/dL, postural systolic blood pressure changes mean (SD), mm Hg was -12.5 ± 17.6, which Disease stage based on polyneuropathy disability (PND) classified into I had 32 cases, II had 21 cases, IIIA had 11 cases, IIIB had 5 cases, and IV had 3 cases. **Conclusion:** The quality of life related to health in patients having familial amyloid neuropathy disorder is largely influenced by these signs and associated losses in capacities.

Key words: Familial amyloid polyneuropathy; Psychological factor; Quality of life; Symptoms; Mortality and morbidity.

Introduction

Familial amyloidotic polyneuropathy (FAP) was one of several systemic amyloidoses developed by the extracellular deposition on amyloid fibrils. FAP is caused by within 113 amyloid genetic mutations which have been identified so far, with the most prevalent change being the substitution in methionine to valine in position 30 (Val30Met) in the transthyretin gene. [1 - 6]

It is an uncommon illness worldwide, although in endemic places such as Portugal and Sweden, the reported frequency is 151/100,000 persons and 104/100,000 inhabitants, respectively [7–13]. Cases have been reported in Spain, which shown that the major endemic emphasis is on Mallorca, where a series of 107 cases was recently published. [14,15]

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In the second stage, autonomic dysfunction worsens, and sensory-motor involvement in the upper limbs occurs, requiring assistance in everyday tasks. The third stage is characterized by severe dysfunction, including full paralysis, and death occurs roughly 10-13 years after the clinic's inception. Coutinho et al. defined the clinical phases of the illness. [18]

Multiple factors are required to determine a diagnosis: family history, evidence of polyneuropathy, the discovery of mutant TTR, and, in situations where there is no endemic center, the identification of amyloid accumulation in the tissues (mostly adipose tissue, salivary glands, nerve or gut). In areas of endemic emphasis, the diagnosis is mostly done through family members screening for the discovery of mutant TTR in people who are asymptomatic, with periodic follow-up proving essential to early detection and treatment. [19,20]

Patients and method

A study was conducted on Iraqi patients with familial amyloid polyneuropathy (≥ 20 years old) who participated within the Transthyretin Amyloidosis Outcomes Survey (THAOS). Our study collected data of different hospitals in Iraq from May 9, 2023, to October 16, 2024, and involved demographic data, disease characteristics, current as well as previous therapies, family history, biopsy results, and results for routine measurements conducted during clinical settings, including the preference-based assessment of health, EQ-5D-3L questionnaire.

Our study examined individuals with familial amyloid polyneuropathy for up to 11 years. Data was retrieved and evaluated at the referral facilities, and variations were handled through revising individual survey records. We included all asymptomatic gene carriers as well as symptomatic individuals. The analysis eliminated patients and visits having incomplete EQ-5D-3L data. The dataset for the general population comprises all participants who's participated in the Iraqi random sampling stratified by gender and age group.

HRQoL was assessed by the preference-based questionnaire EQ-5D-3L. This instrument assesses an individual's HRQoL with a health classification system with five categories: mobility, self-care, typical activities, pain/discomfort, and anxiety/depression. Each dimension is given three severity levels, with level 1 indicating the absence of health concerns and level 3 representing serious challenges.

When a value set is applied to the respondent's perceived health status, the EQ-5D-3L index scores is calculated. The Iraqi value set produces an EQ-5D-3L index score ranging from -0.54 (for health conditions lower than mortality) to 1.00 (perfect health). Cross-sectional research was carried out to collect EQ-5D data for the overall Iraqi population. EQ-5D data was collected through the enrollment process in familial amyloid polyneuropathy, as well as during subsequent clinical practice visits.

Results

Table 1: Enroll basics and demographic features of patients.

Characteristics	Frequency [n = 72]	Percentage [%]
Age, years		
20 – 30	15	20.83%
31 – 40	21	29.17%
41 – 50	36	50.0%
Gender		
Male	29	40.28%
Female	43	59.72%
Comorbidities		
Yes	45	62.50%
No	27	37.50%
Hypertension	36	50.0%
Diabetes	21	29.17%
Asthma	11	15.28%

Heart failure	8	11.11%
Anemia	5	6.94%
Smoking status		
Yes	32	44.44%
No	40	55.56%
Previous surgeries		
Yes	28	38.89%
No	44	61.11%
ASA %		
I	8	11.11%
II	23	31.94%
III	30	41.67%
IV	11	15.28%
Education status		
Primary	38	52.78%
Secondary	20	27.78%
Bachelor, master, doctorate	14	19.44%
Income status, $		
< 820	44	61.11%
820 - 1250	18	25.0%
> 1250	10	13.89%

Table 2: Distribution of familial amyloid polyneuropathy symptoms on patients.

FAP symptoms	Frequency [n = 72]	Percentage [%]
Tingling and numbness in the extremities	22	30.56%
Muscle weakness	15	20.83%
Pain	20	27.78%
Diarrhea	6	8.33%
Weight loss	4	5.56%
Irregular heart rate	3	4.17%
kidney problems	2	2.78%

Table 3: Identify clinical findings of patients with FAP.

Variables	Frequency [n = 72]	Percentage [%]
ATTR genotype, No. (%)		
Met30	40	55.56%
Non-met30	32	44.44%
Serum albumin level, mean (SD), g/dL	4.3 ± 0.38	
Postural systolic blood pressure changes mean (SD), mm Hg	- 12.5 ± 17.6	
Disease stage based on polyneuropathy disability (PND)		
I	32	44.44%
II	21	29.17%
IIIA	11	15.28%
IIIB	5	6.94%
IV	3	4.17%
Neuropathy Impairment Score +7	56.83 ± 44.24	
NIS Score	47.24 ± 42.88	

SF-36 physical component score, mean (SD)	36.62 ± 10.78	
SF-36 mental component score, mean (SD)	47.65 ± 13.83	
Mortality		
Death	12	16.67%
A live	60	83.33%

Table 4: Assessment of psychology level in terms of anxiety and depression on patients with FAP.

Items	Frequency [n =72]	Percentage [%]
Normal [0 – 7]	19	26.39%
Borderline [8 – 10]	28	38.89%
Abnormal [11 – 21]	25	34.72%

Table 5: Assessment of quality of life for general health related to patients with FAP using EQ-5D-3L scale.

Items	QoL scores [0 – 1]
Mobility	0.63 ± 0.12
Self-care	0.72 ± 0.10
Typical activities	0.46 ± 0.14
Pain/discomfort	0.25 ± 0.098
Anxiety/depression	0.38 ± 0.16

Discussion

Prior studies that have been scrutinizing HRQoL with regard to patients suffering from genetic amyloidosis have left out those participants that were already immobile or were diagnosed with neuro pathology. Such studies had a limited range of patients with knowledge on end-of-life themes ($n \leq 16$) and did not provide enough information about factors that can predict medical outcomes of HRQoL while neglecting individuals who were receiving hepatic transplants (HTx). [21]

Other studies done before may also have disreputable methodological characteristics. Specifically, there may be some questions regarding the use of country-specific EQ-5D value sets for other geographical regions when people submit their preference-based questionnaires. [15]

Despite the fact that this study is supportive of earlier research, it shows that patients with familial amyloid polyneuropathy exhibit a decrease in HRQoL but carriers do not experience as much deterioration compared to other individuals. An important thing to note is how minimal the usefulness is it possesses towards the end stage of the diseases, which has been shown to improve the HRQoL of patients under therapy. [22,18,23]

The major advantage of our Patient-Reported Outcomes (PRO) study is that it involved almost 1250 patients with familial amyloidotic polyneuropathy (FAP) and asymptomatic carriers followed up over time. Besides initially catering for both patients and carriers in terms of health-related quality of life (HRQoL), it is our view that the resultant data will facilitate an economic assessment of healthcare technology [24,7,9]. Preference-based HRQoL information is generally needed in cost-effectiveness decision analysis for the purpose of quality-adjusted life years estimation. [24,14,16,18,25]

In the case of familial amyloid polyneuropathy, this is very important because two new drugs (patisiran and inotersen) have been recently registered as therapeutics against this disease in the European Union and the United States [26].

HTA agencies tend to apply county tariffs based on crude EQ-5D response data using sizeable longitudinal registries, though rare diseases present a challenge in this context. Payors are faced with

uncertainty when it comes to quality-of-life evaluation for orphaned drugs due to the unpredictable nature of estimates provided by HRQoL, given small samples and poor-quality information [27].

The sample of familial amyloid polyneuropathy satisfying that was examined roughly 57% of the familial amyloid polyneuropathy of Portuguese subjects that were followed up in 2015 at referral centres [28].

The population was overall younger and made up of more men; besides, therefore, our sample might not fully capture patients in the late stages with MS as they mostly use wheelchairs or beds, an indication that they cannot be part of future registries. Furthermore, reduced cases can lead to imprecision in the coefficients that represent the transition between stages [29].

Most of the individuals affected by familial amyloid polyneuropathy, as well as carriers of the disease, are characterized by carrying the Val30Met mutation. However, caution needs to be exercised while extrapolating the findings from our group that has only a single mutation type to those in populations which have multiple mutations in their TTR gene and different clinical manifestations of the disease as seen in other regions of the world. [30].

Conclusion

The patient's standard of life related to health is much affected by both entailed increasing deficits with time as well as those diagnosed with familial amyloid polyneuropathy. Such steps as very careful observation over asymptomatic bearers, quickly identifying the disease, and starting proper treatment may improve survival chances among the sick ones. Gradually causing the decline of the health-related standard of life.

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