Correlation of X-Linked Dystonia-arkinsonism Severity to the Quality of Life of Primary Caregivers in an Outpatient Clinic in the Philippines

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Abstract

X-linked dystonia-parkinsonism (XDP) is an inherited, progressive movement disorder characterized by a combination of dystonia (involuntary muscle contractions that cause repetitive movements or abnormal postures) and parkinsonism (symptoms similar to Parkinson's disease, such as tremors, rigidity, and bradykinesia). Patients in advanced stages of XDP become dependent upon family members and require permanent help from caregivers. This leads to a decrease in the quality of life of caregivers.

The primary objective of this study was to investigate the impact of X-linked dystonia Parkinsonism (XDP) severity of patients being seen at an outpatient clinic in the Philippines on the quality of life (QoL) of patients' respective primary caregivers.

The study demonstrated a strong negative correlation between disease severity and caregiver well-being. The significant associations with lifestyle factors such as diet and physical activity further emphasize the need for comprehensive support systems addressing both medical and psychosocial needs.

INTRODUCTION

X-linked Dystonia Parkinsonism leads to considerable social and economic consequences. It is well known that a chronically disabled person may often distort and disorganize the life of the entire family and disrupt the existing balance among them. Patients in advanced stages of the disease become dependent upon family members and require permanent help from the caregivers, resulting in a declining former professional life, and abilities to manage the household and to perform self-care. The need for permanent care and help to the chronically disabled person leads to a decrease in the quality of life of caregivers.

BACKGROUND / SIGNIFICANCE OF THE STUDY

There have been numerous studies written on the impact of Parkinson's disease on the lives of caregivers, but as of yet, there are currently no known studies on the impact of X-linked Dystonia Parkinsonism on the quality of life of caregivers. In conducting this study, the investigators hoped to highlight the social value of caregivers and their role in the care of the XDP patient.

OBJECTIVES OF THE STUDY

General Objectives

This study aimed to investigate the impact of X-linked dystonia Parkinsonism (XDP) severity of patients being seen at the Makati Medical Center from April 2024 to July 2024 on the quality of life (QoL) of patients' respective primary caregivers.

Specific Objectives

1. Describe the clinical and sociodemographic characteristics of XDP patients and their respective primary caregivers,
2. Describe the XDP severity of patients in the study,
3. Describe the QoL of primary caregivers in the study,
4. Determine the correlation between the XDP severity of patients being seen at the Makati Medical Center from April 2024 to June 2024 measured by XDP-MDSP on the QoL of patients' respective primary caregivers measured by Scale of Quality of Life of Caregivers (SQLC), and
5. Determine the association between XDP severity of patients being seen at the Makati Medical Center from April 2024 to June 2024 measured by XDP-MDSP on the QoL of patients' respective primary caregivers measured by SQLC while controlling for possible confounders.

REVIEW OF RELATED LITERATURE

X-Linked Dystonia Parkinsonism

X-linked dystonia-parkinsonism (XDP), locally known as "Lubag" is a progressive neurodegenerative disease affecting mainly male Filipinos. It is an adult-onset, sex-linked, predominantly male, progressive movement disorder with high penetrance and a high frequency of generalization (Lee et al., 2011; Rosales, 2010). As of February 2010 in the latest XDP registry by Lee and cohorts, there are now 505 cases from 253 families in the registry, and the prevalence of XDP in the Philippines is at 0.31 per 100,000. Currently, there are no published studies on the prevalence of XDP specifically worldwide, however, in a study by Steeves, et al in 2012, the prevalence of primary dystonia worldwide is at 16.43 per 100,000.

Quality of Life and Caregiver Burden

Most chronically ill subjects are cared for by an informal support system comprising relatives, friends, or other non-professional caregivers. Caring for patients with chronic and disabling diseases means that these types of caregivers bear physical and psychological distress, limitations on their personal and social activities, as well as a financial burden.

The consequences, not only for individuals but also for the healthcare system, of the impact exerted by chronic patients on caregivers, merit attention for several important reasons. An example of this is the fact that the caring capacity of such informal caregivers tends to be a key factor in determining the institutionalization of patients. This is because family caregivers will usually only place patients in a long-term institution when their caring capacity is overwhelmed by the physical, emotional, or economic load. Furthermore, the distress caused by looking after disabled friends and relatives may have major adverse consequences for caregivers' physical and psychological health.

In a study by Martin et al in 2005, caregivers should be assessed to identify the characteristics of and factors associated with the strain that they are experiencing. Knowledge of this type may help design effective interventions targeted at improving caregiver distress. Alleviating the burden and thereby allowing for a better caregiver quality of life, will lead to an ensuing extension of patients' permanency at home and a better quality of care.

In the advanced stages of the disease, patients with XDP present with diverse degrees of disability resulting from physical and mental impairment. As a consequence, persons closest to XDP patients are burdened with a strain derived from their role as caregivers of patients with progressive disease.

The XDP-MDSP Rating Scale

Pasco et al., in cooperation with the Movement Disorder Society of the Philippines (MDSP), developed the XDP-MDSP Rating Scale, validated in 2017, to utilize it for clinical and research purposes. This validated scale was developed in the hopes that it will be useful to clinicians who manage patients with XDP and clinical researchers who test the effects of various interventions for uniformity in their assessments.

This scale is designed to rate the severity of dystonic, parkinsonian, and non-motor symptoms in patients with X-linked Dystonia Parkinsonism (XDP; DYT-3; Lubag) and their effect on activities of daily living. The ratings depend on using all available information, which is generally provided through the patient’s and caregiver’s report and the clinical interview.

The Scale of Quality of Life of Caregivers (SQLC) Questionnaire

The need for permanent care and help to be given to the chronically disabled person leads to a decrease in the life quality of caregivers. The Scale of Quality of Life of Caregivers (SQLC) questionnaire was developed by Glozman et al in 1998 to evaluate caregivers of patients living with Parkinson’s Disease. The contribution describes an inventory for evaluating the quality of life of Parkinsonian patients’ caregivers and analyzes some factors determining their social disadaptation.

The questionnaire revealed a correlation between the caregivers’ dissatisfaction with their quality of life and the level of their input in helping the patient with everyday living. These results were dependent upon the degree of disability of the Parkinsonian patients, as revealed by neurological and neuropsychological assessment, disease duration and form, subjects’ age, education, and family position.

METHODOLOGY

Participants were extracted from a pool of known gene-positive X-linked dystonia-parkinsonism patients and their caregivers AND previously consulted at the movement disorder clinic of Makati Medical Center and a stable non-professional caregiver. From the list of XDP patients currently being seen at the Movement Disorders Clinic of Makati Medical Center, the investigator reached out via Viber message if the participants were willing to participate in the study. If they consented, an informed consent form was provided for them to sign and send back to the investigator.

An agreed-upon time for the Viber interview was set by the investigator and patient as well as the caregiver. The researcher acquired consent from patients and caregivers qualified to be included in the study. They were contacted through the Viber video conferencing method.

After acquiring basic information about the patient and their caregiver, the XDP-MDSP Rating scale was administered to the XDP patient by the researcher through the teleconferencing method. Only one caregiver per XDP patient was interviewed in a 1:1 ratio. Afterward, the SQLC questionnaire was administered to the caregiver to assess the quality of life of the caregiver.

RESEARCH DESIGN

Study Design

This research employed a cross-sectional, analytical study design examining the relationship of XDP severity of patients being seen at the Makati Medical Center from April 2024 to July 2024 measured by

XDP-MDSP on the Quality of Life (QoL) of patients' respective primary caregivers measured by the Scale of Quality of Life of Caregivers (SQLC) Questionnaire.

Recruitment

From the list of XDP patients currently being seen at the Movement Disorders Clinic of Makati Medical Center, the investigator reached out via Viber message if the participant would like to participate in the study and an informed consent form was sent to them if they consented.

Study Participants

XDP patients and their primary caregivers were the target population of the study. Sampling population included only XDP patients being seen at the Movement Disorders Clinic of Makati Medical Center from April 2024 to July 2024 with their respective primary caregivers. Ratio of patient to caregiver was set to 1:1 to minimize the effect of interdependence of QoL of scores among caregivers coming from the same XDP patient. There were two sets of inclusion and exclusion criteria for the study: one for the XDP patients and another for their primary caregivers.

'Caregiver' was operatively defined as the person who usually cohabited with the patient and who was in some way directly involved in the patient's care or impacted by the patient's health problem (even though the patient was not in need of care). Patients were community-dwelling, thus excluding professional caregivers and carers belonging to social support networks. Pairs were included in the study on the condition that both patients and their respective main caregivers were literate ('able to read, understand and answer the questionnaires').

Inclusion criteria for XDP patients:

a. Patient being seen at the Movement Disorders Clinic of Makati Medical Center from April 2024 to July 2024,
b. Patient diagnosed with XDP certified by neurologists with competence in movement disorders,
c. Patient 18 years old and above,
d. Patient who agreed to be included in the study using a consent form.

Exclusion criteria for XDP patients:

a. Patient with missing or miscoded data,
b. Patient without primary caregivers,
c. Patient with comorbidities that may affect severity of XDP scores (e.g. diabetes, cardiovascular disease, anxiety, clinically diagnosed with anxiety or depression, cancer, anemia), and
d. Patient who refused to continue with the study.

Inclusion criteria for XDP patient's primary caregiver:

a. Primary caregiver currently taking care of and cohabitating with the diagnosed XDP patient for at least one year as of date of answering questionnaire,
b. Primary caregiver 18 years old and above,
c. Primary caregiver cohabitating with XDP patients, and
d. Primary caregiver who agreed to be included in the study using a consent form.

Exclusion criteria for XDP patient's primary caregiver:

a. Primary caregiver deemed as professional caregivers and carers belonging to social support networks,
b. Primary caregiver with missing or miscoded data,
c. Primary caregiver with comorbidities that may affect Quality of Life (QoL) scores (e.g. COPD, diabetes, cardiovascular disease, clinically diagnosed with anxiety or depression, cancer, anemia), and
d. Primary caregiver who refused to continue with the study.

Interview

The interview was done via Viber teleconsult. A short history and physical examination over teleconsult was done. The XDP-MDSP rating scale was conducted by the investigator via teleconsult. As the "rigidity" component could not be assessed over teleconsult, this was subtracted from the total XDP-MDSP score.

After conducting the XDP-MDSP score, the primary caregiver was interviewed separately from the XDP patient in order to assess their SQLC score. The investigator asked the primary caregiver about the details of the SQLC and the data was encoded and tabulated.

STATISTICAL ANALYSIS

Descriptive statistics was done using means and standard deviation for continuous variables while frequencies and percentages for categorical variables. Pearson correlation was used to examine the relationship between XDP severity of patients being seen at the Makati Medical Center from April 2024 to July 2024 measured by XDP-MDSP on the QoL of patients' respective primary caregivers measured by SQLC. T-test was used to test the statistical significance of such correlation. Univariate linear regression was used to determine initial relationship of QoL of primary caregivers with XDP severity of patients and possible confounders. On the other hand, multiple linear regression analysis was used to analyze the association between QoL of primary caregivers and XDP severity of patients while controlling for probable confounders. Z-test was used to test for the significance of regression coefficients. Level of significance was set to a=5% for all hypotheses testing.

WITHDRAWAL OR DISCONTINUATION CRITERIA

Participants were allowed to withdraw or discontinue from the study at any point.

DURATION

The duration of the study was from April 2024 to July 2024.

ETHICAL CONSIDERATIONS/VULNERABILITY

The study was conducted after obtaining approval from the Institutional Review Board (IRB). The protocol was implemented in accordance with the ethical principles of the Declaration of Helsinki and the National Ethics Guidelines for Health Research.

RESULTS

The total number of participants was 35 pairs of XDP patients and caregivers. Males consisted of 100% of the patient population, while females consisted of 100% of the caregiver population. For the patient related variable shown in Table 1, mean age at onset of XDP was at 38.34 (SD = 6.77) and the mean age at evaluation was at 43.40 (SD = 7.01). The mean duration of XDP in years was at 5.06 years (SD = 3.26).

Table 1. Descriptive statistics of patient-related variables.

Patient Variable	Mean	SD	Min	Max
Age at onset of XDP	38.34	6.77	26	50
Age at evaluation	43.40	7.01	31	60

Duration of XDP	5.06	3.26	1	16
Physical Measurements	**Mean**	**SD**	**Min**	**Max**
Body Weight (kg)	66.46	5.12	48	72
Height (cm)	166.66	4.61	159	180
BMI	23.94	1.85	17.63	28.13
Sex	**N = 35**		**Percentage**	
Male	35		100%	
Female	0		0%	
Comorbidities				
Hypertension	1		2.86%	
Type 2 Diabetes Mellitus	0		0%	
Dyslipidemia	0		0%	
Educational Attainment				
Elementary Level	0		0%	
High School Level	13		37.1%	
College Level	22		62.9%	
Post-Graduate	0		0%	
Vocational	0		0%	

For the caregiver data, shown in Table 2, all caregivers are female. Caregivers' ages range from 30 to 58, averaging 42.26 years. The majority (71.4%) are wives of the patients. Most caregivers (65.7%) have a high school level of educational attainment.

Table 2. Descriptive statistics of caregiver-related variables.

Caregiver Variable	**Mean**	**SD**	**Min**	**Max**
Age of caregiver	42.26	6.46	30	58
Years of Being caregiver	5.09	3.23	1	16
Sex	**N = 35**		**Percentage**	
Male	0		0%	
Female	35		100%	

Relationship to Patient		
Wife	25	71.4%
Aunt	2	5.7%
Partner	3	8.6%
Sister	5	14.3%
Educational Attainment		
Elementary Level	0	0%
High School Level	23	65.7%
College Level	12	34.3%
Post-Graduate	0	0%
Vocational	0	0%

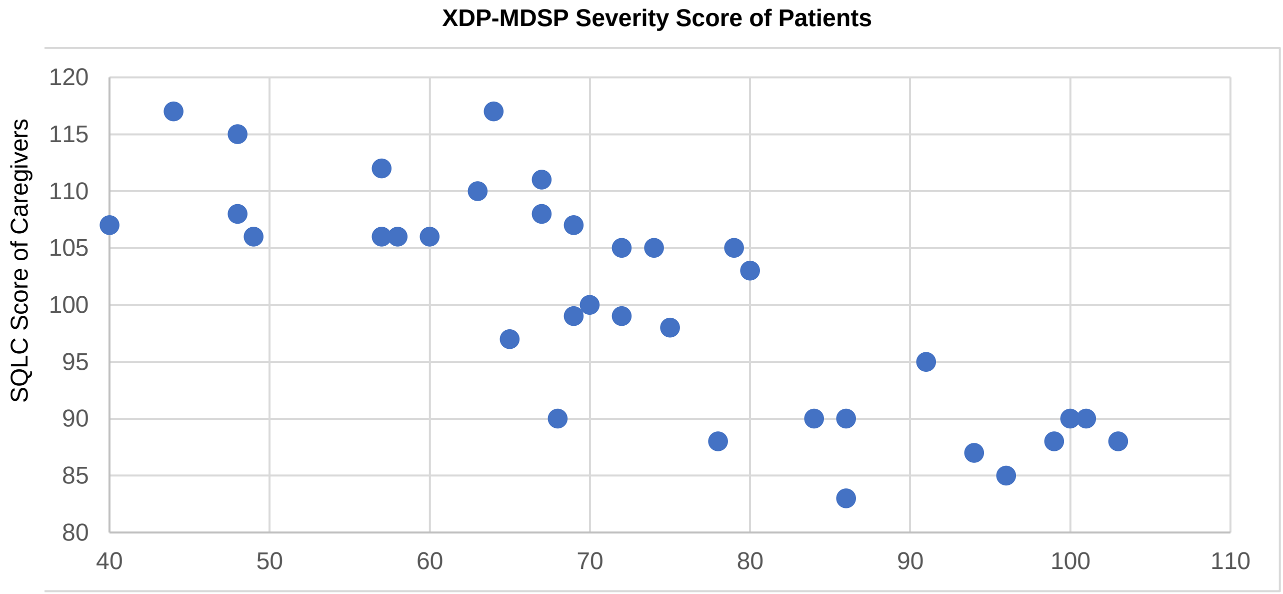

Figure 1. Correlation of XDP-MDSP Score and the SQLC Score of Caregivers

For the correlation of XDP-MDSP severity score and SQLC score, a correlation coefficient of −0.81 is seen, indicating a strong negative correlation between the XDP-MDSP Score and the SQLC Score of the Caregiver. This means that as the XDP-MDSP Score increases (indicating more severe symptoms and greater disability), the SQLC Score of Caregiver (indicating quality of life) tends to decrease, shown as a downward slope in Figure 1. This suggests that more severe symptoms in patients are associated with a lower quality of life for caregivers.

Overall, this strong negative correlation highlights the significant impact that the severity of XDP symptoms in patients has on the well-being of their caregivers.

Table 3. Multiple regression analysis of XDP-MDSP Score and SQLC Score controlling for confounders.

Predictor	**Coefficient**	**Std. Error**	**Z – score**	**P – value**	**Significant at 5%**
Intercept	138.4158	15.907	8.7016	< 0.0001	**Yes**
XDP-MDSP Score	-0.4243	0.088	-4.8069	< 0.0001	**Yes**
Age of Patient at Evaluation	-0.1063	0.146	-0.7272	0.4671	No
Duration of XDP (years)	-0.1118	0.514	-0.2173	0.8279	No
BMI	-0.5936	0.571	-1.0387	0.2989	No
Hypertension (Yes)	-3.9361	3.605	-1.0917	0.2749	No
Smoker (Previous smoker)	-1.2704	2.731	-0.4652	0.6418	No
Alcohol intake (Occasional)	-1.5405	2.468	-0.6242	0.5325	No
Alcohol intake (Previous alcoholic beverage drinker)	-8.4273	3.501	-2.4070	0.0161	**Yes**
Diet (Regular diet as tolerated)	12.8056	5.469	2.3415	0.0192	**Yes**
Diet (Soft diet)	12.5793	4.174	3.0136	0.0026	**Yes**
Physical Activity (Highly Active (3-4 hr))	-3.9361	3.605	-1.0917	0.2749	No
Physical Activity (Sedentary <1 hr)	12.7347	4.061	3.1359	0.0017	**Yes**
Educational Attainment (High School Level)	2.5283	1.967	1.2852	0.1987	No

Multiple regression analysis was done shown in Table 3, controlling for possible confounders. r^2 was calculated at 0.835, indicating approximately 83.5% of the variance in the SQLC Score of the Caregiver can be explained by the model, which included the XDP-MDSP Score and the confounders. The coefficient for the XDP-MDSP Score: -0.4243, meaning for every one-unit increase in the XDP-MDSP Score, the SQLC Score of Caregiver is expected to decrease by approximately 0.4243 units, holding all other variables constant.

In controlling for confounders, a history of alcohol intake showed a significant negative relationship (coef: -8.4273, p-value: 0.025), regular diet as tolerated, showed a significant positive relationship (coef: 12.8056, p-value: 0.029), soft diet showed a significant positive relationship (coef: 12.5793, p-value: 0.006) and physical activity (Sedentary <1 hr) showed a significant positive relationship (coef: 12.7347, p-value: 0.005).

This meant that caregivers of patients with a history of alcohol intake tend to have significantly lower QoL while caregivers of patients with regular diet as tolerated and soft diet tend to have significantly higher QoL. Interestingly, caregivers of patients with sedentary physical activity tend to have significantly higher QoL.

Other confounders such as the Age of Patient at Evaluation, Duration of XDP, BMI, and the rest of the categorical variables did not show statistically significant relationships with the SQLC Score of Caregiver in this model.

The mean XDP score of the 35 XDP patients was 72.37 (range 40-103). For the caregivers, the mean SQLC score was 100.31 (range 83-117). Distribution of SQLC scores by degree of disease severity based on the XDP-MDSP severity scale showed a significant downward trend, indicating significantly worse QoL among caregivers as the severity of the disease among patients rose (p-value <0.0001).

The multiple linear regression analysis confirms that the severity of XDP has a significant negative impact on the QoL of primary caregivers, even when controlling for various potential confounders. Additionally, certain lifestyle factors such as diet and physical activity levels also significantly influence caregiver QoL.

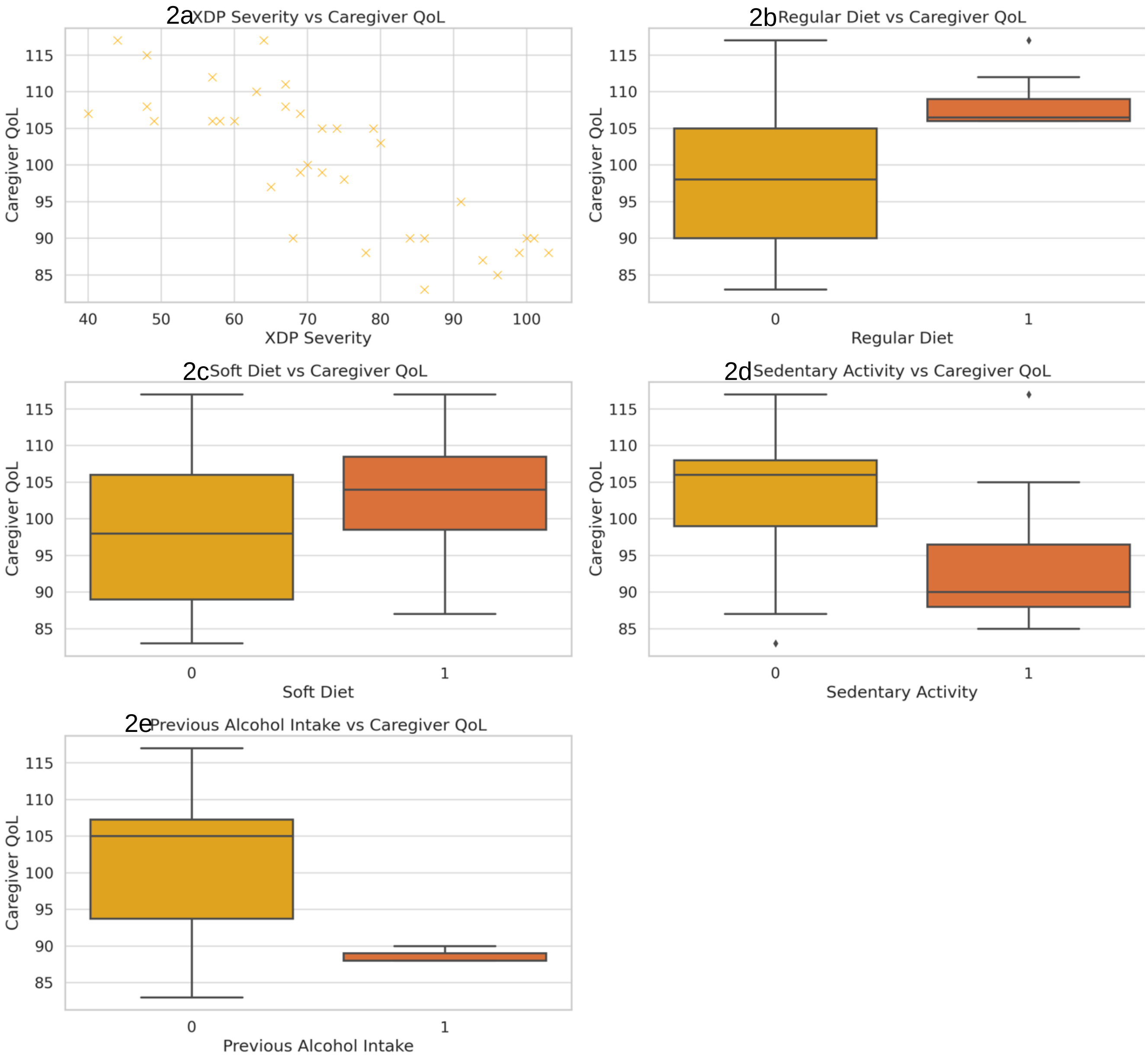

Figure 2a - 2e. Relationships between Caregiver QoL and Key Predictors

Shown in Figures 2a through 2e are the relationships between Caregiver Quality of Life and Key Predictors. In Figure 2a, XDP Severity vs Caregiver QoL**,** a scatter plot shows a negative correlation between XDP severity (XDP-MDSP Score) and caregiver QoL. In Figure 2b, Regular Diet vs Caregiver QoL, a box plot illustrates that caregivers of patients on a regular diet as tolerated tend to have a higher QoL. In Figure 2c, Soft Diet vs Caregiver QoL**,** a box plot shows that caregivers of patients on a soft diet also tend to have a higher QoL. In Figure 2d, Sedentary Activity vs Caregiver QoL, a box plot indicates that caregivers of patients with sedentary physical activity tend to have a higher QoL. Finally, in Figure 2e, Previous Alcohol Intake vs Caregiver QoL, a box plot reveals that caregivers of patients with a history of alcohol intake tend to have a lower QoL.

DISCUSSION

Clinical and Sociodemographic Characteristics

The study included 35 XDP patients with a mean age of onset at 38.34 years and an average disease duration of 5.06 years. Notably, the majority of patients did not present with significant comorbid conditions such as hypertension, diabetes mellitus, or dyslipidemia. XDP, in general, is not known to come in tandem with any comorbidities. Lifestyle factors revealed that most patients were non-smokers and engaged in varying levels of physical activity, with a substantial number adhering to a regular diet as tolerated. Caregivers were exclusively female, predominantly wives of the patients, with an average age of 42.26 years and a mean caregiving duration of 5.09 years.

All of the caregivers were female, be it the XDP patient's wife, sister, aunt, or partner. It has been shown that women are more likely to be caregivers of patients with chronic diseases. In a study by Sharma, et al in 2016, it has been suggested that there are several societal and cultural demands on women to adopt the role of a family caregiver. Stress-coping theories propose that women are more likely to be exposed to caregiving stressors, and are likely to perceive, report, and cope with these stressors differently from men. Many studies, which have examined gender differences among family caregivers of people with mental illnesses, have concluded that women spend more time providing care and carrying out personal-care tasks more often than men. These studies have also found that women experience greater mental and physical strain, greater caregiver burden, and higher levels of psychological distress while providing care.

XDP Severity and Caregiver Quality of Life

The severity of XDP, measured using the XDP-MDSP score, exhibited significant variability among patients, reflecting the heterogeneous nature of the disease. Caregiver QoL, assessed using the SQLC score, ranged from 83 to 117, with a mean score of 100.31, indicating considerable variability in caregiver experiences and challenges.

A robust negative correlation (correlation coefficient = -0.81) was observed between XDP severity and caregiver QoL, suggesting that as XDP symptoms worsen, the QoL of caregivers declines significantly. This relationship was further substantiated by regression analysis, which indicated that a one-unit increase in the XDP-MDSP score corresponds to a decrease of approximately 0.4243 units in the SQLC score, holding other variables constant ($p\text{-value} < 0.001$).

Since XDP is a chronic and progressive disorder, with components of physical and mental impairment and disability, the importance of the caregiver's role in looking after XDP patients has gradually become recognized. The findings highlight the substantial burden placed on caregivers and the diverse challenges they face. Attention should therefore be given to identifying factors influencing caregiver burden and distress.

Influence of Confounding Variables

The study also examined the potential influence of various confounding variables, including patient age at evaluation, duration of XDP, BMI, hypertension, diabetes mellitus, dyslipidemia, smoking status, alcohol intake, diet, physical activity, and educational attainment. Findings showed that:

- **Diet:** Caregivers of patients on a regular diet as tolerated (coefficient = 12.8056, p-value = 0.029) and those on a soft diet (coefficient = 12.5793, p-value = 0.006) reported higher QoL.
- **Alcohol intake:** Previous alcohol consumption by patients was associated with significantly lower caregiver QoL (coefficient = -8.4273, p-value = 0.025).
- **Physical Activity:** Sedentary physical activity levels in patients correlated with higher caregiver QoL (coefficient = 12.7347, p-value = 0.005).

These findings underscore the significant impact of lifestyle factors on caregiver QoL and suggest that interventions targeting these areas could potentially ameliorate the burden on caregivers.

CONCLUSION

The study highlights the profound impact of XDP severity on the QoL of primary caregivers, demonstrating a strong negative correlation between disease severity and caregiver well-being. The significant associations with lifestyle factors such as diet and physical activity further emphasize the need for comprehensive support systems that address both medical and psychosocial needs.

LIMITATIONS OF THE STUDY

Our study has a very limited number of participants due to the stringent inclusion criteria as well as the rarity of the disease. The questionnaire materials used are not all available in the local language of the subject participants, and the interpretation of the questions may not be perceived as intended. The mode through which the interviews are done also limits the motor tests done in Part II of XDP-MDSP (Parkinsonism) as rigidity could not be assessed via teleconsult.

RECOMMENDATIONS

Long-term follow-up with XDP patients as well as their caregivers is recommended to establish the different determinants of caregiver burden and to target specific societal domains to ameliorate the impact of the disease on the XDP patients and the caregivers themselves. This study contributes to the growing body of literature on caregiver burden and underscores the critical importance of holistic care approaches in managing chronic neurodegenerative conditions like XDP.

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