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Caregiving strain is associated with cardiac autonomic imbalance in primary oncology caregivers: A cross-sectional analytical study

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ABSTRACT

Objectives: Oncology caregivers often endure a significant amount of psychosocial stress while going through the experience of caregiving for their dependents. Exposure to chronic stress disrupts the cardiac autonomic balance and increases the risk of cardiovascular events. There is a paucity of research on the association between caregiving strain and cardiac autonomic status of primary oncology caregivers. This study aimed to assess the cardiac autonomic balance and its association with the levels of perceived strain and quality of life (QOL) of primary oncology caregivers.

Materials and Methods: Forty-six individuals (30 males and 16 females) who have been primary caregivers of patients under the treatment for cancer at the Regional Cancer Centre over the past 3 months–1 year were recruited in this cross-sectional study. Cardiac autonomic status was assessed by heart rate variability (HRV) technique. The level of strain perceived and QOL of the study participants were assessed using the Modified Caregiver Strain Index (MCSI) and Caregiver QOL-Cancer (CQOL-C) questionnaires, respectively. Comparison of study parameters based on MCSI scores (low strain vs. moderate-high strain) was done using the Independent Student's *t*-test. Spearman rank correlation coefficient test was performed to assess the correlation between sympathovagal balance (Low frequency [LF]/high frequency [HF]) and other study parameters. Multiple linear regression analysis was performed to predict the LF/HF ratio with independent variables MCSI score and CQOL-C score. $P < 0.05$ was considered statistically significant.

Results: Significantly high blood pressure, LF power, LF nu (LF normalised units) and LF/HF ratio were observed among caregivers with moderate-to-high caregiving strain as compared to those with low strain levels, while significantly low HF nu (HF normalised units) and CQOL-C scores were noted among the moderate-to-high caregiving strain subgroup as compared to the low caregiving strain subgroup. LF/HF ratio revealed a significant positive correlation with the level of caregiving strain ($r = 0.563$, $P < 0.001$) and a significant negative correlation with the QOL ($r = -0.489$, $P = 0.001$) of caregivers. However, on regression analysis, the level of caregiving strain was found to be a significant predictor of autonomic dysfunction unlike the caregivers' QOL.

Conclusion: Increased caregiving strain is associated with cardiac autonomic imbalance in primary oncology caregivers.

Keywords: Cardiac autonomic balance, Heart rate variability, Oncology caregivers, Caregiving strain, Quality of life

INTRODUCTION

Cancer is one of the most important causes of morbidity and mortality, both in developed and developing countries. In India, cancer prevails as the second most common cause of adult death in urban and the third most common cause of death in rural areas.[1]

The caregivers of cancer patients endure a significant amount of stress while supporting their dependents during their treatment process. Importantly, these caregivers also report decreased quality of life (QOL) in physical and psychological domains compared with population norms. This is attributed to their increased caregiving responsibilities and numerous stressors such as financial burden, interruptions in daily routines, role strain, poor quality and quantity of sleep and uncertainty regarding the patient's prognosis.[2,3]

Exposure to psychosocial stressors is known to be linked with a higher risk of acute myocardial infarction even after adjusting for risk factors associated with cardiovascular disease.[4] In addition, psychological disturbances such as depression and anxiety associated with chronic stress are strongly related to an increased risk of cardiovascular morbidity and mortality.[5]

Chronic stress is known to alter the normal rhythm of the Hypothalamo-Pituitary-Adrenal (HPA) axis, characterised by increased activity of the sympathetic and reduced activity of the parasympathetic nervous system. The alteration in the HPA axis rhythm eventually results in autonomic imbalance, a potential causative factor for untoward cardiovascular events.[6,7] Factors such as increased oxidative stress, platelet activation, endothelial dysfunction and abnormal increase in inflammatory biomarkers and cytokines may further increase the risk of cardiovascular disease independent of the disturbances in the HPA axis in individuals exposed to prolonged stress.[5]

It is expected that the cardiac autonomic balance would be altered in oncology caregivers due to their high levels of stress and psychological distress. However, there is a paucity of data on the association between caregiving strain and the cardiac autonomic status of these individuals.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Physiology in collaboration with the Departments of Radiation Oncology and Medical Oncology (Regional Cancer Center) at a tertiary care hospital in South India from July 2021 to August 2021. The study (project number JIP/IEC/2020/217) was reviewed and approved by the Institute Research and Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki (2013).

Sample size estimation

The sample size was estimated based on the sample size formula for the estimation of the mean for the low frequency (LF)/high frequency (HF) (sympathovagal balance) parameter. Considering the standard deviation of LF/HF to be 2.07 (based on the pilot study conducted in the Institute) and the absolute precision of 0.6 units, a total sample size of 46 was estimated at a 5% level of significance.

Inclusion criteria

Individuals of both genders aged >18 years, who were primary caregivers of patients undergoing treatment for solid tumours with metastasis over the past 3 months–1 year, were recruited for the study. The primary caregiver was the individual who helped the patient the most among the relatives and accompanied them for treatment at the institution. The study participants were recruited from the Medical and Radiation Oncology outpatient departments or wards (Regional Cancer Centre) during their dependents' treatment.

Exclusion criteria

Individuals with a known history of acute or chronic medical illness and a prior history of clinical depression or other psychiatric illnesses were excluded from the study.

Study procedure

Following the consecutive sampling technique, 46 individuals (30 males and 16 females) fulfilling the above-mentioned criteria were chosen for the study. The study procedure was explained and written informed consent was obtained from the participants before data collection. The sociodemographic details were collected and recorded in the pro forma sheet.

Assessment of basal cardiovascular parameters

On the day of recording, the study participants reported at the Autonomic Function Testing laboratory in the Department of Physiology, between 9 am and 11 am, 2–3 h after a light breakfast.

Blood pressure (BP) recording

Following the American Heart Association guidelines,[8] BP was recorded after 5 min of rest in the sitting posture using an automated BP apparatus (Omron® SEM 1 Model, Omron Healthcare Co. Ltd, Kyoto, Japan). Two BP recordings were taken at an interval of 1 min and the mean of the two values was taken as the participant's BP.

Mean arterial pressure (MAP) was calculated as MAP = Diastolic BP (DBP) +1/3 Pulse pressure (PP) [PP is the difference between systolic and DBP].

Rate Pressure Product (RPP), a measure of myocardial workload and oxygen consumption, was calculated as RPP = Systolic BP (SBP) × Heart Rate (HR) × 10^{-2}.[9]

The basal HR reading was taken from the BP apparatus.

Assessment of cardiac sympathovagal indices

Following 10 min of rest in the supine posture, 5-min Electrocardiogram (ECG) was recorded in the subjects in Lead II configuration using a data acquisition system (BIOPAC Inc., Goleta, CA, USA). Recordings were done at a room temperature of 25–28°C in light and noise-minimised room. Short-term HR variability (HRV) analysis was done as per the European Taskforce Guidelines.[10] After screening for ectopic beats and noise, R-R intervals were obtained from the 5-min ECG data and fed to 'Kubios version 2.0' software for HRV analysis. The following time and frequency domain indices were included in the study.

Time Domain Indices:

1. SDNN –Standard deviation of all normal to normal (NN) R-R intervals-indicative of total HRV
2. RMSSD – Square root of the mean of the sum of the squares of differences between adjacent NN intervals – indicative of cardiac parasympathetic activity.
3. pNN50 – Percentage of the number of pairs of adjacent NN intervals differing by more than 50 ms in the entire recording divided by the total number of all NN intervals – indicative of cardiac parasympathetic activity.

Frequency Domain Indices:

1. LF power (0.04–0.15 Hz) – indicative of cardiac sympathetic and parasympathetic activity
2. LF normalised units (LF nu) – LF/(Total power [TP]-VLF) × 100 –indicative of cardiac sympathetic activity
3. HF power (0.15–0.40 Hz) – indicative of cardiac parasympathetic activity
4. HF normalised units (HF nu) – HF/(TP - VLF) × 100 – indicative of cardiac parasympathetic activity
5. LF/HF ratio – indicative of cardiac sympathovagal balance
6. TP – indicative of total HRV

Assessment of caregiver strain

The level of caregiver's strain was assessed using the 'Modified Caregiver Strain Index (MCSI),[11] a 13-item, simple and easy-to-administer self-reported questionnaire with good internal reliability (Cronbach's $\alpha = 0.9$). Caregivers' perceived strain in personal, physical, social, psychological and financial domains was assessed using this questionnaire. A score of 2 was given for 'yes,' 1 for 'sometimes,' and 0 for 'no response' for the items in the questionnaire. High MCSI scores were a reflection of increased caregiver strain. Based on the final score, the caregiving strain was classified as low (0–8), moderate (9–18) and high (19–26).[12] In this study, the moderate and high strain categories were grouped for comparison with the low strain category.

Assessment of QOL of caregivers

The caregiver's QOL was assessed using the 'Caregiver QOL-Cancer – (CQOL-C)'[13] questionnaire, a 35-item self-reported questionnaire. The items in the questionnaire helped in assessing the mental and social effects of cancer on the following domains of the caregiver: Burden of disease (ten items), family disruption (seven items), positive adaptation by caregiver (seven items) and financial concerns during cancer treatment (three items). Eight additional undefined items were not related to the major subdomains. Caregivers responded to each statement in the questionnaire on a 4-point Likert scale (0-4), with '4' representing that an individual item correlates strongly with the caregiver. Responses for 27 items contributed as deductions to the caregiver's overall score, while eight responses contributed as positive additions. The total score varied from 0 to 140. High CQOL-C scores indicated good QOL among caregivers.

The MCSI and CQOL-C questionnaires were translated to the local language (Tamil) and the translated versions were tested in a pilot study on a few caregivers before their usage for the present study.

Statistical analysis

The data were entered into an Excel datasheet and SPSS Version 19.0 was used for the statistical analysis.

Descriptive statistics

The continuous variables age, caregiving duration, cardiovascular parameters, SBP, DBP, MAP, RPP, HR, pNN50, RMSSD, SDNN, LF power, LF nu, HF power, HF nu, LF/HF, TP, MCSI score and CQOL-C score were summarised using mean with standard deviation or median with the interquartile range depending on the distribution of the variable.

Test of significance

Comparison of study variables based on MCSI scores (low strain vs. moderate-high strain) was done using the Independent Student's *t*-test/Mann–Whitney U test based on the distribution of data. Similarly, a gender-based comparison of the study variables was performed using the

Independent Student's *t*-test/Mann–Whitney U test based on the distribution of data. The linear relationship between LF/HF ratio and other HRV indices, perceived levels of strain and QOL was assessed using the Spearman rank correlation coefficient.

Regression analysis

Multiple linear regression analysis was performed to predict the LF/HF ratio with independent variables MCSI score and CQOL-C score. Adjusted regression coefficient (β) along with the 95% confidence interval was estimated. All the analyses were performed at 5% level of significance and *P*-value < 0.05 was considered statistically significant.

RESULTS

Forty-six primary caregivers (30 males and 16 females) of individuals diagnosed with and undergoing treatment for solid metastatic tumours over the past 3 months–1 year were recruited for the study. The mean age of the study participants was 36.20 ± 12.92 years [Table 1]. The mean MCSI and CQOL-C scores were 11.44 ± 5.04 and 79.65 ± 20.86, respectively [Table 1]. The participants with a final MCSI score of 0–8 were categorised into the low strain group and those with scores of 9–26 were categorised into the moderate-to-high strain group. Comparison of cardiovascular and HRV parameters between the low strain and moderate-to-high strain groups revealed significantly high SBP (101.81 ± 11.40 mmHg vs. 118.20 ± 12.61 mmHg, $P < 0.001$), DBP (64.50 ± 4.41 mmHg, vs. 77.97 ± 11.69 mmHg, $P < 0.001$), MAP (76.94 ± 5.28 vs. 91.38 ± 11.31, $P < 0.001$), RPP (79.52 ± 17.89 mmHg/min vs. 91.75 ± 13.56 mmHg/min, $P = 0.013$), LF power (164.50 [104.25-308.75] ms^2 vs. 331.50 [231.75 - 592.00] ms^2, $P = 0.011$), LF nu (29.05 [20.45–56.98] vs. 60.60 [50.95–71.823], $P < 0.001$) and LF/HF ratio (0.45 [0.26–1.33] vs. 1.55 [1.04–2.55], $P < 0.001$) and significantly low HF nu (62.58 ± 18.12 vs. 39.66 ± 13.17, $P < 0.001$) and CQOL-C score (94.81 ± 14.32 vs. 71.57 ± 19.35, $P < 0.001$) in the moderate-high strain group [Table 2]. Gender-based subgroup analysis of the study parameters revealed a significantly high DBP (75.83 ± 11.33 vs. 68.50 ± 11.14, $P = 0.043$) and LF/HF ratio (1.41 [0.95–2.55] vs. 0.86 [0.42–1.71], $P = 0.021$) and significantly low HF nu (43.71 ± 18.08 vs. 54.97 ± 17.57, $P = 0.049$) among male caregivers compared to females [Table 3]. Significant positive correlations were observed between LF/HF ratio (a measure of sympathovagal balance) and BP [(SBP, r = 0.560, $P < 0.001$), (DBP, r = 0.537, $P < 0.001$), (MAP, r = 0.597, $P < 0.001$) and (RPP, r = 0.592, $P < 0.001$)] [Table 4]. However, statistically significant negative correlations were observed between LF/HF ratio and HRV indices indicative of parasympathetic activity ([pNN50, r = −0.455, $P = 0.002$), (RMSSD, r= −0.533, $P < 0.001$)] and total HRV ([SDNN, r = −0.395, P=0.007]) [Table 4]. While a significant positive correlation was observed between LF/HF ratio and MCSI score (r = 0.563, $P < 0.001$), a significant negative correlation was observed between LF/HF ratio and CQOL-C score (r = −0.489, $P = 0.001$) [Table 4]. The linear regression analysis was performed to regress the outcome variable LF/HF ratio (a measure of cardiac autonomic balance) with independent variables MCSI score and CQOL-C score. The multiple linear regression model fitted was found to be statistically significant in predicting the outcome variable, LF/HF (F value = 8.90, *P*-value = 0.001). The adjusted R^2 value for the model was estimated to be 26%, which was low to moderate. It was estimated in multiple linear regression that with a unit increase in the MCSI score, the LF/HF ratio increased by 0.116 (95% confidence interval: 0.046, 0.185; *P*-value = 0.002) but the effect of CQOL-C score on LF/HF ratio was estimated to be 0.003 (95% confidence interval: −0.014, 0.020; *P*-value = 0.701) which was not found to be statistically significant [Table 5].

Table 1: Characteristics of study participants.

Parameters	Values (*n*=46)
Age, years	36.20±12.92
Caregiving Duration, months	7.30±3.39
Cardiovascular Parameters	
SBP, mmHg	112.50±14.42
DBP, mmHg	73.28±11.67
MAP, mmHg	86.35±11.84
RPP, mmHg/min	87.49±16.12
HR, beats/min	77.97±12.28
Time-domain indices of HRV	
pNN50 (%)*	4.50 (0.58–21.52)
RMSSD, ms*	28.35 (17.55–39.78)
SDNN, ms	36.37±13.82
Frequency domain indices of HRV	
LF power (ms^2)*	272 (157.27–514.25)
LF nu	52.15±18.77
HF power (ms^2)*	254 (83.50–542.25)
HF nu	47.63±18.52
LF/HF*	1.20 (0.64–2.05)
Total power (ms^2)*	1126.50 (574.25–1781.25)
MCSI score	11.44±5.04
CQOL-C score	79.65±20.86

Value expressed as mean±standard deviation. *Value expressed as median (interquartile range). SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, RPP: Rate pressure product, HR: Heart rate, HRV: Heart rate variability, pNN50: Percentage of NN50 count divided by the total number of all NN intervals, RMSSD: Square root of the mean of the sum of the squares of differences between adjacent NN intervals, SDNN: Standard deviation of normal-to-normal intervals, LF power: Low frequency power, LF nu: low frequency power normalised units, HF power: High frequency power, HF nu: High frequency power normalised units, LF/HF: ratio of low to high-frequency power, MCSI: Modified caregiver strain index, CQOL-C: score, caregiver quality of life-cancer score

Table 2: Comparison of study variables based on MCSI scores.

Parameters	Low Strain (MCSI Score 0–8) (*n*=16)	Moderate-to-high Strain (MCSI Score 9–26) (*n*=30)	*P*-value
Age, years	37.69±14.83	35.40±11.98	0.573
Cardiovascular parameters			
SBP, mmHg	101.81±11.40	118.20±12.61	<0.001
DBP, mmHg	64.50±4.41	77.97±11.69	<0.001
MAP, mmHg	76.94±5.28	91.38±11.31	<0.001
RPP, mmHg/min	79.52±17.89	91.75±13.56	0.013
HR, beats/min	77.84±13.98	78.04±11.53	0.959
Time-domain indices of HRV			
pNN50 (%)*	10.00 (0.35–25.53)	2.95 (1.05–18.83)	0.936
RMSSD, ms*	33.20 (17.45–43.93)	24.75 (17.40–38.30)	0.628
SDNN, ms	35.62±13.96	36.78±13.97	0.790
Frequency domain indices of HRV			
LF power (ms^2)*	164.50 (104.25–308.75)	331.50 (231.75–592.00)	0.011
LF nu*	29.05 (20.45–56.98)	60.60 (50.95–71.83)	<0.001
HF power (ms^2)*	371.50 (117.00–628.00)	244.50 (80.00–503.25)	0.338
HF nu	62.58±18.12	39.66±13.17	<0.001
LF/HF*	0.45 (0.26–1.33)	1.55 (1.04–2.55)	<0.001
Total power (ms^2)*	1094.50 (410.75–1704.5)	1137.50 (595.25–1799.75)	0.612
CQOL-C score	94.81±14.32	71.57±19.35	<0.001

Value expressed as mean±standard deviation. Data analysed by Independent Student's *t*-test - *P* value. *Value expressed as median (interquartile range). Data analysed by Mann–Whitney U-test - *P* Value. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, RPP: Rate pressure product, HR: Heart rate, HRV: Heart rate variability, pNN50: Percentage of NN50 count divided by the total number of all NN intervals, RMSSD: Square root of the mean of the sum of the squares of differences between adjacent NN intervals, SDNN: Standard deviation of normal-to-normal intervals, LF power: Low frequency power, LF nu: Low frequency power normalised units, HF power: High frequency power, HF nu: High frequency power normalised units, LF/HF: Ratio of low-to-high-frequency power, MCSI: Modified caregiver strain index, CQOL-C score: Caregiver quality of life-cancer score.

Table 3: Gender-based differences in study variables.

Parameters	Males (*n*=30)	Females (*n*=16)	*P*-value
Age, years	36.73±14.09	35.19±10.75	0.680
CV Parameters			
SBP, mmHg	113.77±15.16	110.12±13.05	0.401
DBP, mmHg	75.83±11.33	68.50±11.14	0.043
MAP, mmHg	88.48±11.74	82.37±11.31	0.095
RPP, mmHg/min	85.48±15.83	91.27±16.49	0.250
HR, beats/min	75.17±10.65	83.23±13.71	0.032
Time-domain indices of HRV			
pNN50 (%)*	4.50 (1.12-19.50)	7.20 (0.42-26.07)	0.853
RMSSD, ms*	28.35 (21.15-39.32)	29.30 (15.20-45.15)	0.773
SDNN, ms	36.78±13.23	35.71±15.29	0.824
Frequency domain indices HRV			
LF power (ms^2)*	314 (159.50-592)	251 (73.50-399.75)	0.222
LF nu	55.95±18.54	45.03±17.57	0.058
HF power (ms^2)*	244.50 (80.25-505)	366.50 (100.75-645.75)	0.695
HF nu	43.71±18.08	54.97±17.57	0.049
LF/HF*	1.41 (0.95-2.55)	0.86 (0.42-1.71)	0.021
Total power (ms^2)*	1126.50 (493.75-1737)	1139 (616.25-2309.75)	0.747
MCSI score	11.77±5.20	10.81±4.85	0.540
CQOL-C score	77.63±21.48	83.44±19.73	0.364

Value expressed as mean±standard deviation. Data analysed by Independent Student's *t*-test - *P* value. *Value expressed as median (interquartile range). Data analysed by Mann–Whitney U-test - *P* value. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, RPP: Rate pressure product, HR: Heart rate, HRV: Heart rate variability, pNN50: Percentage of NN50 count divided by the total number of all NN intervals, RMSSD: Square root of the mean of the sum of the squares of differences between adjacent NN intervals, SDNN: Standard deviation of normal-to-normal intervals, LF power: Low frequency power, LF nu: Low frequency power normalised units, HF power: High frequency power, HF nu: High frequency power normalised units, LF/HF: Ratio of low to high-frequency power, MCSI: Modified caregiver strain index, CQOL-C score: Caregiver quality of life-cancer score

DISCUSSION

Forty-six participants (30 males and 16 females) who were primary caregivers of cancer patients undergoing treatment for 3 months–1 year were recruited for this study. The mean duration of caregiving was 7.30 ± 3.39 months. Cardiac autonomic activity, caregiving strain and QOL of these individuals were assessed by HRV, MCSI and caregiver QOL-Cancer (CQOL-C) questionnaires. The cardiac sympathovagal balance revealed a significant positive correlation with the level of caregiving strain and a significant negative correlation with the QOL of these caregivers.

The extent of caregiving strain as assessed by the MCSI questionnaire revealed a mean MCSI score of 11.44 ± 5.04 among the study participants. This value is higher than the mean MCSI score reported in a study by Saimaldaher and Wazqar.[12] on cancer caregivers. The study by Dhandapani *et al.* on caregivers of patients suffering from intracranial tumours reported a median MCSI score of 6.[14] Manir and Ghosh, in their study on caregivers' strain for head-and-neck cancer patients, reported an MCSI H Score of 22.[15]

Table 4: Correlation between LF/HF and various study variables of cancer caregivers.

Parameters	r-value	*P*-value
Age, years	0.044	0.773
SBP, mmHg	0.560	<0.001
DBP, mmHg	0.537	<0.001
MAP, mmHg	0.597	<0.001
RPP, mmHg/min	0.592	<0.001
HR, beats/min	0.330	0.024
pNN50 (%)	−0.455	0.002
RMSSD, ms	−0.533	<0.001
SDNN, ms	−0.395	0.007
MCSI score	0.563	<0.001
CQOL-C score	−0.489	0.001

R values are Spearman's rank correlation coefficient - *P* value, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, RPP: Rate pressure product, HR: Heart rate; HRV: Heart rate variability, pNN50: Percentage of NN50 count divided by the total number of all NN intervals, RMSSD: Square root of the mean of the sum of the squares of differences between adjacent NN intervals, SDNN: Standard deviation of normal-to-normal intervals, MCSI: Modified caregiver strain index, CQOL-C score: Caregiver quality of life-cancer score

These differences in the level of caregiving strain could be attributed to various reasons, such as the severity of the disease, accompanying symptoms, patient's performance status and prognosis, caregiving duration and caregiver's QOL (physical, mental and social status).

In this study, the caregiver's QOL as assessed by the CQOL-C questionnaire revealed a mean total score of 79.65 ± 20.86, a finding similar to those reported in the previous studies.[16-19] Data from the previous reports suggest poor psychological health and low social support as potential reasons for the lower QOL in cancer caregivers.[20]

Responsibility for caregiving is a chronic stressor that negatively impacts the physiological, psychological and overall well-being of the caregivers. A study by Rajeshwari *et al.* has shown that caregivers of oncology patients report significant distress, especially in the areas of emotional and family problems.[21] Chronic stress causes dysregulation of the HPA axis and the autonomic nervous system leading to an increased sympathetic and decreased parasympathetic tone, thus affecting the cardiovascular parameters and the cardiac autonomic status.[6,7] In addition, stress-induced reduction in baroreflex sensitivity, one of the major cardioprotective autonomic reflex mechanisms along with changes in cortisol levels and altered immune and inflammatory reactions, may also increase the risk of cardiovascular events in chronic stress.[22-24]

The comparison of the study variables based on the categorisation of participants into the subgroups of low strain and moderate-to-high strain revealed several notable findings. The cardiovascular parameters (SBP, DBP, MAP and RPP) were significantly higher in participants with moderate-to-high MCSI scores, indicating a potential risk of cardiovascular disorders in these individuals. In line with this result, a higher LF/HF ratio characterised by increased sympathetic and decreased parasympathetic activity was observed in the group with moderate-to-high MCSI scores as compared to individuals with low MCSI scores. The significant positive correlation of LF/HF ratio with the MCSI score reinforces the fact that the burden of caregiving may function as a chronic stressor leading to cardiac autonomic dysregulation. In addition, the significant positive correlation observed between LF/HF ratio and **BP** (SBP, DBP and

Table 5: Linear regression analysis of factors associated with LF/HF.

Variables	Regression coefficient (β)	95.0% confidence interval for β		t	*P*-value
		Lower bound	Upper bound		
MCSI score	0.116	0.046	0.185	3.363	0.002
CQOL-C score	0.003	−0.014	0.020	0.386	0.701
Constant	−0.127	−2.104	1.849	−0.130	0.897

MCSI: Modified caregiver strain index, CQOL-C score: Caregiver quality of life-cancer

MAP) establishes that increased sympathetic activity in caregivers could contribute to the raised BP observed in these individuals. Similar findings have also been reported in the study by Lucini *et al*.[25] The study by Pakkala *et al*. on caregivers of patients with locomotor deficits following cerebrovascular accidents reported decreased HRV and a drift towards sympathetic dominance in these individuals.[26] Similarly, the study by Corà *et al*. reported an increased HR, systolic and DBP among relative caregivers of terminally ill patients.[27] In addition, the statistically significant negative correlation observed between LF/HF ratio and CQOL-C in this study indicates the plausible role of decreased QOL as a psychological stressor in cancer caregivers leading to autonomic imbalance and risk of cardiovascular morbidity in these individuals.[28-30] This is reflected well through the MCSI subgroup analysis, which shows a significantly decreased QOL among caregivers with moderate-to-high strain as compared to individuals with low strain. Interestingly, on regression analysis, the level of caregiving strain was found to be a significant predictor of autonomic dysfunction unlike the caregivers' QOL.

The gender-based analysis of study variables revealed a significantly higher D**BP** among male caregivers compared to female caregivers pointing towards increased sympathetic activity in these individuals. Increased cardiac sympathetic activity reduces the total HRV (TP), a known risk marker of cardiovascular morbidity and mortality. In line with this statement, the LF/HF ratio, a measure of the cardiac sympathovagal balance, was significantly higher among males. However, the HR was found to be significantly higher in females than in males; this may be attributed to the influence of sex hormones and gender-based differences in the intrinsic rhythmicity of the pacemaker.[31]

The meta-analysis by Pinquart and Sörensen[32] and studies by Schrank *et al*.[33] and Ketcher *et al*.[34] have documented high-stress levels among female caregivers compared to male caregivers. On the contrary, the level of caregiver's perceived strain as assessed by the MCSI scores was not significantly different between male and female caregivers in this study.

The present study had the following limitations that need to be considered to interpret its findings accurately. First, the small sample size could be a major limitation of the study. Second, the study's cross-sectional design could not establish the cause-effect relationship among the study parameters. Third, parameters such as the caregiver strain index and QOL of the study participants were assessed using self-reported questionnaires, which could introduce potential subjective bias. Finally, considering the age group of the study participants, the study results cannot be generalised to the entire population. In spite of all these constraints, the association between caregiving strain, caregiver's QOL and autonomic status of primary oncology caregivers is well established in this study. Further, the findings of the study also point towards the need for regular periodic assessments of the cardiovascular and autonomic status of cancer caregivers to prevent impending adverse cardiovascular events.

Strength

This is the first study to have reported the cardiac autonomic status and its association with levels of caregiving strain and QOL of primary oncology caregivers.

CONCLUSION

The cardiac autonomic imbalance in primary caregivers of cancer patients is associated with their level of caregiving strain. Regular health check-ups are recommended to assess the overall well-being of these individuals during their caregiving period.

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Declaration of patient consent

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Conflicts of interest

There are no conflicts of interest.

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