Quality of life of mild cognitive impairment patients with type 2 diabetes mellitus and hypertension

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\textbf{ABSTRACT}
Mild cognitive impairment (MCI) is a progressive neurodegenerative disease on which diabetes mellitus and hypertension play an important role as major risk factors. This study aims to assess the quality of life of MCI patients with type 2 diabetes and hypertension. A cross sectional study was carried out in a tertiary care teaching hospital. Cognitive status of patients were assessed by Addenbrooke’s Cognitive Examination III (ACE-III) and Montreal Cognitive Assessment (MoCA). Mild Cognitive Impairment Questionnaire (MCQ) was used to score the quality of life. SPSS 21.0 was used to perform statistical analysis. Kruskal-Wallis test and Mann Whitney U test were used to analyze the relationship between quality of life and demographic parameters. Totally 1887 patients with type 2 DM and hypertension were screened to detect MCI patients. The prevalence of MCI in the population was found to 24.64%. Mean age of the population was 45.12 ± 10.54. Quality of life of patients was affected due to MCI with diabetes and hypertension in early ages. Patients employed in Govt or private sector (p=0.021) and disease duration less than 10 years (p=0.025) had significantly better quality of life. Two domains of MCQ, such as emotional concern and practical concern were assessed separately found that MCI patient’s practical concern scores did not differ significantly from emotional concern scores (p= 0.874). Quality of life was affected in MCI patients with diabetes and hypertension in early ages. Routine clinical examination should consider the quality of life as an important parameter during the patient visit and necessary modifications should be given to enhance the quality of life as well as patient satisfaction.

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\textbf{INTRODUCTION}
Mild cognitive impairment (MCI) is the decline of cognitive function more than expected for a person’s age without notable interference with his daily life activities. Majority of MCI patients may remain stable or normal over time, but some develop dementia and alzheimer’s on later stages (Gauthier \textit{et al.}, 2006). Considering the lacunae for dementia treatment, there is substantial interest to identify potential modifiable risk factors and to control such factors to prevent the progression to alzheimer’s disease risk (Bendlin, 2019). Among risk factors of MCI,
type 2 diabetes mellitus (DM) and hypertension (HTN) has been consistently related to a higher risk of neurodegenerative diseases (Luchsinger et al., 2007).

Quality of Life (QoL) is important in healthcare to ascertain the real impact of disease and treatment in human life, particularly in chronic disorders (Muldoon et al., 1998). The World Health Organization (WHO) defined QoL as the individual’s perception of their position in life in the context of culture and value system in which they live and in relation to their goals, expectations, and standards (WHOqol Group, 1995). The behavioural, cognitive and functional changes seen in dementia may have a major effect on the QoL of patients. QoL is an indicator of the progression of the neurodegenerative disease for individuals with cognitive impairment and dementia (Bárrios et al., 2013; Logsdon et al., 2007). There are numerous approaches for dementia-related QoL conceptualization, several studies using different rating scales indicate reduced QoL in subjects with dementia compared to cognitively normal elderly subjects (Sublett et al., 2020; Reitz et al., 2007). Since clinical manifestations with ongoing dementia are present in MCI, mild reductions in QOL may also be expected in MCI patients.

QoL of patients with any disease is majorly assessed by any validated scales or questionnaires, which are patient reported outcome measures. So it is essential to use a validated patient-reported outcome measure to assess QoL in the MCI population. Studies assessing QoL of MCI population with type DM and HTN using validated patient-reported outcome measure questionnaires and/or scales are limited and results can’t be generalized to everyone. Investigators analysed various QOL indices and found mixed results (Kalaria, 2000; Vermeer et al., 2003). The possible reason for these diverse outcomes remains unclear but may be associated with comparatively small sample sizes of the study and/or the use of general scales to measure QoL, that may be less sensitive to assess the MCI-related potential QOL changes.

By considering potential limitations and mixed results from previous study reports, the current study aimed to screen a large cohort of type 2 DM and HTN patients to identify confirmed MCI patients with type 2 DM and HTN, assessing the QoL of these patients by a validated patient-reported outcome measure tool to assess QoL in people with MCI. The screening for MCI identification and specific QoL questionnaire for MCI patients will help to synthesize accurate results of QoL in type 2 DM and HTN patients with MCI.

MATERIALS AND METHODS

Study design, study centre and ethics approval
A cross sectional study was conducted at Government medical college hospital, Calicut, Kerala, India, a tertiary care teaching hospital after getting ethics committee approval from the hospital. The study was conducted in compliance with ethical guidelines for research involving human participants. Participants interested in participating after explaining the study were included for this study after receiving a signed informed consent form. Confidentiality of included patients details are strictly maintained.

Inclusion and exclusion Criteria
Inclusion criteria of the study were (i) patients with type 2 DM and hypertension receiving medications for the management of the disease; (ii) adequate hearing and vision for neuropsychological testing; (iii) population aged between 30 to 64 years were the inclusion criteria’s for the study, whereas the exclusion criteria’s for the study are (i) patients with dementia, alzheimer’s and psychiatric disorders; (ii) patients with familial history MCI, dementia and alzheimer’s disease; (iii) patients with a history of depression, trauma, head injury or central nervous system infarct, infection or focal lesions of clinical significance; (iv) pregnant and lactating women; (v) patients who are not willing to participate in the study, as these conditions could interfere with study findings.

Patient recruitment and data collection
The sample size for this study was calculated using the OpenEpi (Version 3.01) and G*Power (Version 3.1.9.4) (Sullivan et al., 2009). Based on the inclusion and exclusion criteria, participants were enrolled in the study. Initially, the participants were screened to assess MCI using 2 questionnaires such as Montreal Cognitive Assessment Questionnaire (MoCA) and Addenbrooke’s Cognitive Examination-III (ACE-III) questionnaire. Patients identified with MCI using both the questionnaires were included into the study to enhance the accuracy of findings. Identified MCI populations demographic characteristics, duration of disease, medication chart, treatment duration and QoL were collected in the designed data collection form. QoL is assessed by using the Mild Cognitive Impairment Questionnaire (MCQ).

Scales used
(i) Montreal Cognitive Assessment
MoCA malayalam (language spoken in the Indian
state of Kerala) version was used to assess the cognitive status of eligible patients. MoCA includes executive function, higher-level language, and complex visuospatial processing to enable detection of mild impairment with less ceiling effect. The total score of MoCA is 30 and a score of 26 or above is considered as normal or no cognitive decline. The subjects with less than or equal to 12 years of education were provided with 1 score extra. Increased sensitivity has been reported for MoCA in identifying cognitive decline in AD, dementia and stroke patients. A higher association of MoCA with neuropsychological measures for memory, visuospatial and executive functioning than MMSE was reported by Lam et al. These are the reasons for selecting MoCA for identifying MCI (Nasreddine et al., 2005).

(ii) Addenbrooke’s Cognitive Examination-III (ACE-III) questionnaire

ACE-III is a neuropsychological measure used to assess cognitive decline. It has five cognitive domains: measuring attention/orientation (18 points), memory (26 points), fluency (14 points), language (26 points), and visuospatial function (16 points)–100 in total. Higher scores indicate higher levels of cognitive function (Hodges et al., 2017).

(iii) Mild Cognitive Impairment Questionnaire (MCQ)

MCQ contains 13 questions that assess two constructs – Practical Concerns (7 items) and Emotional Concerns (6 items). Each of the 13 questions on the MCQ is scored in the same way with the score increasing as the reported practical/emotional concerns increase. All questions are laid out similarly with raw response categories denoting no concerns scoring 0 and those representing greatest severity scoring 4. The recommended raw scoring for responses is thus: None 0, Rarely 1, Sometimes 2, Often 3 and Always 4. Transformed scores are presented on a metric of 0 (no problems as measured by the MCQ) to 100 (maximum impact of MCI as measured by the MCQ). Interpretation of scale scores, which is based on the Likert scale underlying each of the domains, could be used: a scale score of 0 – 20 indicates ‘never’ experiencing the phenomena represented by the domain, 21 - 40 ‘rarely’ experiencing them, 41 – 60 ‘sometimes’ experiencing them, 61 – 80 ‘often’ experiencing them and ‘81 – 100 ‘always’ experiencing them (Dean et al., 2014).

Statistical Analysis

Statistical analysis was performed by using SPSS version 21.0. The continuous variable are represented as mean ± standard deviation (SD) and categorical variables were presented as frequency (percentage). All continuous data were tested for normally with skewness, kurtosis and Kolmogorov-Smirnov test. Comparison of continuous data among groups was performed with the Mann Whitney U test and independent sample Kruskal-Wallis Test.

RESULTS

A total of 1887 type 2 DM and hypertension patients were screened with MoCA and ACE-III questionnaires to identify MCI. 465 patients were identified to have MCI and included in the research. Due to insufficient QoL questionnaire information given, 24 participants were excluded. The prevalence of MCI was found to 24.64%.

Demographic characteristics

Socio - demographic characteristics, social habits, disease status and lifestyle, were represented in Table 1. The mean age (mean ± SD) of the population was 45.12 ± 10.54. The MoCA score (mean ± SD) for the included patients was 20.06 ± 1.89 and ACE-III score (mean ± SD) was 77.71 ± 1.89. Our study populations mean MoCA and ACE-III score confirmed that the included population was having MCI.

The recruited patients are on a combination of different antihypertensive and anti diabetic medications. A total of 27 different antihypertensive and anti diabetic medications combinations were identified and listed these combinations in Table 2. Glimepiride, metformin and metoprolol combination was used by the majority of population and metformin, insulin & amlodipine was used by the least number of patients.

Quality of life

Quality of life of the patients were assessed with MCQ (Table 3) and the relation between various socio demographic, social habit, lifestyle and disease status characteristics with total MCQ percent score were assessed and represented in Table 4. QoL of patients is affecting in early ages due to DM and HTN with MCI. A total of 64.4% reported that QoL is affected sometimes. Statistically, significant difference were observed with occupation (p=0.021) and disease duration (p=0.025).

Employed patients in either Govt or private sector had a better quality of life compared with self employed, unemployed or retired patients. Disease duration of less than 10 years had a better quality of life than others. Age related quality of life is not assessed as the age related decline in QoL is well established. All the remaining socio demographic,
Table 1: Baseline Characteristics of the study participants

| Characteristics                          | Categories                          | Frequency | Percentage |
|------------------------------------------|-------------------------------------|-----------|------------|
| **Socio-demographic Factors**            |                                     |           |            |
| Gender                                   | Female                              | 211       | 45.38      |
|                                          | Male                                | 254       | 54.62      |
| Marital status                           | Married                             | 363       | 78.06      |
|                                          | Widowed/Separated/Unmarried          | 102       | 21.93      |
| Occupation                               | Skilled/Self employed                | 44        | 9.46       |
|                                          | Unemployed/Homemaker                 | 264       | 56.77      |
|                                          | Govt/Private employed                | 133       | 28.60      |
|                                          | Retired                              | 24        | 5.16       |
| Socioeconomic status                     | Low                                 | 239       | 51.40      |
|                                          | Middle                               | 200       | 43.01      |
|                                          | High                                 | 26        | 5.59       |
| Education                                | Illiterate                          | 0         | 0          |
|                                          | Primary                              | 0         | 0          |
|                                          | Middle                               | 0         | 0          |
|                                          | High School                          | 80        | 17.20      |
|                                          | Higher Secondary                     | 122       | 26.24      |
|                                          | Graduate & above                      | 263       | 56.56      |
| **Social Habits**                        |                                     |           |            |
| Alcohol                                  | Women (Yes)                          | 13        | 6.16       |
|                                          | Women (No)                           | 198       | 93.84      |
|                                          | Men (Yes)                            | 248       | 97.64      |
|                                          | Men (No)                             | 6         | 2.36       |
| Tobacco (Chewing)                        | Women (Yes)                          | 10        | 4.74       |
|                                          | Women (No)                           | 201       | 95.26      |
|                                          | Men (Yes)                            | 26        | 10.24      |
|                                          | Men (No)                             | 228       | 89.76      |
| Cigarette Smoking                        | Women (Yes)                          | 0         | 0          |
|                                          | Women (No)                           | 211       | 100        |
|                                          | Men (Yes)                            | 224       | 88.19      |
|                                          | Men (No)                             | 30        | 11.81      |
| **Disease Status (years)**               |                                     |           |            |
| Disease duration of Type 2 DM and hypertension | <10            | 84        | 18.06      |
|                                          | 10-19                                | 368       | 79.14      |
|                                          | 20-29                                | 11        | 2.37       |
|                                          | >30                                  | 2         | 0.43       |
| Treatment duration of Type 2 DM and hypertension | <10            | 137       | 29.46      |
|                                          | 10-19                                | 320       | 68.82      |
|                                          | 20-29                                | 7         | 1.51       |
|                                          | >30                                  | 1         | 0.22       |
| **LifeStyle**                            |                                     |           |            |
| Regular Exercise Habit                   | Yes                                  | 45        | 9.68       |
|                                          | No                                   | 420       | 90.32      |
| Food Habit                               | Vegetarian                           | 67        | 14.41      |
|                                          | Non-Vegetarian                       | 398       | 85.59      |
Table 2: Type of treatment

| Sl no | Diabetes medication | Add on anti-diabetes drugs | Antihypertensive medication | Add on antihypertensive drug | Frequency | Percentage |
|-------|---------------------|-----------------------------|----------------------------|-----------------------------|-----------|------------|
| 1     | Insulin             | No second drug              | Nifedipine                 | No Second Drug              | 2         | 0.43       |
| 2     | Insulin             | No second drug              | Enalapril                  | No Second Drug              | 2         | 0.43       |
| 3     | Insulin             | No second drug              | Losartan                   | No Second Drug              | 11        | 2.37       |
| 4     | Insulin             | No second drug              | Metoprolol                 | No Second Drug              | 9         | 1.94       |
| 5     | Glimepiride         | No second drug              | Nifedipine                 | No Second Drug              | 2         | 0.43       |
| 6     | Glimepiride         | No second drug              | Enalapril                  | No Second Drug              | 11        | 2.37       |
| 7     | Glimepiride         | No second drug              | Metoprolol                 | No Second Drug              | 4         | 0.86       |
| 8     | Glimepiride         | Metformin                   | Nifedipine                 | No Second Drug              | 38        | 8.17       |
| 9     | Glimepiride         | Metformin                   | Amlodipine                 | No Second Drug              | 39        | 8.39       |
| 10    | Glimepiride         | Metformin                   | Amlodipine                 | Losartan                    | 11        | 2.37       |
| 11    | Glimepiride         | Metformin                   | Enalapril                  | No Second Drug              | 42        | 9.03       |
| 12    | Glimepiride         | Metformin                   | Losartan                   | No Second Drug              | 19        | 4.09       |
| 13    | Glimepiride         | Metformin                   | Metoprolol                 | No Second Drug              | 103       | 22.15      |
| 14    | Glimepiride         | Insulin                     | Nifedipine                 | No Second Drug              | 13        | 2.80       |
| 15    | Glimepiride         | Insulin                     | Nifedipine                 | Losartan                    | 7         | 1.51       |
| 16    | Glimepiride         | Insulin                     | Enalapril                  | No Second Drug              | 5         | 1.08       |
| 17    | Glimepiride         | Insulin                     | Metoprolol                 | No Second Drug              | 7         | 1.51       |
| 18    | Metformin           | No Second Drug              | Nifedipine                 | No Second Drug              | 19        | 4.09       |
| 19    | Metformin           | No Second Drug              | Enalapril                  | No Second Drug              | 39        | 8.39       |
| 20    | Metformin           | No Second Drug              | Losartan                   | No Second Drug              | 4         | 0.86       |
| 21    | Metformin           | No Second Drug              | Metoprolol                 | No Second Drug              | 42        | 9.03       |
| 22    | Metformin           | insulin                     | Nifedipine                 | No Second Drug              | 16        | 3.44       |
| 23    | Metformin           | insulin                     | Nifedipine                 | Losartan                    | 4         | 0.86       |
| 24    | Metformin           | insulin                     | Amlodipine                 | No Second Drug              | 1         | 0.22       |
| 25    | Metformin           | insulin                     | Enalapril                  | No Second Drug              | 4         | 0.86       |
| 26    | Metformin           | insulin                     | Losartan                   | No Second Drug              | 2         | 0.43       |
| 27    | Metformin           | insulin                     | Metoprolol                 | No Second Drug              | 9         | 1.94       |

Social habit, lifestyle and disease status characteristics were not statistically significant.

**Difference between Practical and Emotional concerns**

Individual patients practical and emotional concern scores were evaluated against different socio demographic, social habit, lifestyle and disease status characteristics (Table 4). Related samples Wilcoxon-Signed Rank test was performed to assess the difference between practical and emotional concerns. Practical concern scores inpatients (Mdn = 50) did not differ significantly from emotional concern scores (Mdn = 50), $T = -1.58, p = 0.874, r = -0.008$.

**DISCUSSION**

The evaluation of health related QoL is a significant part of the clinical evaluation of patients in regular practice, especially given the evidence that the disease has an adverse impact on the quality of life and, secondly, the interest in conducting trials of potentially disease-modifying therapies for dementia is growing in patients with MCI who have a high rate of conversion to dementia. Moreover, the generally available QoL measures, the patient reported outcome measure specifically developed for MCI patients QoL assessment would be more beneficial to predict the exact QoL of the affected population.

A systematic review conducted by Ward *et al.* reported that prevalence of MCI is varying widely across the international studies and found to be 3% - 42% (*Ward et al.*, 2012). A study by Wu *et al.* reported that the prevalence of MCI in hypertensive patients is 16.5% (*Wu et al.*, 2016) and study by JA Luchsinger *et al.* reported that the prevalence of MCI among type 2 DM patients is 8.8% (*Luchsinger et al.*, 2007).

The main findings of the study was QoL of patients was affected by MCI in patients with DM and HTN
### Table 3: Quality of life

| Practical Concern Inference | Emotional Concern Inference | Total MCQ Inference |
|-----------------------------|-----------------------------|---------------------|
| Frequency | Percent | Particulars | Frequency | Percent | Particulars | Frequency | Percent | Particulars |
| Never | 3 | 0.7 | Never | 11 | 2.5 | Never | 1 | 0.2 |
| Rarely | 115 | 26.1 | Rarely | 111 | 25.2 | Rarely | 84 | 19.0 |
| Sometimes | 212 | 48.1 | Sometimes | 200 | 45.4 | Sometimes | 284 | 64.4 |
| Often | 103 | 23.4 | Often | 111 | 25.2 | Often | 70 | 15.9 |
| Always | 8 | 1.8 | Always | 8 | 1.8 | Always | 2 | 0.5 |
| Total | 441 | 100 | Total | 441 | 100 | Total | 441 | 100 |

### Table 4: QoL compared with various socio demographic characteristics

| Socio demographic Variables | N   | MCQ Score | Std. Deviation | Significance |
|-----------------------------|-----|-----------|----------------|--------------|
| Gender                      |     |           |                |              |
| Female                      | 208 | 50.397    | 10.9508        | 0.795        |
| Male                        | 203 | 49.884    | 10.1251        |              |
| Marital status              |     |           |                |              |
| Widowed/Separated/Unmarried | 80  | 52.5241   | 11.51670       | 0.068        |
| Married                     | 361 | 49.5952   | 10.21936       |              |
| Occupation                  |     |           |                |              |
| Skilled/Self Employed       | 43  | 46.1986   | 9.15091        | 0.021        |
| Unemployed/Homemaker        | 262 | 50.3157   | 10.49691       |              |
| Govt/Private employed       | 133 | 51.2147   | 10.74495       |              |
| Retired                     | 3   | 41.6667   | 6.17764        |              |
| Education                   |     |           |                |              |
| HS                          | 56  | 47.219    | 11.1350        | 0.092        |
| HSS                         | 122 | 50.4727   | 9.15270        |              |
| G&A                         | 263 | 50.5851   | 10.90162       |              |
| Socio-Economic Status       |     |           |                |              |
| Low                         | 215 | 49.8033   | 9.99612        | 0.220        |
| Middle                      | 200 | 50.9136   | 10.88700       |              |
| High                        | 26  | 46.7458   | 11.35407       |              |
| alcohol use                 |     |           |                |              |
| Yes                         | 245 | 49.9217   | 10.09943       | 0.785        |
| No                          | 196 | 50.3826   | 11.03046       |              |
| Tobacco chewing             |     |           |                |              |
| Yes                         | 17  | 55.6559   | 11.30448       | 0.060        |
| No                          | 424 | 49.9049   | 10.43401       |              |
| smoking                     |     |           |                |              |
| Yes                         | 221 | 49.7392   | 10.02454       | 0.666        |
| No                          | 220 | 50.5157   | 10.99232       |              |
| food habit                  |     |           |                |              |
| Veg                         | 65  | 51.2132   | 10.05434       | 0.450        |
| NonVeg                      | 376 | 49.9387   | 10.59268       |              |
| regular exercise            |     |           |                |              |
| No                          | 397 | 50.2520   | 10.69741       | 0.407        |
| Yes                         | 44  | 48.9945   | 8.70430        |              |
| Disease duration of Type 2  |     |           |                |              |
| DM and hypertension         |     |           |                |              |
| Less than 10 years          | 83  | 54.3691   | 10.01497       | 0.025        |
| 10-19 years                 | 358 | 44.7845   | 9.85214        |              |
| Treatment duration of Type  |     |           |                |              |
| 2 DM and hypertension       |     |           |                |              |
| Less than 10 years          | 135 | 52.6541   | 11.23014       | 0.372        |
| 10-19 years                 | 306 | 50.6321   | 10.85620       |              |
mild cognitive impairment was prevalent among patients with type 2 diabetes mellitus and hypertension. Quality of life was affected in mild cognitive impairment patients with diabetes and hypertension in early ages. Future studies should consider the quality of life assessment as well as different approaches which can enhance the quality of life of disease population across all age groups.

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Conflict of interest

The authors declare that they have no conflict of interest for this study.

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