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Late-onset depression: A risk factor for major neurocognitive disorder?

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ABSTRACT

Background: Depression and dementia/major neurocognitive disorder (MNCD) are the most common psychiatric morbidities in elderly people.
Objectives: To assess whether late-onset depression (LOD)—defined as onset of first major depressive episode occurring at or above 50 years—and other socio-demographic and clinical variables are risk factors for MNCD in those aged 60 years or above.
Methods: A hospital-based, case-control study was undertaken, with 170 cases of MNCD and 172 controls without MNCD (as assessed using Malayalam adaptation of Addenbrooke's Cognitive Examination). Participants were evaluated for LOD using Structured Clinical Interview for Diagnostic and Statistical Manual for Mental Disorders-Fourth Edition-Text Revision- Research Version.
Results: LOD had a crude OR of 1.22 (95% CI = 0.75–2.00). On univariate analysis, age group ≥80 years, family history of MNCD, hypertension, hyperlipidaemia, movement disorder, normal pressure hydrocephalus and history of treatment for depression were found to be significant risk factors and low income a significant protective factor. After adjusting for socio-demographic and clinical variables using multiple logistic regression, LOD was not found to be a significant risk factor for MNCD (adjusted OR = 0.62, 95% CI = 0.32–1.20). Age ≥80 years, female sex, history of treatment for depression, family history of MNCD, hyperlipidaemia and movement disorders were significant risk factors for MNCD, in the model.
Conclusions: LOD does not increase the risk of MNCD significantly in elderly population. Increasing age, female sex, a positive family history of MNCD and medical comorbidities like hyperlipidaemia and movement disorders were significant risk factors along with a history of treatment for depression.

1. Introduction

In India, the proportion of older adults constitute 8.6% of the total population. During 2009–13, Kerala had the maximum proportion of elderly—12.6%—and had the highest life expectancy at birth among the states and union territories of India.[1] With increasing longevity, the probability of psychiatric morbidity in elderly population also tends to increase.

The first World report on ageing and health identified depression and dementia among the greatest causes of years lived with disability in people older than 60 years.[2] A cross-sectional survey conducted in South India, found the prevalence of depression in elderly population to be 21.7%.[3] The prevalence of dementia in India was found to vary from 0.6 to 3.5% in rural areas and 0.9–4.8% in urban areas.[4] Subjective memory deficits are consistently reported in both dementia and depression. Although cognitive impairment in elderly persons with depression is considered to be reversible with treatment, in a subset of patients, it persists even after successful treatment of depression. This suggests that cognitive impairment in depression could be a harbinger for dementia.[5]

The interrelationship between depression and dementia is complex and not well understood. Depression could be a psychological reaction to cognitive decline and may be an early symptom of dementia. It is also

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proposed as a risk factor for dementia.[6] Studies assessing depression as a risk factor for dementia in elderly have produced contradictory findings. The Framingham Heart Study found that, on follow-up, depression at baseline was associated with increased risk of dementia in elderly people.[7] The MIRAGE study, a case-control study, reported an association between depression symptoms and Alzheimer's disease (AD).[8] A longitudinal study done in men in Western Australia reported that the association is apparent only during the initial five years of follow-up, suggesting that depression is more likely to be a marker of incipient dementia than a truly modifiable risk factor.[9] The Whitehall II cohort study found that baseline depressive symptoms was not associated with increased risk of dementia.[10] Other studies also have reported that late-life depressive symptoms did not increase the risk of dementia,[11,12] but appeared to be early manifestations, rather than predictors of dementia.[13]

Various mechanisms have been hypothesized to link depression and dementia: vascular disease, alteration in glucocorticosteroids, hippocampal atrophy, increased beta-amyloid deposition, inflammatory changes and deficits of growth factors and neurotrophins are some of them.[14] Studies examining late-onset depression (LOD) as a risk factor for dementia/AD have yielded inconsistent results. Many of these studies have assessed symptoms of depression rather than the syndrome of depression. Lack of energy and impairment in sleep, appetite, concentration and functioning are symptoms of depression which are frequently reported by elderly population, even in the absence of depressive disorder. Hence, while evaluating depression as a risk factor for dementia, it would be appropriate to assess depressive disorder as a syndrome. Review of literature did not reveal any studies in Indian setting assessing LOD as a risk factor for dementia. The Diagnostic and Statistical Manual for Mental Disorders-Fifth Edition (DSM-5) has used the term 'major neurocognitive disorder' for defining what was called 'dementia' earlier.[15] This study was conducted with the objective of assessing whether LOD is a risk factor for major neurocognitive disorders (MNCD) in those aged 60 years or above attending a tertiary care center. The secondary objective was to assess other socio-demographic and clinical risk factors for MNCD in this population.

2. Materials and methods

A hospital-based, case-control study was undertaken in the departments of Psychiatry, Neurology and General Medicine of a tertiary care, teaching hospital in Kerala over a period of four years from 2015. Cases were defined as those aged 60 years or above diagnosed as per DSM-5 criteria for MNCD and having scores below the education-specified norms of the Malayalam adaptation of Addenbrooke's Cognitive Examination (M-ACE).[16,17] Controls were those aged 60 years or above not satisfying the DSM-5 criteria for MNCD and having scores above the education-specified norms of the M-ACE, attending the departments of Neurology and General Medicine, but not Psychiatry. Those who were diagnosed to have schizophrenia, bipolar disorder and other psychotic disorders as per Diagnostic and Statistical Manual for Mental Disorders-Fourth Edition-Text Revision (DSM-IV-TR) criteria[18] from the history/clinical evaluation and using Structured Clinical Interview for DSM IV-TR-Axis I Disorders-Research Version (SCID-1-RV),[19] as well as those who were in delirium or un-co-operative to participate in the evaluation were excluded from the study. So also, those who or whose relative refused to give consent and those who did not have a reliable informant were excluded. Taking α as 5%, β as 20%, the prevalence of depression in elderly population as 22%[3] and the expected OR as 2, sample size was calculated to be 165 in each arm and rounded off as 170 in each arm. Approval of the institutional Human Ethics Committee was obtained before starting the study. Consecutive cases of MNCD and concurrent controls were recruited for the study. Those diagnosed to have current major depressive disorder (MDD) were referred for psychiatric care.

2.1. Variables studied and tools used

The study variable was late-onset depression, defined as onset of first major depressive episode occurring at or above 50 years, diagnosed by DSM-IV-TR criteria[18] using SCID-I-RV,[19] as per the information obtained from subject and/or informant. Unlike DSM-5 criteria, DSM-IV-TR criteria for major depressive episode excludes bereavement. Socio-demographic variables like age, sex, educational status and monthly income were also studied. Clinical variables studied included duration since the onset of first-episode of depression, early-onset depression, number of episodes of depression, history of treatment for depression, past history of alcohol use disorder as assessed by DSM-IV-TR criteria,[18] using SCID-I-RV,[19] family history suggestive of MNCD and depression, history of medical conditions like cerebro-vascular disorders, coronary artery disease, hypertension, diabetes mellitus, hyperlipidaemia, movement disorders, renal failure, hepatic failure, thyroid dysfunction, traumatic brain injury, normal pressure hydrocephalus and medications used, as reported by the participant and/or informant or from treatment documents.

M-ACE, a global cognitive screening battery adapted to Malayalam, was used to assess the cognitive functioning of the participants to differentiate cases from controls. It evaluates six cognitive domains. A maximum score of 100 is weighted as follows: orientation (10), attention (8), memory (35), verbal fluency (14), language (28), and visuo-spatial ability (5). It can be administered in 15–20 min.[16] The internal consistency reliability was good (Cronbach's alpha- 0.78). Education-stratified norms have been developed for this questionnaire for the local population.[17] SCID-I-RV is a semi-structured interview schedule for making DSM-IV Axis-I diagnoses. Modules are available for mood episodes and psychotic disorder—both current and past.[19] A moderate inter-rater reliability of 0.66 has been reported for MDD.[20] Permission was obtained from the authors for using all these questionnaires. SCID-I-RV was translated to the local language and back-translated by experts in both the languages and subject. A pro-forma was developed to collect details of the other socio-demographic and clinical variables and pilot-tested before administering to the study participants.

2.2. Analysis

Analysis was done using IBM SPSS Statistics for Windows version 21.0.[21] In addition to the descriptive statistics, comparisons were done using independent samples' *t-test* for continuous variables and χ^2 test/-Fisher's exact test for proportions. Bivariate and multivariate analyses–using multiple logistic regression–were also done to identify and adjust for the confounding variables.

3. Results

There were 170 cases and 172 controls. The mean age of cases was 70.8 years (SD-8.02) and controls 69.2 years (SD-6.17) ($t = 2.13$, $df = 340$, $p = 0.03$). The mean scores of M-ACE were 29.47 (SD-13.80) for cases and 60.82 (SD-14.85) for controls ($t = -20.22$, df-340, $p = 0.0001$). See Table 1 for the distribution of socio-demographic variables between the cases and controls. A statistically significant difference was observed between the age groups of cases and controls ($p = 0.003$). For further univariate analysis, the socio-demographic variables were dichotomized, taking the group comprising 50% of the participants as the cut-off. Only for age groups, 80 years or above was taken as the cut-off, considering the greater risk reported for increasing age. Majority of the informants of cases were sons/daughters/siblings (57.6%), while that for controls were spouses (46.5%). There was no significant difference between the informants of the two groups in their mean age, sex, educational status or mean duration of staying with the patient.

On univariate analysis, LOD was not found to be a significant risk factor for MNCD (crude OR [cOR] = 1.22, 95% Confidence Interval [CI] = 0.75–2.00, $p = 0.42$). The median duration since onset of first-episode

Table 1
Distribution of socio-demographic variables among cases and controls.

Variable		Cases (n1 = 170) No. (%)	Controls (n2 = 172) No. (%)	*P* value
[a]Age group (years)	60–69	85 (50.0)	96 (55.8)	0.003
	70–79	55 (32.4)	67 (39.0)	
	80–89	25 (14.7)	8 (4.7)	
	≥90	5 (2.9)	1 (0.6)	
[b]Sex	Female	85 (50.0)	69 (40.1)	0.07
	Male	85 (50.0)	103 (59.9)	
[a]Educational status	Illiterate	22 (12.9)	22 (12.8)	0.96
	Primary school	74 (43.5)	70 (40.7)	
	High school	61 (35.9)	62 (36.0)	
	Pre-degree	5 (2.9)	6 (3.5)	
	Degree	4 (2.4)	5 (2.9)	
	PG/ Professional	4 (2.4)	7 (4.1)	
[b]Monthly income (INR)	≤5000/-	67 (39.4)	78 (45.3)	0.14
	5001-10000/-	40 (23.5)	50 (29.1)	
	10001-20000/-	33 (19.4)	25 (14.5)	
	> Rs. 20000/-	30 (17.6)	19 (11.0)	

INR –Indian rupees, PG – Post-graduation.
[a] – Fisher's exact test.
[b] – $\chi 2$ test.

of depression was 12 months (Inter-quartile range [IQR] = 6–48) for cases and 12 months (IQR = 3.25–48) for controls; the difference was not statistically significant (Mann-Whitney $U = 905.00$, $p = 0.90$). There was no significant difference in the number of depressive episodes between the two groups ($p = 0.38$). As the control group also was recruited from clinical population with multiple medical comorbidities and were on a plethora of medications including antihypertensives, hypoglycemic agents, lipid-lowering agents, etc., the comparison of medication use between the two groups was not meaningful. Belonging to the age group of 80 years or above was found to be a significant risk factor for MNCD. Lower income (up to Rs. 10,000/-) was found to be a significant protective factor. See Table 2 for details of univariate analysis of socio-demographic variables. Among the clinical variables, family history of MNCD, hypertension, hyperlipidaemia, movement disorders, normal pressure hydrocephalus and history of treatment for depression were found to be significant risk factors. Among other variables, early-onset depression was also not found to be a significant risk factor for MNCD. See Table 3 for details.

Table 2
Univariate analysis of socio-demographic variables.

Variable		Cases (n1 = 170) No. (%)	Controls (n2 = 172) No. (%)	cOR (95% CI)	*P* value
[a]Age group (years)	[b]≥ 80	30 (17.6)	9 (5.2)	3.88	0.0001
	60–79	140 (82.4)	163 (94.8)	(1.78–8.45)	
Sex	[b]Female	85 (50.0)	69 (40.1)	1.49	0.07
	Male	85 (50.0)	103 (59.9)	(0.97–2.29)	
Educational status	[b]< HS	96 (56.5)	92 (53.5)	1.13	0.58
	HS or above	74 (43.5)	80 (46.5)	(0.74–1.73)	
[a]Monthly income (INR)	[b] ≤ 10000/-	107 (62.9)	128 (74.4)	0.58	0.02
	>10000/-	63 (37.1)	44 (25.6)	(0.37–0.93)	

cOR – crude Odds Ratio, HS – High school, INR – Indian rupees.
[a] – P value < 0.05.
[b] – Reference category for each variable.

Bivariate analysis was done for all variables. Confounding was observed for movement disorders and history of treatment for depression. Logistic regression (LR) was done including the study variable—LOD—and all variables with P value < 0.10 in enter model. LOD had an adjusted OR (aOR) of 0.62 (95% CI - 0.32-1.20, p = 0.16). Age ≥80 years, female sex, history of treatment for depression, family history of MNCD, hyperlipidaemia and movement disorders were found to be significant risk factors for MNCD. The model had adequate goodness of fit—Hosmer and Lemeshow test was not significant (p value = 0.96) and −2 Log likelihood ratio was 376.06. See Table 4 for details.

4. Discussion

In this study, LOD was not found to be a significant risk factor for MNCD. Other studies have made similar observations. In a community-based, prospective study, the Monongahela Valley Independent Elders Survey (MoVIES), 1366 cognitively normal participants, aged 65 years or above, were evaluated biennially for depressive symptoms using a modified Center for Epidemiological Studies-Depression scale (CES-D) and for cognitive decline using the MoVIES cognitive test battery for an average of 7.1 years. It was found that depression at baseline did not increase the risk for development of dementia subsequently [Relative risk (RR)-1.27 (95% CI = 0.55–2.93)], after adjusting for confounders. The risk of developing depression in early dementia (aOR- 5.19 [95% CI-1.78-15.15]) and AD (aOR- 6.45 [95% CI-2.18-19.14]) was found to be significant. They concluded that depressive symptoms could be early manifestations than predictors of dementia and AD.[11] From the same study, Ganguli et al. (2006) reported that depressive symptoms at baseline were not associated with the rate of cognitive decline over time. Using random effects model, it was found that depression was associated with baseline cognitive scores, but not with decline on any cognitive scores. It was suggested that substantial cognitive decline does not occur in the absence of incipient dementia, and hence cannot be attributed to depression.[22] The Whitehall II cohort study assessed depressive symptoms using General Health Questionnaire and CES-D and found an increased risk of dementia in those reporting depressive symptoms for a mean follow-up of 11 years, but not in those with a mean follow-up of 28 years. Using mixed models and a backward time scale, retrospective depressive trajectories were analyzed over 28 years. Differences in depressive symptoms in those with dementia compared to those without became more than nine times larger at the year of diagnosis. This suggested that depressive symptoms are a prodromal feature of dementia.[10] In these studies, depressive symptoms, not the syndrome of depression, were assessed. Various other studies have found depressive symptoms to be a risk factor for dementia.[7,8] In most of these studies, including the MIRAGE study, depressive symptoms were assessed using a single question or a questionnaire and/or diagnostic criteria. In our study, past major depressive episode was assessed using a structured, diagnostic interview schedule—SCID-I-RV. The median duration of onset of first episode of depression in cases was 12 months prior to the study. This suggests that, on an average, the first depressive episode occurred one year prior to the point of evaluation of the cases, which indicates that these episodes could be a prodrome or part of the early symptoms of dementia. Becker et al. (2009) had suggested that depression can exert its "effect" on cognition by having the unwanted fellow travellers of medical disease.[12] In our study, the control group was constituted by subjects with one or more medical comorbidities, attending the Geriatric Clinic and Neurology department of the institution. Patients with chronic medical conditions are found to have higher prevalence of co-morbid depression.[23] So also, the possibility of misclassification of early or mild cases of dementia as controls cannot be ruled out, but this was not influenced by the exposure status. These could have contributed to underestimating the risk associated with depression.

Increasing age, female sex and family history of MNCD has been

Table 3
Univariate analysis of clinical variables.

Variable		Cases (n1 = 170) No. (%)	Controls (n2 = 172) No. (%)	cOR (95% CI)	P value
Late-onset depression	[b]Yes	46 (27.1)	40 (23.3)	1.22	0.42
	No	124 (72.9)	132 (76.7)	(0.75–2.00)	
[a]F/H MNCD	[b]Yes	41 (24.1)	20 (11.6)	2.42	0.003
	No	129 (75.9)	152 (88.4)	(1.35–4.33)	
F/H depression	[b]Yes	9 (5.3)	8 (4.7)	1.15	0.78
	No	161 (94.7)	164 (95.3)	(0.43–3.04)	
P/H AUD	[b]Yes	18 (10.6)	21 (12.2)	0.85	0.64
	No	152 (89.4)	151 (87.8)	(0.44–1.66)	
[a]Hypertension	[b]Yes	62 (36.5)	39 (22.7)	1.96	0.005
	No	108 (63.5)	133 (77.3)	(1.22–3.15)	
Diabetes mellitus	[b]Yes	81 (47.6)	91 (52.9)	0.81	0.33
	No	89 (52.4)	81 (47.1)	(0.53–1.24)	
[a]Hyperlipidaemia	[b]Yes	87 (51.2)	47 (27.3)	2.79	0.0001
	No	83 (48.8)	125 (72.7)	(1.78–4.37)	
CVA	[b]Yes	76 (44.7)	76 (44.2)	1.02	0.92
	No	94 (55.3)	96 (55.8)	(0.67–1.57)	
CAD	[b]Yes	38 (22.4)	46 (26.7)	0.79	0.35
	No	132 (77.6)	126 (73.3)	(0.48–1.29)	
[a]Movement disorders	[b]Yes	82 (48.2)	35 (20.3)	3.65	0.0001
	No	88 (51.8)	137 (79.7)	(2.26–5.88)	
Renal failure	[b]Yes	4 (2.4)	2 (1.2)	2.05	0.45
	No	166 (97.6)	170 (98.8)	(0.37–11.33)	
Hepatic failure	[b]Yes	1 (0.6)	1 (0.6)	1.01	1.00
	No	169 (99.4)	171 (99.4)	(0.06–16.31)	
Thyroid dysfunction	[b]Yes	14 (8.2)	19 (11.0)	0.72	0.38
	No	156 (91.8)	153 (89.0)	(0.35–1.49)	
TBI	[b]Yes	15 (8.8)	7 (4.1)	2.28	0.07
	No	155 (91.2)	165 (95.9)	(0.91–5.74)	
[a]NPH	[b]Yes	23 (13.5)	6 (3.5)	4.33	0.001
	No	147 (86.5)	166 (96.5)	(1.72–10.92)	
Early-onset depression	[b]Yes	9 (5.3)	7 (4.1)	1.32	0.59
	No	161 (94.7)	165 (95.9)	(0.48–3.62)	
[a]History of treatment for depression	[b]Yes	20 (11.8)	7 (4.1)	3.14	0.008
	No	150 (88.2)	165 (95.9)	(1.29–7.64)	

AUD – alcohol use disorder, CAD – coronary artery disease, cOR – crude Odds Ratio, CVA – cerebrovascular accident, F/H – family history of, P/H – past history of, MNCD– major neurocognitive disorder, NPH – normal pressure hydrocephalus, TBI – traumatic brain injury.
[a] - P value < 0.05.
[b] - Reference category for each variable.

Table 4
Results of multiple logistic regression analysis.

Variable	aOR (95% CI)	P value
Late-onset depression	0.62 (0.32–1.20)	0.16
*Age ≥80 years	3.97 (1.71–9.22)	0.001
*Female sex	2.38 (1.40–4.03)	0.001
Income ≤ INR 10,000/-	0.67 (0.39–1.14)	0.14
*Treatment for depression	4.91 (1.64–14.74)	0.005
*Family history of MNCD	2.65 (1.38–5.07)	0.003
Hypertension	1.38 (0.76–2.51)	0.29
*Hyperlipidaemia	2.24 (1.27–3.93)	0.005
*Movement disorders	4.35 (2.39–7.91)	0.0001
Normal pressure hydrocephalus	2.66 (0.94–7.57)	0.07
Traumatic brain injury	2.29 (0.78–6.69)	0.13
−2 log likelihood ratio = 376.06, Nagelkerke $R^2 = 0.332$, Cox & Snell $R^2 = 0.249$, Hosmer and Lemeshow test – P value = 0.96		

aOR – adjusted Odds Ratio, INR – Indian rupees, MNCD – Major neurocognitive disorder; *- P value < 0.01.

identified as significant risk factors for dementia, in this study. Hyperlipidaemia and movement disorders were found to be significant risk factors after adjusting for confounding variables including LOD, while other medical comorbidities like hypertension, traumatic brain injury and NPH lost significance on LR. The EURODEM pooled analyses of four cohort studies had found that increasing age, female sex and low levels of education increased the risk for AD significantly, while family history of dementia did not.[24] Other studies have found inconclusive or contradictory evidence for various medical conditions as risk factors of dementia.[25–27] The English Longitudinal Study of Ageing found that cardiometabolic abnormalities like hypertension, diabetes mellitus, etc. were not associated with increased risk of dementia[25]; while the Alzheimer's Association evaluated the evidence for cardiometabolic risk factors and concluded that management of these factors may reduce the risk for dementia.[26] A case-control study conducted in North India had found hyperlipidaemia to be a significant risk factor for dementia.[27] A population-based, nested case-control study had found that Parkinson's disease was associated with increased risk for dementia, even after adjusting for age, sex, education and social class.[28] History of treatment for depression was also identified as a significant risk factor in this study. But the details of medications used were not available. Antidepressants, benzodiazepines and neuroleptics could have been used for the treatment of depression. A meta-analysis had reported increased risk of dementia with antidepressant use—a pooled RR of 1.75 (95% CI - 1.03-2.96) for selective serotonin reuptake inhibitors and 2.13 (95% CI-1.43-3.18) for tricyclic antidepressants.[29] Treatment for depression could also be suggestive of more severe depressive episode, which could have contributed to increasing the risk for dementia.

The inter-relationship between LOD and MNCD being complex, it can be proposed that in some subjects, insight regarding an imminent cognitive decline can lead to a depressive reaction. It can also be that depression is the response to another medical condition, like hypertension or cerebrovascular accident, which is also a risk factor for dementia.[6] The 'Vascular Depression' hypothesis posits that cerebrovascular disease can predispose, precipitate or perpetuate some geriatric depressive symptoms. Focal vascular damage and white matter lesions in specific tracts are associated with late-life depression and cognitive dysfunction. Ageing- and disease-related pro-inflammatory states and immune activation can precipitate depressive symptoms and cognitive deficits. Cerebral hypoperfusion, mediated by vascular risk factors like hypertension, diabetes mellitus and atherosclerosis can contribute to the development of affective and cognitive symptoms.[30] Thus, LOD can be a psychological reaction to early dementia or it can be a manifestation of the same neuropathological processes which precipitates dementia. It could also be proposed that in a subset of aged population, depression, being associated with chronic stress and hypercortisolism, can lead to hippocampal damage and thereby cognitive dysfunction. Further studies are needed to delineate the neuropathological processes involved in

these different subgroups of patients.

4.1. Strengths of the study

Literature review did not find any other studies in the Indian context assessing whether LOD is a risk factor for MNCD. Hence, the relevance of this study. This study had assessed past history of LOD as a syndrome, using a structured diagnostic interview schedule, rather than depressive symptoms. Moreover, by using DSM-IV-TR criteria, bereavement was also ruled out. Those with bipolar and psychotic disorders—which could lead to cognitive impairment—were also excluded. Hence the exposure variable was assessed stringently. To address recall bias, information was obtained from the participant and a reliable informant.

4.2. Limitations of the study

The prevalence of depression in general population in later studies was found to be lower than that used for calculating the sample size for this study.[31] Hence, this study might have lacked adequate power to find a significant association between LOD and MNCD. Being a hospital-based study, the findings lack external validity. Excluding the more severe, un-co-operative patients and those in delirium could have led to survivor bias. The possibility of early or mild cases of dementia being misclassified as controls cannot be ruled out, leading to non-differential misclassification bias. Subtyping of MNCD was not done due to logistic reasons. The exact duration of onset of the symptoms of MNCD could not be ascertained. Hence the temporal correlation of the exposure and outcome could not be assessed. The control group was selected from a clinic-based population, with multiple medical co-morbidities and a greater possibility of comorbid depression. This could have also contributed to reducing the observed risk for the exposure variable and other medical conditions. This also prevented a meaningful comparison of medication use between the two groups, as both groups were receiving multiple medications.

5. Conclusions

This study found that LOD did not increase the risk for MNCD significantly in elderly population. Increasing age and female sex were significant sociodemographic risk factors; while family history of MNCD, history of treatment for depression, hyperlipidaemia and movement disorders were significant clinical risk factors for MNCD. Further research, including community controls and longitudinal follow-up studies of LOD, is needed to understand the complex relationship between LOD and MNCD in elderly population.

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CRediT author statement

Indu Pankajakshan Vijayanthi: Conceptualization, Methodology, Investigation, Formal analysis, Data curation, Writing – Original draft, Review and editing.**Saboora Beegum M:** Conceptualization, Supervision, Writing – Review and editing**Krishna A Kumar:** Conceptualization, Supervision, Writing – Review and editing**Karunakaran Vidhukumar:** Conceptualization, Methodology, Formal analysis, Writing –Reviewand editing **Prabhakaran S Sarma:** Methodology, Formal analysis, Writing –Review and editing.

Declaration of competing interest

There are no conflicts of interest to report.

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