



RESEARCH ARTICLE

REVISED Prevalence and patterns of multi-morbidity in the productive age group of 30-69 years: A cross-sectional study in Pathanamthitta District, Kerala. [version 2; peer review: 2 approved]

Rohini C, Panniyammakal Jeemon

Achutha Menon Centre for Health Science Studies, Sree Chitra Tirunal Institute of Medical Sciences and Technology, Trivandrum, Kerala, 695011, India

V2 First published: 08 Oct 2020, 5:233
<https://doi.org/10.12688/wellcomeopenres.16326.1>
 Latest published: 15 Dec 2020, 5:233
<https://doi.org/10.12688/wellcomeopenres.16326.2>

Abstract

Background: Multi-morbidity is the coexistence of multiple chronic conditions in individuals. With advancing epidemiological and demographic transitions, the burden of multi-morbidity is expected to increase in India.

Methods: A cross-sectional representative survey was conducted among 410 participants aged 30-69 years in Pathanamthitta District, Kerala to assess the prevalence of multi-morbidity. A multi-stage cluster sampling method was employed to identify households for the survey. We interviewed all eligible participants in the selected households. A structured interview schedule was used to assess socio-demographic variables, behavioral risk factors and prevailing clinical conditions. We used the PHQ-9 questionnaire for depression screening. Further, we conducted active measurements of both blood sugar and blood pressure. Multiple logistic regression was used to identify variables associated with multi-morbidity.

Results: Overall, the prevalence of multi-morbidity was 45.4% (95% CI: 40.5-50.3%). Nearly a quarter of the study participants (25.4%) reported only one chronic condition (21.3-29.9%). Further, 30.7% (26.3-35.5), 10.7% (7.9-14.2), 3.7% (2.1-6.0) and 0.2% reported two, three, four and five chronic conditions, respectively. At least one person with multi-morbidity was present in around seven out of ten households (72%, 95% CI: 65-78%). Further, one in five households (22%, 95% CI: 16.7-28.9%) reported more than one person with multi-morbidity. Diabetes and hypertension was the most frequent dyad (30.9%, 95% CI: 26.5-35.7%), followed by hypertension and depression (7.8%, 95% CI: 5.5-10.9%). Diabetes, hypertension and ischemic heart disease was the common triad in males (8.5%, 95% CI: 4.8-14.1%), while it was diabetes, hypertension and depression (6.9%, 95% CI: 4.2-11.1%) in females. Age, sex, and employment status were associated with multi-

Open Peer Review**Reviewer Status**

Invited Reviewers

1

2

version 2(revision)
15 Dec 2020**version 1**

08 Oct 2020



report



report

1. **Pallab K Maulik** , George Institute for Global Health, New Delhi, India

2. **GK Mini** , Ananthapuri Hospitals and Research Institute, Trivandrum, India

Any reports and responses or comments on the article can be found at the end of the article.

morbidity.

Conclusion: Multi-morbidity is prevalent in one of two participants in the productive age group of 30-69 years. Further, seven of ten households have at least one person with multi-morbidity. The high burden of multi-morbidity calls for integrated management strategies for multiple chronic conditions.

Keywords

Multi-morbidity, cross-sectional, household, rural, India, pattern



This article is included in the [Wellcome Trust/DBT India Alliance](#) gateway.

Corresponding author: Panniyammakal Jeemon (jeemon@sctimst.ac.in)

Author roles: **C R:** Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Project Administration, Resources, Writing – Original Draft Preparation; **Jeemon P:** Conceptualization, Funding Acquisition, Methodology, Resources, Supervision, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: This work was supported by the Wellcome Trust through a Wellcome Trust/DBT India Alliance Clinical and Public Health Intermediate Fellowship to Panniyammakal Jeemon [IA/CPHI/14/1/501497].

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Copyright: © 2020 C R and Jeemon P. This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: C R and Jeemon P. **Prevalence and patterns of multi-morbidity in the productive age group of 30-69 years: A cross-sectional study in Pathanamthitta District, Kerala. [version 2; peer review: 2 approved]** Wellcome Open Research 2020, 5 :233 <https://doi.org/10.12688/wellcomeopenres.16326.2>

First published: 08 Oct 2020, 5:233 <https://doi.org/10.12688/wellcomeopenres.16326.1>

REVISED Amendments from Version 1

We have made amendments to the data on 'employment status' presented in Table 1. We have highlighted that in the multi-variate regression model, a sandwich variance estimator was used for accounting for clustering. We have also added the definition of marital status in the footnotes of Table 3.

Any further responses from the reviewers can be found at the end of the article

Introduction

Globally, several countries are going through an epidemiological transition in which degenerative diseases are displacing infections and nutritional disorders as the major cause of mortality and morbidity¹. An increasing trend of life expectancy due to good living conditions, increased income per capita, advances in health care and education are reported globally^{2,3}. However, the added years of life due to increase in life expectancy are often complicated by poor health and disability, resulting from the high burden of chronic diseases, especially non-communicable diseases (NCDs)⁴. Available evidence suggests that the majority of patients diagnosed with chronic diseases have more than one chronic co-existing condition⁵. Co-existence of more than one chronic condition in the same individual is known as multi-morbidity⁶.

Prevalence estimates of multi-morbidity vary widely depending on method of data collection⁴, age of the population studied, definition of chronic condition, definition of multi-morbidity, and number and types of chronic conditions included in the analysis. In addition to the complexities related to the definition, there is a lack of an explicit validated tool to measure the components of multi-morbidity uniformly for reporting the magnitude of diseases⁷. However, available evidence indicates that prevalence, pattern and complexity associated with multiple chronic conditions have been increasing over the years⁸.

The increasing burden of multi-morbidity may cause considerable financial burden, especially in low- and middle-income countries (LMICs). If preventive and management strategies are not integrated and coordinated across multiple chronic conditions, it can lead to duplication and health system inefficiency. Data from LMICs on multi-morbidity are very limited. Further, India does not have population level estimates on multi-morbidity. Given the rising burden of NCDs in India, with the onset of disease at least a decade earlier than their Western counterparts⁹, it is important to characterize the multi-morbidity pattern in this population.

The state of Kerala in India is in an advanced stage of epidemiological transition as compared to other states in India^{10,11}. Therefore, it is highly likely that the prevalence of multi-morbidity will be higher in Kerala. However, very limited data on prevalence of multi-morbidity are available from Kerala. A better understanding of the epidemiology of multi-morbidity is crucial for re-organization of health care services to provide integrated care for multiple chronic conditions. The objective

of our study was to assess the community level prevalence and pattern of multi-morbidity in Kerala.

Methods**Ethical statement**

The Institutional Ethics Committee (IEC) of Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum approved the study (SCT/IEC/1455/NOV-2019). The questionnaire interview and all measurements were conducted after obtaining a written informed consent from each study participant. Privacy was ensured during the time of interview and confidentiality of all the information collected was maintained. The participants agreed to report or publish the data collected during the study except any information that could lead to the identification of any individual, by signing a consent form prepared in local language. The participants had the freedom to refuse participation at the beginning or during any stage of data collection.

Study design

A cross-sectional survey was conducted in Pathanamthitta district of Kerala, India using a structured interview schedule.

Study setting

Pathanamthitta is a southern district of Kerala with the highest proportion of elderly population (18%), lowest total fertility rate (1.3)¹² and highest literacy rate (96.9%)¹³. The population size of Pathanamthitta district is close to 1.2 million as per the 2011 census¹⁴. A high prevalence of diabetes is also noted in Pathanamthitta district¹⁵.

Study population

We included eligible participants aged 30 to 69 years. The participants were residents of rural areas of Pathanamthitta district for a minimum period of one year. Those who did not give informed consent, were physically or mentally not in a condition to answer the questions and/or undergo clinical measurements as part of the study, or were pregnant or lactating within six weeks post-partum were excluded. All eligible participants in a selected household who satisfied the inclusion criteria were included in the study.

There are eight community development blocks (CDB) in Pathanamthitta district. The CDBs were the primary sampling units. Of these eight CDBs, three were randomly selected by simple random sampling. We used computer generated random numbers for the random selection of CDBs. In the second stage, four panchayats were selected from each CDB using computer generated random numbers (a total 12 of Panchayats were selected from three blocks). From these 12 panchayats, one ward each was randomly selected using computer generated random numbers. Further, 16 to 18 alternate houses were visited in each ward. One of the authors (RC) was responsible for the selection of households and participants for the study. After locating the center and the main junction of the ward, by pen rotation, the first household was identified. Subsequently, every alternate household was visited. In case the selected house was empty or locked, the next nearest one was visited. All the houses visited were on the right hand side of the

road. All the eligible participants in the selected households were interviewed. In case any of the potential participants were not present in the house during the time of interview, one more attempt was made at a later time point.

Data collection

A medically qualified primary care doctor (RC) conducted the data collection from all participants. A community health worker (ASHA) assisted RC in the survey. A structured interview schedule¹⁶ was used to assess variables such as socio-demographic factors, behavioral risk factors and prevailing clinical conditions. We used the translated patient health questionnaire (PHQ-9) in *Malayalam* (local language in the state of Kerala) for screening of depression. Random capillary blood sugar (Onetouch Verio Flex Meter) and blood pressure (Omron Blood pressure monitor-upper arm BP7100) measurements were also undertaken. Three readings were recorded at five minutes intervals in the non-dominant arm by getting the participant to sit comfortably for five minutes and keeping the machine at the same level of his/her heart. The average of the three values was calculated and considered as the blood pressure of the participant. Elderly (above 60 years) participants were asked about their living arrangements. Females were asked about their history of menopause. The period of data collection was from 01.01.2020 to 28.02.2020.

Definitions

The operational definition of 'multi-morbidity' was 'co-existence of more than one of the 11 listed chronic conditions in the same individual'. Hypertension was defined as per Joint National Committee-7 guidelines¹⁷. Depression was defined as a PHQ-9 score of 10 or above. Diabetes mellitus was defined as a random capillary blood glucose value above 140mg/dl. The remaining conditions viz ischemic heart disease, heart failure, stroke, chronic kidney disease, chronic obstructive airway disease, arthritis, thyroid hormone disorders and cancer were self-reported by the participants and verified with corresponding patient-held medical records, which were present with them. The patient-held medical records included consultation details, diagnostic details and treatment details. Those who ever used any form of tobacco were defined as tobacco users and those who ever used alcohol were defined as alcohol users. Recommended level of physical activity was defined as walking/jogging/engaging in sport for at least 30 minutes a day on five days in a week. A household was defined as a group of persons who live together and share a common kitchen. The age of starting formal education in the state of Kerala is six years. Low education group were those who studied up to 7th standard. Those who studied above 7th standard were defined as high education group.

Sample size

A prevalence of 30% was anticipated¹⁸ and the precision assumed was 6%. A design effect of 1.5 was assumed, as we employed a multi-stage cluster sampling to identify the participants. We accounted for 10% attrition. The sample size required was estimated as 403 and it was rounded off to 410.

Data management and data analysis

Data were collected using paper forms and later entered into Microsoft Excel 2013 (v 15.0) sheets¹⁶. Data cleaning and data analysis were done using R software version 3.6.3¹⁹. We used the R packages "summarytools" and "ggplot2". Continuous variables were presented as mean and standard deviation and categorical variables as proportions. The overall prevalence and prevalence across socio-demographic variables were calculated with 95% confidence intervals (CIs). Logistic regression analyses were performed to estimate odds ratios (ORs) of various socio-demographic factors associated with multi-morbidity. We present both un-adjusted and adjusted multi-variate model (with sandwich variance estimator) results.

Results

General characteristics

Out of the 430 participants approached, we collected data from 410 participants (95% response rate)¹⁶. The mean age of the study population was 53 (SD=11.7) years (Table 1). Three of five participants in the study population were females (59.8%). Females were younger (mean=52, SD=12.2 years) compared to males (mean=55, SD=10.7 years). Nearly one-third of the participants (32%) reported education up to seventh standard. Nearly half (49%) of the study population were homemakers (49%). One of five participants (20%) were ever users of tobacco. Alcohol use (ever use) was prevalent in 14.6% of the study population. Recommended level of physical activity was reported in one of five participants (20%).

Prevalence of multi-morbidity

More than a quarter (29.3%) of the study participants did not report any one of the 11 included chronic conditions (Figure 1A). Nearly a quarter of the study participants (25.4%) reported only one condition (95% CI: 21.3-29.9). Further, 30.7% (95% CI: 26.3-35.5), 10.7% (95% CI: 7.9-14.2), 3.7% (95% CI: 2.1-6.0) and 0.2% reported two, three, four and five co-existing conditions, respectively (Figure 1A). Overall, 45.4% (95% CI: 40.5-50.3) of the study population reported two or more conditions or multi-morbidity.

Around seven in ten households (72%) reported at least one person in the household with multi-morbidity. Additionally, one in five households (22%) reported more than one person with multi-morbidity (Figure 1B). Overall, 28% of the households did not report any one with multi-morbidity.

Pattern of multi-morbidity

We present common patterns of multi-morbidity in Table 2. Diabetes and hypertension were the most frequently co-existing conditions (31%, 95% CI: 26.5-35.7%) (Figure 2). The second most common pair in females was hypertension-depression (11%, 95% CI: 7.8-16.2%), followed by diabetes-depression (10%, 95% CI: 6.5-14.4%). However, in males it was hypertension-ischemic heart disease (11.5%, 95% CI: 7.2-17.6%) followed by diabetes-ischemic heart disease (8%, 95% CI: 4.9-14.1%).

Table 1. General characteristics of the study population.

Characteristics	Females N=245	Males N=165	Total N=410
Age (mean, SD)	51.9 (12.2)	55.0 (10.7)	53.2 (11.7)
Age group, n (%)			
30-39	48 (19.6)	15 (9.1)	63 (15.4)
40-49	59 (24.1)	37 (22.4)	96 (23.4)
50-59	53 (21.6)	43 (26.1)	96 (23.4)
60-69	85 (34.7)	70 (42.4)	155 (37.8)
Religion, n (%)			
Hindu	131(53.5)	92 (55.8)	223 (54.4)
Christian	110 (44.9)	72 (43.6)	182 (44.4)
Muslim	4 (1.6)	1 (0.6)	5 (1.2)
Marital status, n (%)			
Married	192 (78.4)	152 (92.1)	344 (83.9)
Divorced/separated	5 (2.0)	2 (1.2)	7 (1.7)
Widowed	43 (17.6)	4 (2.4)	47 (11.5)
Unmarried	5 (2.0)	7 (4.2)	12 (2.9)
Education, n (%)			
No schooling	1 (0.4)	1 (0.6)	2 (0.5)
1st-7th standard	85 (34.7)	45 (27.3)	130 (31.7)
8th -10th standard	109 (44.5)	75 (45.5)	184 (44.9)
Higher secondary	17 (6.9)	29 (17.6)	46 (11.2)
Graduation and above	33 (13.5)	15 (9.1)	48 (11.7)
Employment, n (%)			
Daily wager/self-employed	24(9.8)	89 (53.9)	113(27.6)
salaried	12 (4.9)	10 (6.1)	22 (5.4)
Unemployed	209(85.3)	66 (40)	275 (67.1)
Monthly income, n (%)			
>=25000 INR	51 (20.8)	33 (20.0)	84 (20.5)
<25000 INR	194 (79.2)	132 (80.0)	326 (79.5)
Ever used tobacco, n (%)	1 (0.4)	81 (49.1)	82 (20.0)
Ever used alcohol, n (%)	0 (0.0)	60 (36.4)	60 (14.6)
Recommended physical activity, n (%)	28 (11.4)	54 (32.7)	82 (20.0)

INR, Indian Rupee; SD, standard deviation.

Multi-morbidity in sub-groups of population

The prevalence of multi-morbidity increased from 3.2% in the 30–39 age group to 69.7% in the 60–69 age group ($p < 0.001$).

More than half of the study participants (53.1%) in the 50–59 age group reported multi-morbidity (Table 3). In the multiple logistic regression analysis, a 10% increase in

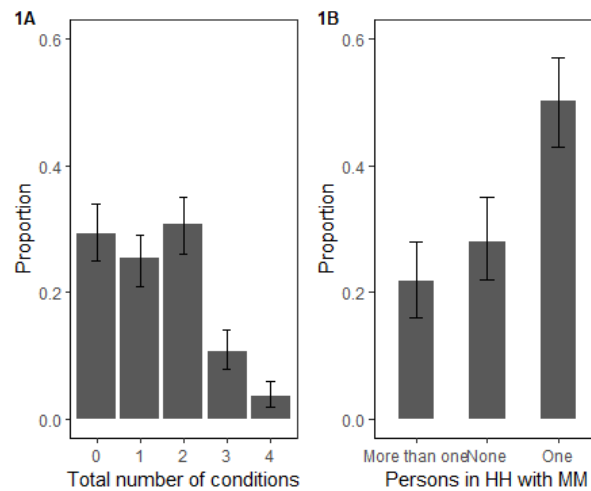


Figure 1. A) Distribution of morbidities among the participants **B)** Proportion of households (HH) with and without multi-morbidity (MM).

Table 2. Common pairs of chronic conditions (pattern of multi-morbidity) among the study population.

Common dyads, n (%)	Total (N=410)	Males (N=165)	Females (N=245)
Diabetes – Hypertension	127 (30.9)	51 (30.9)	76 (31.0)
Hypertension – Depression	32 (7.8)	4 (2.4)	28 (11.4)
Hypertension – Ischemic heart disease	31 (7.5)	19 (11.5)	12 (4.9)
Diabetes – Depression	26 (6.3)	2 (1.2)	24 (9.8)
Diabetes – Ischemic heart disease	23 (5.6)	14 (8.4)	9 (3.7)
Hypertension – Thyroid hormone disorders	23 (5.6)	2 (1.2)	21 (8.6)
Diabetes – Thyroid hormone disorders	16 (3.9)	2 (1.2)	14 (5.7)
Hypertension – Stroke	10 (2.4)	7 (4.2)	3 (1.2)
Common triads, n (%)			
Diabetes – Hypertension – Ischemic heart disease	23 (5.6)	14 (8.5)	9 (3.6)
Diabetes – Hypertension – Depression	19 (4.6)	2 (1.2)	17 (6.9)
Diabetes – Hypertension – Thyroid hormone disorders	11 (2.6)	1 (0.6)	10 (4.1)
Diabetes – Hypertension – Stroke	6 (1.4)	3 (1.8)	3 (1.2)
Diabetes – Thyroid hormone disorders – Depression	4 (0.9)	0 (0.0)	4 (1.6)

propensity for multi-morbidity with every one year increase in age was observed (OR=1.1; 95% CI: 1.1-1.2, $p<0.001$). The prevalence of multi-morbidity was relatively higher in females (48.2%) as compared to males (41.2%). Similarly, the odds for multi-morbidity were lower in males as compared to females (OR=0.4, 95% CI: 0.2-0.8, $p=0.015$). The low education group had a higher prevalence (53%) of multi-morbidity than the high education group (41.7%) ($p=0.04$). However, in the multi-variate

model, after accounting for other socio-demographic variables, participants in the low education category had lower odds of multi-morbidity as compared to individuals in the high education category (OR=0.40; 95% CI: 0.2-0.7, $p<0.001$). The unemployed group had a higher prevalence of multi-morbidity as compared to others ($p<0.001$). Marital status, income, alcohol and tobacco intake in males and living arrangement of elderly did not influence the propensity for multi-morbidity.

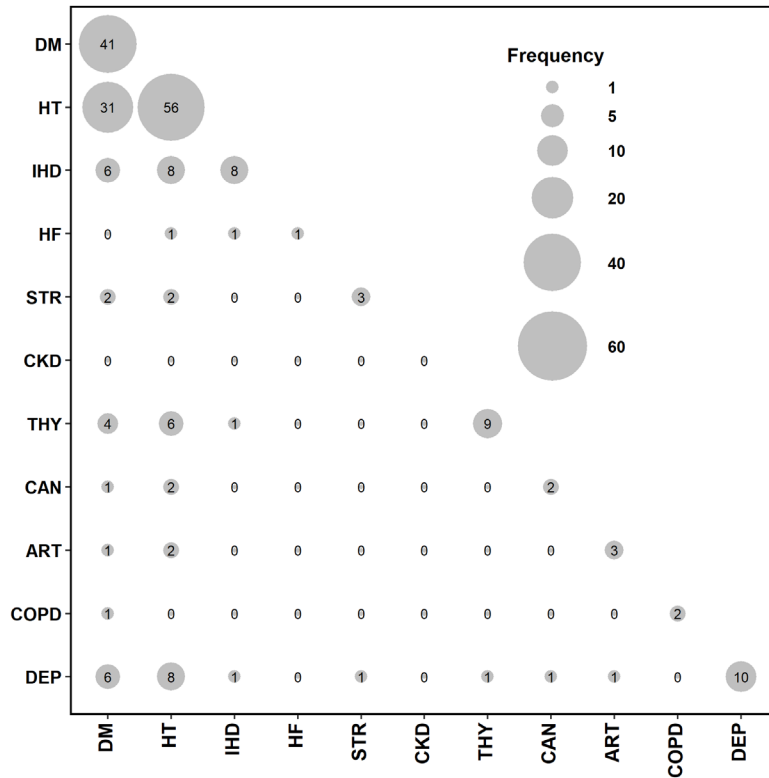


Figure 2. Pattern of co-existence of conditions. DM, diabetes mellitus; HT, hypertension; IHD, ischemic heart disease; HF, heart failure; STR, stroke; CKD, chronic kidney diseases; THY, thyroid hormone disorders; CAN, cancer; ART, arthritis; COPD, chronic obstructive airway disease; DEP, depression.

Among the 245 female participants, 63.3% had reached menopause. Among those who had reached menopause, the prevalence of multi-morbidity was 66.5%. However, the prevalence of multi-morbidity was 16.7% among females who did not reach menopause.

Discussion Highlights

Multi-morbidity, the co-existence of multiple chronic conditions in the same individual, is prevalent in one of two adult individuals in the age group of 30–69 years in Pathanamthitta district of Kerala. The prevalence of multi-morbidity increases with advancing age. We also document that seven in ten households have at least one individual with multi-morbidity. Further, one in five households report more than one person with multi-morbidity. Diabetes and hypertension are the most common co-existing conditions. However, we find differences in the second and third most common dyads and triads of co-existing chronic conditions between males and females. Multi-morbidity assessment in management of chronic conditions is essential given its high prevalence and the differences in health care utilization and quality of life in individuals with different combinations of co-existing chronic conditions²⁰.

Comparison of multi-morbidity prevalence with other studies

Direct comparison of prevalence of multi-morbidity across studies is almost impossible due to varying definitions of multi-morbidity, methods of data collection and the number of conditions included. In a systematic review, the prevalence of multi-morbidity ranged from 4.5% to 83% in the South Asian population²¹. Additionally, in a previous study conducted in Kerala among the age group of 45 years and above, the prevalence of multi-morbidity was substantially lower than our study estimates²². Most of the studies on multi-morbidity in India and other LMICs rely on self-reported data on chronic conditions from the participants and are often subjected to several biases. In our study, we incorporated active measurements for diabetes, hypertension and depression assessment. Further, the medical records of the participants were verified by a medical doctor to confirm the self-reported data on other chronic conditions. The number of chronic conditions included in our assessment for multi-morbidity was also higher than other studies conducted in LMICs.

Multi-morbidity assessment at the household level

The household is an important unit of intervention for chronic disease prevention and control. Although the data on the

Table 3. Prevalence of multi-morbidity (MM) according to socio-demographic characteristics.

	No MM N=224	MM N=186	Crude OR	Adjusted OR*	P value
Age per one year increase			1.1 (1.08-1.13)	1.1 (1.1-1.2)	<0.001
Age groups, n (%)				Not included	
30-39	61 (96.8)	2 (3.2)	Reference		
40-49	71 (74)	25 (26)	10.7 (2.4-47.2)		
50-59	45 (46.9)	51 (53.1)	34.6 (7.9-149.4)		
60-69	47 (30.3)	108 (69.7)	70.1 (16.4-298.6)		
Gender, n (%)					
Female	127 (51.8)	118 (48.2)	Reference		
Male	97 (58.8)	68 (41.2)	0.7 (0.5-1.1)	0.4 (0.2-0.8)	0.015
Marital status, n (%)					
Currently not married***	25 (37.9)	41 (62.1)	Reference		
Married	199 (57.8)	145 (42.2)	0.4 (0.2-0.7)	0.7 (0.3-1.5)	0.324
Education, n (%)					
Above primary	162 (58.3)	116 (41.7)	Reference		
Primary	62 (47.0)	70 (53.0)	1.6 (1.03-2.4)	0.4 (0.2-0.7)	<0.001
Employment, n (%)					
Daily wage/self-employed	81 (71.7)	32 (28.3)	Reference		
Unemployed	126 (45.8)	149 (54.2)	2.9 (1.8-4.8)	1.9 (1.03-3.6)	0.041
Salaried	17 (77.3)	5 (22.7)	0.7 (0.2-2.2)	0.9 (0.3-3.1)	0.529
Income, n (%)				*	
High income	38 (45.2)	46 (54.8)	Reference		
Low income	186 (57.1)	140 (42.9)	0.6 (0.4-1.0)		
Ever had tobacco**, n (%)				*	
Yes	49 (60.5)	32 (39.5)	0.7 (0.4-1.2)		
No	48 (57.1)	36 (42.9)	Reference		
Ever had alcohol**, n (%)				*	
Yes	36 (60)	24 (40)	0.7 (0.4-1.3)		
No	61 (58.1)	44 (41.9)	Reference		
Living arrangement-elderly, n (%)				*	
With spouse (n=116)	42 (36.2)	74 (63.8)	0.5 (0.2-1.1)		
Without spouse(n=39)	8 (20.5)	31 (79.5)	Reference		

*Only variables that showed statistical significance (p<0.05) in unadjusted analyses were entered into adjusted multi-variate analysis. **Analysis was done only for male participants as females did not report alcohol or tobacco use. MM, multi-morbidity; OR, odds ratio. ***Currently not married means either unmarried or divorced/separated or widowed

prevalence of multi-morbidity at the household level are limited, available data suggest strong concordance of chronic conditions within the co-residing adults²³. Existence of at least one person with a chronic disease among seven out of ten

households in Kerala is alarming. Further, multi-morbidity was prevalent in more than one individual in one of five households. The alarming prevalence at the household level calls for innovative models for prevention and control of multi-morbidity.

Family-based models such as the Programme of Lifestyle Intervention in Families (PROLIFIC study)²⁴ may be more appropriate to reduce the burden and progression of multi-morbidity in LMICs. A family centered approach for lifestyle changes and self-care for cardiovascular risk reduction, and involvement of non-physician health workers for care-coordination were the key strategies in the PROLIFIC study. It is envisaged that in a family focused approach, the proposed lifestyle changes and self-care strategies are more achievable and sustainable for both the individuals and their family members²⁵.

Multi-morbidity prevalence in sub-groups and their implications

The prevalence of multi-morbidity increases with age. In our study, the highest prevalence of multi-morbidity was among the age group of 60–69 years. Similar findings were reported in studies from other countries^{21,26–28}. Although seven out of ten participants in the 60–69 age group reported multiple chronic conditions in our study, it was evident that multi-morbidity is a substantial problem even in the younger population. The relatively high burden of multi-morbidity in the most productive age group is a cause for concern as it has serious implications in terms of productivity loss, higher health care utilization²⁰ and health expenditure²⁹.

In our study the prevalence of multi-morbidity among females was higher in comparison to males. Several other studies from India and other Asian countries reported a higher prevalence of multi-morbidity in females^{22,29,30}. Further, high prevalence of multi-morbidity among unmarried, divorced/separated/widowed individuals are also reported in other studies^{31,32}. Gender differences in multi-morbidity pattern and care utilization should be explored in detail in future studies.

There is contrasting evidence regarding the association of education or socio-economic status with multi-morbidity. Data from high-income countries suggest an inverse relationship with education³³, while the relationship is positive and linear (prevalence increases with increase in educational level) in studies from LMICs³¹. Further, some studies from India and Kerala failed to establish any relationship between educational status and multi-morbidity^{34,35}. Our study indicates a higher prevalence in individuals with relatively low education levels. However, on adjustment for other socio-demographic characteristics, individuals with less than primary school education had lower propensity for multi-morbidity as compared to individuals with more than primary school level education. Under-reporting of self-reported chronic conditions, especially in the low education group³⁶, often results in positive associations of education with multi-morbidity. We recommend further investigation to profile the pattern of multi-morbidity according to attained educational status and related inequality.

Multi-morbidity pattern and their implications

The most common pair of coexisting chronic conditions in our study was diabetes and hypertension in males and females. This finding is consistent with the results of the study conducted by Singh and colleagues²⁷. The second most common pair was hypertension and depression for females, while it was

hypertension and ischemic heart disease for males. Similarly, the most common triad in females was diabetes, hypertension and depression, while in males it was diabetes, hypertension and ischemic heart disease. Higher health care utilization and poor quality of life²⁰ in individuals with multiple chronic conditions calls for integrated prevention and control strategies to address the burden of multi-morbidity.

Strengths and limitations

In our survey, we achieved a high response rate (95%) and incorporated measures for active screening of under-diagnosed chronic conditions such as hypertension, diabetes and depression. Further, a medically qualified primary care physician reviewed the medical records of all participants to confirm the self-reported status of other chronic conditions. However multi-morbidity assessment was done by simple counting and the severity of the conditions were not taken in to consideration. Random blood sugar for identification of individuals with diabetes may have under-estimated the true burden of diabetes. Association observed in our study does not imply causality due to the cross-sectional study design.

Conclusion

Multi-morbidity is a major public health problem in Kerala that affects almost half of adult individuals in the productive age group and seven out of ten households. Diabetes, hypertension, depression and ischemic heart disease are the most common co-existing conditions. However, the pattern of multi-morbidity is different across gender and other socio-economic groups. Future research is recommended to identify the progression of single chronic conditions to multi-morbidity over the life-course using prospective study designs.

Data availability

Underlying data

<https://doi.org/10.6084/m9.figshare.12494681.v4>

Figshare: Prevalence and patterns of multi-morbidity among 30–69 years old population of rural Pathanamthitta, a district of Kerala, India: A cross-sectional study. <https://doi.org/10.6084/m9.figshare.12494681.v4>¹⁶.

This project contains the following underlying data:

- Multilatest v2 - Copy.xls (demographic and clinical data for all participants)
- Codes used in multilatest v2-converted.pdf (data dictionary)

Extended data

Figshare: Prevalence and patterns of multi-morbidity among 30–69 years old population of rural Pathanamthitta, a district of Kerala, India: A cross-sectional study. <https://doi.org/10.6084/m9.figshare.12494681.v4>¹⁶.

This project contains the following extended data:

- Interview schedule english version 3-converted.pdf (interview schedule in English)

- Table for interview english version 1-converted.pdf (interview schedule table in English)
- Interview schedule malayalam version2.pdf (interview schedule in Malayalam)
- Table for interview malayalam version1-converted.pdf (interview schedule in Malayalam)

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](#) (CC-BY 4.0).

Acknowledgements

We acknowledge the wholehearted support of the study participants and the community health workers (ASHAs).

References

1. Omran AR: **The Epidemiologic Transition: A Theory of the Epidemiology of Population Change.** *Milbank Q.* 2005; **83**(4): 731–57. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
2. GBD 2016 Mortality Collaborators: **Global, regional, and national under-5 mortality, adult mortality, age-specific mortality, and life expectancy, 1970–2016: a systematic analysis for the Global Burden of Disease Study 2016.** *Lancet.* 2017 [cited 2020 Jul 18]; **390**(10100): 1084–1150. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
3. Houweling TA, Kunst AE, Mackenbach JP: **World Health Report 2000: inequality index and socioeconomic inequalities in mortality.** *Lancet.* 2001; **357**(9269): 1671–2. [PubMed Abstract](#) | [Publisher Full Text](#)
4. Smith SM, O'Dowd T: **Chronic diseases: what happens when they come in multiples?** *Br J Gen Pract.* 2007; **57**(537): 268–70. [PubMed Abstract](#) | [Free Full Text](#)
5. Fortin M, Bravo G, Hudon C, *et al.*: **Prevalence of Multimorbidity Among Adults Seen in Family Practice.** *Ann Fam Med.* 2005; **3**(3): 223–8. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
6. van den Akker M, Buntinx F, Knottnerus JA: **Comorbidity or multimorbidity: what's in a name? A review of literature.** *Eur J Gen Pract.* 1996; **2**(2): 65–70. [Publisher Full Text](#)
7. Diederichs C, Berger K, Bartels DB: **The Measurement of Multiple Chronic Diseases—A Systematic Review on Existing Multimorbidity Indices.** *J Gerontol A Biol Sci Med Sci.* 2011; **66**(3): 301–11. [PubMed Abstract](#) | [Publisher Full Text](#)
8. Pefoyo AJK, Bronskill SE, Gruneir A, *et al.*: **The increasing burden and complexity of multimorbidity.** *BMC Public Health.* 2015; **15**: 415. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
9. Arokiasamy P: **India's escalating burden of non-communicable diseases.** *Lancet Glob Health.* 2018; **6**(12): e1262–3. [PubMed Abstract](#) | [Publisher Full Text](#)
10. India State-Level Disease Burden Initiative Collaborators: **Nations within a nation: variations in epidemiological transition across the states of India, 1990–2016 in the Global Burden of Disease Study.** *Lancet.* 2017; **390**(10111): 2437–60. [PubMed Abstract](#) | [Free Full Text](#)
11. Sivasankaran S, Thankappan KR: **Prevention of non-communicable diseases requires a life course approach: A case study from Kerala.** *Indian J Med Res.* 2013; **137**(5): 874–7. [PubMed Abstract](#) | [Free Full Text](#)
12. Guillmoto CZ, Rajan I: **Fertility at District Level in India: Lessons from the 2011 Census.** 34. [Reference Source](#)
13. Census of India Website: **Office of the Registrar General & Census Commissioner, India.** [cited 2020 Jul 26]. [Reference Source](#)
14. **Indian Districts by Population, Sex Ratio, Literacy 2011 Census.** [cited 2020 Jul 18]. [Reference Source](#)
15. Irudaya Rajan S; Centre for Enquiry into Health & Allied Themes (Mumbai I): **Population ageing and health in India.** Mumbai: Centre for Enquiry into Health and Allied Themes; 2006. [Reference Source](#)
16. Rohini JP: **Prevalence and patterns of multi-morbidity among 30-69 years old population of rural Pathanamthitta, a district of Kerala, India: A cross-sectional study.** *figshare.* Dataset. 2020. <http://www.doi.org/10.6084/m9.figshare.12494681.v4>
17. Chobanian AV, Bakris GL, Black HR, *et al.*: **Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.** *Hypertension.* 2003; **42**(6): 1206–52. [PubMed Abstract](#) | [Publisher Full Text](#)
18. Mini GK, Thankappan KR: **Pattern, correlates and implications of non-communicable disease multimorbidity among older adults in selected Indian states: a cross-sectional study.** *BMJ Open.* 2017; **7**(3): e013529. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
19. R: **The R Project for Statistical Computing.** [cited 2020 Jun 5]. [Reference Source](#)
20. Sum G, Salisbury C, Koh GCH, *et al.*: **Implications of multimorbidity patterns on health care utilisation and quality of life in middle-income countries: cross-sectional analysis.** *J Glob Health.* 2019; **9**(2): 020413. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
21. Pati S, Swain S, Hussain MA, *et al.*: **Prevalence and outcomes of multimorbidity in South Asia: a systematic review.** *BMJ Open.* 2015; **5**(10): e007235. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
22. Arokiasamy P, Uttamacharya, Jain K: **Multi-Morbidity, Functional Limitations, and Self-Rated Health Among Older Adults in India: Cross-Sectional Analysis of LASI Pilot Survey, 2010.** *SAGE Open.* 2015; **5**(1). [Publisher Full Text](#)
23. Patel SA, Dhilon PK, Kondal D, *et al.*: **Chronic disease concordance within Indian households: A cross-sectional study.** *PLoS Med.* 2017; **14**(9): e1002395. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
24. Jeemon P, Hari Krishnan S, Sanjay G, *et al.*: **A PROgramme of Lifestyle Intervention in Families for Cardiovascular risk reduction (PROLIFIC Study): design and rationale of a family based randomized controlled trial in individuals with family history of premature coronary heart disease.** *BMC Public Health.* 2017 [cited 2020 Jul 26]; **17**(1): 10. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
25. Joseph LM, Lekha TR, Boban D, *et al.*: **Perceived facilitators and barriers of enrolment, participation and adherence to a family based structured lifestyle modification interventions in Kerala, India: A qualitative study [version 2; peer review: 3 approved].** *Wellcome Open Res.* 2019; **4**: 131. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
26. Garin N, Koyanagi A, Chatterji S, *et al.*: **Global Multimorbidity Patterns: A Cross-Sectional, Population-Based, Multi-Country Study.** *J Gerontol A Biol Sci Med Sci.* 2016; **71**(2): 205–14. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
27. Singh K, Patel SA, Biswas S, *et al.*: **Multimorbidity in South Asian adults: prevalence, risk factors and mortality.** *J Public Health (Oxf).* 2019; **41**(1): 80–9. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
28. Violan C, Foguet-Boreu Q, Flores-Mateo G, *et al.*: **Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies.** *PLoS One.* 2014 [cited 2019 Aug 3]; **9**(7): e102149. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
29. Pati S, Agrawal S, Swain S, *et al.*: **Non communicable disease multimorbidity and associated health care utilization and expenditures in India: cross-sectional study.** *BMC Health Serv Res.* 2014 [cited 2019 Aug 3]; **14**: 451. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
30. Pati S, Swain S, Hussain MA, *et al.*: **Prevalence, correlates, and outcomes of multimorbidity among patients attending primary care in Odisha, India.** *Ann Fam Med.* 2015; **13**(5): 446–50. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
31. Himanshu H: **Prevalence of Multimorbidity (Chronic NCDs) and Associated Determinants Among Elderly in India.** 2017; 69–76. [Reference Source](#)
32. Muksor A, Dixit P: **Rural-Urban Differentials in NCD Multimorbidity in Adult Population in India: Prevalence and Cost of Care.** 2018; **2018**(02): 12. [Reference Source](#)
33. Agborsangaya CB, Lau D, Lahtinen M, *et al.*: **Multimorbidity prevalence and patterns across socioeconomic determinants: a cross-sectional survey.** *BMC Public Health.* 2012; **12**(1): 201. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
34. Banjare P, Pradhan J: **Socio-economic inequalities in the prevalence of multi-morbidity among the rural elderly in Bargarh District of Odisha**

- (India). Chaturvedi S, editor. *PLoS One*. 2014; **9**(6): e97832.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
35. Vargese SS, Mathew E, Johny V, *et al.*: **Prevalence and pattern of multimorbidity among adults in a primary care rural setting.** *Clin Epidemiol Glob Health*. 2019 [cited 2020 Apr 11]; **8**(2): 482–485.
[Publisher Full Text](#)
36. Vellakkal S, Millett C, Basu S, *et al.*: **Are estimates of socioeconomic inequalities in chronic disease artefactually narrowed by self-reported measures of prevalence in low-income and middle-income countries? Findings from the WHO-SAGE survey.** *J Epidemiol Community Health*. 2015; **69**(3): 218–25.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

Open Peer Review

Current Peer Review Status:  

Version 2

Reviewer Report 21 December 2020

<https://doi.org/10.21956/wellcomeopenres.18178.r41845>

© 2020 Maulik P. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Pallab K Maulik 

George Institute for Global Health, New Delhi, Delhi, India

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Mental health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 11 November 2020

<https://doi.org/10.21956/wellcomeopenres.17948.r41074>

© 2020 Mini G. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



GK Mini 

Global Institute of Public Health, Ananthapuri Hospitals and Research Institute, Trivandrum, Kerala, India

Comments and suggestions:

The study is well conducted and should be of interest to the readership, my congratulations to the authors for picking up the topic, multi-morbidity. However, there are some minor problems that need to be addressed by the authors.

Abstract:

The abstract is concise, specific, representative of the article, and in the correct form, which accurately summarizes the essential information.

- The first sentence in the abstract, "Multi-morbidity is the coexistence of multiple chronic conditions in individuals and families," is slightly different from the definition of multi-morbidity given in the methodology. Better to avoid "families" from abstract.
- The objective is not given in the abstract.

Methods:

The methodology of the study is thorough and presented clearly. The researchers have done a good job describing the study population, data collection, definitions of terms used, and sample size.

- Since all the eligible participants in the selected households were interviewed, there is a possibility for the clustering of multiple respondents within the houses, which is not addressed in the analysis.
- The details of the number of households surveyed were not given in the abstract. This is important in the context of the discussion on multi-morbidity assessment at the household level.
- Only elderly participants were asked about their living arrangements. This needs further explanation.
- Under the sub-title 'Data Collection,' "Malayalam" can be put in italics and bracket (local language), helping international readers.
- The justification for selecting the 11 listed chronic conditions in the study were not given.
- There is no mention of the type of treatment for the selected diseases.
- Patients with multi-morbidity are at increased risk for polypharmacy. Since the authors verified the medical records, it would have been easy for them to get details of medication and the treatment from different systems.

Results:

The results are clearly described. Some points for consideration are as follows:

- The study used multi-stage cluster sampling. Correction for clustering was not performed in data analysis.
- Depression was measured using PHQ-9. However, no detail on the prevalence of depression is presented in the manuscript.
- The results derived from the logistic regression analysis presented in Table 3, age standardization would have helped estimate the true prevalence of multi-morbidity in this population, which would also help the readers to compare results from other studies.

- The classification of employment status presented in Table 1 & Table 3 is different. I'd suggest making these consistent.
- In Table 2, the authors gave details of common pairs of chronic conditions. However, I couldn't find the prevalence of individual diseases anywhere in the manuscript.
- In Table 3, in employment classification, better to club the 'salaried' with the first category is 'daily wage/self-employed' so that it becomes two categories as employed and not employed.
- In Table 3, marital status classification needs to be verified, specifically the term 'currently not married.'
- Prevalence of the recommended level of physical activity was given in the manuscript. It would be better to analyze the recommended level of physical activity with multi-morbidity considering the association of physical activity with decreased risk of chronic conditions and mortality.

Discussion:

The discussion section is very well presented as it covers all of the components associated with the study. The conclusion is based on the study's findings, and the recommendations made would help future related studies.

- In the results section, the association of menopause and multi-morbidity was given, and there is a significantly increased prevalence of multi-morbidity among those who reached menopause. However, no further discussion is seen in this association. Higher age of menopause women may be considered in this case.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Chronic Disease Epidemiology, Quantitative Research Methods

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 09 Dec 2020

Panniyammakal Jeemon, Sree Chitra Tirunal Institute of Medical Sciences and Technology, Trivandrum, India

Thank you very much for the positive comments. We have included our detailed response to the comments in the section below:

Comment 1: The first sentence in the abstract, "Multi-morbidity is the coexistence of multiple chronic conditions in individuals and families," is slightly different from the definition of multimorbidity given in the methodology. Better to avoid "families" from abstract. ○○ **The objective is not given in the abstract.**

As per the suggestion we have removed the word "families" from the abstract. We have also added the main objective of the study in the abstract.

Comment 2a: Since all the eligible participants in the selected households were interviewed, there is a possibility for the clustering of multiple respondents within the houses, which is not addressed in the analysis.

We had included all eligible participants to assess the multi-morbidity burden at the household level. The household level multi-morbidity is a new concept and has important implications in prevention and control of chronic conditions. We had included 193 households (clusters) in the study and used a sandwich variance estimator in the regression model.

Comment 2c: Only elderly participants were asked about their living arrangements. This needs further explanation.

We were interested in generating some pilot data on the relationship between living arrangements and multi-morbidity burden in the elderly population. It was not part of the main objective of the study.

Comment 2d: Under the sub-title 'Data Collection,' "Malayalam" can be put in italics and bracket (local language), helping international readers.

We have inserted a bracket and mentioned that it is the local language in Kerala.

Comment 2e: The justification for selecting the 11 listed chronic conditions in the study were not given.

This is purely because of pragmatic reasons and based on consensus opinion from experts in the field.

Comment 2f: There is no mention of the type of treatment for the selected diseases.

Patients with multi-morbidity are at increased risk for polypharmacy. Since the authors verified the medical records, it would have been easy for them to get details of medication and the treatment from different systems.

Yes. As the reviewer correctly pointed out the patients with multi-morbidity are at increased risk of poly-pharmacy. Although we collected details of medications, we could not analyze the data as there was no uniformity regarding the type of treatment especially between various systems of medicine. We will need to discuss this with experts in alternative systems of medicine to complete the data analysis.

Comment 3a: The study used multi-stage cluster sampling. Correction for clustering was

not performed in data analysis.

We had included 193 households (clusters) in the study and used a sandwich variance estimator in the regression model.

Comment 3b: Depression was measured using PHQ-9. However, no detail on the prevalence of depression is presented in the manuscript

Prevalence of individual conditions are also presented in Figure 2.

Comment 3c: The results derived from the logistic regression analysis presented in Table 3, age standardization would have helped estimate the true prevalence of multi-morbidity in this population, which would also help the readers to compare results from other studies.

We agree that age-standardization would have helped for comparison of data with other studies. However, since it was a study conducted in one of the districts in Kerala, it may not be useful even if we age standardize to the world standard or Indian population.

Comment 3e: In Table 2, the authors gave details of common pairs of chronic conditions. However, I couldn't find the prevalence of individual diseases anywhere in the manuscript.

Prevalence of individual conditions are also presented in Figure 2.

Comment 3f: In Table 3, in employment classification, better to club the 'salaried' with the first category is 'daily wage/self-employed' so that it becomes two categories as employed and not employed.

Thank you for this suggestion. We have made the changes as per the suggestion.

Comment 3g: In Table 3, marital status classification needs to be verified, specifically the term 'currently not married.'

We have added a footnote to explain the definition of this variable.

Comment 3h: Prevalence of the recommended level of physical activity was given in the manuscript. It would be better to analyze the recommended level of physical activity with multi-morbidity considering the association of physical activity with decreased risk of chronic conditions and mortality.

The limitation of the study design made the assessment difficult as many of the participants started doing the recommended level of physical activity only after they have been diagnosed with one or more of the chronic conditions.

Comment 4: In the results section, the association of menopause and multi-morbidity was given, and there is a significantly increased prevalence of multi-morbidity among those who reached menopause. However, no further discussion is seen in this association. Higher age of menopause women may be considered in this case.

As the reviewer pointed out, there was a higher prevalence of multi-morbidity among females who attained menopause. However, after adjusting for age this difference was marginal.

Competing Interests: None

Reviewer Report 26 October 2020

<https://doi.org/10.21956/wellcomeopenres.17948.r40796>

© 2020 Maulik P. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Pallab K Maulik 

George Institute for Global Health, New Delhi, Delhi, India

It is good paper ascertaining multimorbidities in the south Indian state of Kerala (one district). Overall, I have a few observations which are now not modifiable, but something that needs to be addressed in the discussion:

1. The district chosen seems one of the more extreme districts of Kerala in many ways as already indicated by the author and Kerala itself is one of the odd states in India - health indicator wise. This does bring into question issues about generalizability of the data and more discussion needs to be given to that.
2. The study excluded pregnant and lactating women. Not sure about the rationality as it definitely takes out the possibility of perinatal depression and some other pregnancy related health issues.
3. There is no information about the temporality of the occurrence of the diseases. If that data was not collected, one needs to include that in the limitations and comment on it.
4. While the study may not be powered to provide gender-based analysis, some preliminary indications of trends could be useful, especially given that the results were affected by gender.
5. The author may want to look into the Academy of Medical Science, UK report on multimorbidity.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Mental health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 09 Dec 2020

Panniyammakal Jeemon, Sree Chitra Tirunal Institute of Medical Sciences and Technology, Trivandrum, India

We thank the reviewer for their positive comments. Our detailed response to the comments are given below;

Comment 1: The district chosen seems one of the more extreme districts of Kerala in many ways as already indicated by the author and Kerala itself is one of the odd states in India – health indicator wise. This does bring into question issues about generalizability of the data and more discussion needs to be given to that.

We agree that the results may not be generalisable to other population with different population structure. We have therefore given the name of the district and the state in the title itself. Further, we have described the socio-demographic pattern of the selected district in the study settings.

Comment 2: The study excluded pregnant and lactating women. Not sure about the rationality as it definitely takes out the possibility of perinatal depression and some other pregnancy related health issues.

We agree that exclusion of pregnant and lactating women would have underestimated the prevalence of multi-morbidity. However, some of the chronic conditions like depression may be relatively transient (not very chronic) in this group of participants. Further, it is a standard methodology to exclude pregnant women from similar surveys.

Comment 3: There is no information about the temporality of the occurrence of the diseases. If that data was not collected, one needs to include that in the limitations and comment on it.

Yes. As the design of the study is cross-sectional, temporality cannot be ensured. We accept it as a limitation of this study design.

Comment 4: While the study may not be powered to provide gender-based analysis, some preliminary indications of trends could be useful, especially given that the results were affected by gender.

We have presented the common pairs of chronic conditions stratified by gender in Table 2.

Comment 5: The author may want to look into the Academy of Medical Science, UK report on multi-morbidity.

Thank you for this suggestion. We were motivated to conduct this assessment after reading the Academy of Medical Science, UK report on multi-morbidity.

Once again we thank the reviewer for his positive comments.

Competing Interests: None to declare

