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Emerging multimorbidity patterns and their links with selected health outcomes in a working-age population group

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Key words

Latent class analysis • Multimorbidity • Self-rated health • Quality of life • Primary care.

Summary

Background. The study aims to identify recurrent multimorbidity pattern among individuals in the age-group 15-64 years. Further, the study examines the association of these identified patterns with sociodemographic variables and selected health outcomes.

Methods. The study utilized data on 2912 individuals in the agegroup 15-64 years collected under the burden of diseases study among patients attending public health care settings of Odisha. A latent class analysis was used to identify commonly occurring disease clusters.

Results. The findings suggested that 2.4% of the individuals were multimorbid. Two latent disease clusters were identified, low co-morbidity and Hypertension-Diabetes-Arthritis. Findings

Introduction

Multimorbidity is defined as the coexistence of two or more chronic conditions [1]. With the rise of chronic non-communicable diseases (NCDs) and increased life expectancy, multimorbidity is becoming a norm rather than the exception. In low- and middle-income countries (LMICs) such as India, the impact of these changes are more explicit due to changes in the lifestyle and environmental exposures which contribute to NCDs (such as an increase in obesity and physical inactivity) along with aging [1]. But the healthcare system is still oriented towards treatment for single conditions and acute diseases. Even the treatment guidelines are based on particular conditions rather than holistic treatment of multiple co-morbid conditions. Consequently, patients with multimorbidity need to often visit multiple healthcare providers, which increases the treatment burden, leads to low patient satisfaction and poor health outcomes [2-4].

A global multi-country study has reported the prevalence of multimorbidity to be high (ranging from 45-71%) across LMICs [5]. In another study, covering 28 LMICs, the mean world standardized multimorbidity prevalence for LMICs was 7.8%, among population aged \geq 18 years [6]. Prevalence of multimorbidity varied from 4.5% to 83.0% in South Asia [7, 8]. Community-based studies from India such as the WHO SAGE survey conducted in 2007-2010

highlighted that age, belonging to a non-aboriginal ethnicity and urban area increased the risk of being in the 'Hypertension-Diabetes-Arthritis' group. Furthermore, 50% of the individual in the 'Hypertension-Diabetes-Arthritis' group reported poor quality of life, whereas 30% reported poor self-rated health compared to only 11% by their counterparts. Additionally, the mean health score reported by the individuals in the 'Hypertension-Diabetes-Arthritis' group was 39.9 compared to 46.9 by their counterparts. **Conclusions**. The study findings hint towards increasing burden of multimorbidity among the working age population, which depicts a shift in causation of diseases as a result of which preventive measures also need to be taken much prior.

among those aged \geq 18 years, reported a prevalence of 20% [9]. Another study conducted among rural elderly reported a prevalence of 60% [10]. In primary care settings the prevalence of multimorbidity increased from 6% among 18-29 year olds to 44% among those aged \geq 70 years [11]. In all the studies multimorbidity increased with age. Of note, those with multimorbidity were reported to have higher mortality as compared to those with single morbidity [8]. Although most studies have focused on older patients, multimorbidity is more prevalent in absolute terms in those aged under 65 years. However, the impact of multimorbidity in those aged between 15-64 years is underresearched, and we know little about the clinical and sociodemographic characteristics of the working age population with multimorbidity, their patterns of health and social care use, and the potential changes that could be made to services to manage these patients better.

In another study, the number of people with multimorbidity and the prevalence of multimorbidity seems to have increased in recent years [6, 11]. Recent studies examining comorbidity patterns in non-centenarian populations using correlation analysis [12, 13] and latent class analysis revealed that diseases are not independent and tend to compound and interact. Seven comorbidity classes emerged from the data in a study of a large representative sample of Danish adults [14]. While 59% were classified as having no or just one condition, the other six classes had a very high prevalence of multimorbidity. The most prevalent classes included hypertension (14%), musculoskeletal disorders (10%), and mental disorders (7%).

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Thus, there is a need to understand the common patterns of multimorbidity defined as chronic diseases that cluster together most frequently [14]. There were studies which describe disease clusters that occur with the highest frequency or prevalence. However, it may be more meaningful to focus on the associations beyond chance or patterns of diseases, known as associative multimorbidity [15]. Associative multimorbidity is derived by different statistical methodologies, such as observed to expected ratios or odds ratios among the most commonly dyads or triads of chronic conditions, or cluster and factor analyses to identify systematic clusters among diseases. We need a better understanding of the clustering of multimorbidity patterns in the population. Thus, we aimed to explore the profiles of multimorbidity patterns in outpatients of different levels of public health care facilities. Our hypothesis was (a) the presence of distinct patterns with a small but existing proportion of individuals and (b) that these patterns would be associated with sociodemographic factors (gender, age) and selected health outcomes.

Materials and methods

DATA SOURCE AND SAMPLING DESIGN

The present study utilized data from the survey "burden of diseases among patients attending public health care settings of Odisha-2015", undertaken across ten public health care facilities. The project was conducted under the stewardship of the Department of Health and Family Welfare, Government of Odisha, India. The survey utilized a stratified random sampling design to select the study participants [16]. Considering the non-response rate of 10%, a total of 3377 participants were included in the survey in the age-range of 14-95 years. However, as the study is based on the working age-group population, data on 2912 individuals in the age-group 15-64 years as derived from the original dataset for the purpose of the present study.

ETHICAL CONSIDERATION

All the survey tools and documentations received an ethical approval from the Public Health Foundation of India (PHFI) research ethics committee [16]. They were performed in accordance with the relevant guidelines and regulations. Additionally, all essential prior official permission was acquired to conduct the study at health facilities. An informed consent was obtained from all the study participants after disclosing the purpose and procedure of the study. Confidentiality and anonymity were maintained at all stages of data collection and dissemination [16].

MEASURES

The present study utilized information of 18 self-reported chronic diseases including acid peptic disease, arthritis, chronic back pain, diabetes, epilepsy, filariasis, hearing disorder, heart disease, hypertension, kidney disease, lung diseases, mental disorder, osteoarthritis, skin diseases, stroke, tuberculosis, thyroid diseases and vision disorder to identify frequently occurring diseases groups among the working population (15-64 years) in Odisha, India.

The correlates of the identified latent disease classes were further computed, utilizing variables age-group (15-34 years/ 35-49 years/50-64 years), sex (male/female), ethnicity (aboriginal/non-aboriginal), schooling (no education/ primary/secondary and above), current marital status (in union/not in union), socio economic status (above poverty line/below poverty line), place of living (rural/ urban), health insurance (no/yes), and health care facility visited (primary/secondary/tertiary) as predictors and identified latent disease classes as outcome of interest.

Furthermore, the present study utilized three perceptionbased health outcomes, namely poor self-rated health, poor quality of life and health score. Self-rated Health (SRH) was computed by recoding the responses received from the question, "Would you say that your health is?" The responses for the question had five categories, excellent, very good, good, fair and poor, which were recoded into binary variable poor SRH/not poor SRH.

Furthermore, quality of life was assessed utilizing 81 items which were classified into five domains related to quality of life. These domains included acute and chronic symptoms, self-care, mobility, physical activities and usual activities. All the items were recoded to provide a logical direction (unidirectional). Further, a Cronbach' alpha statistics was utilized check the scale reliability (alpha = 0.87), which suggested the scale to reliable for further computation. A principal component analysis was utilized to compute a quality of life (QoL) score, which was further segmented into two parts, namely "poor QoL/non-poor QoL". A detailed description of the items used in the generated of QoL scores is provided in the Additional Document 1.

The third health outcome was a health score, which was based on the question: "Think about a scale of 0-100, with zero being least desirable state of health that you could imagine and 100 being the perfect health. What number, from 0 to 100 would you give to the state of your health. On average over the last three days?

DATA ANALYSIS

A descriptive analysis was used to study the background characteristics of the working age sample under consideration. Additionally, a weighted prevalence was computed for all the 18 chronic disease conditions included in the present study. To identify multimorbidity patterns among the working age-group population a latent class analysis (LCA) approach was carried out [14, 17, 18]. All the eighteen chronic diseases, namely acid peptic disease, arthritis, chronic back pain, diabetes, epilepsy, filariasis, hearing disorder, heart disease, hypertension, kidney disease, lung diseases, mental disorder, osteoarthritis, skin diseases, stroke, tuberculosis, thyroid diseases and vision disorder were included as observed indicators. Four latent classes were included in the study. Fit indices Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) (lowest values were indicative of the best

fitting model) were used to identify the optimal number of latent classes to be included in the study [14, 17, 19]. After identification of the optimal number of latent disease classes, all the units (sampled individual/participants) were segregated into one of the identified latent class using the computed probability of membership [14, 17, 19]. Additionally, item-response probabilities were utilized to assign labels to the identified latent disease classes, i.e. the labels were based on the item(s) (disease(s)) with higher probabilities [14, 17, 19].

In the present analysis only two latent disease classes were identified, out of which the first group had low item-response probabilities of all the eighteen-disease included, and was therefore labelled as 'low comorbidity' group. This 'low comorbidity' group was considered as the base outcome for the unadjusted (bivariate) and adjusted (multivariable) binary logistic regression. Multivariable binary logistic regression was adjusted for age, sex, ethnicity, education level, marital status, socio-economic status, residence, health insurance, and type of facility and was used to identify the correlates of being in the second latent disease class as compared to 'low co-morbidity' group. Linkages of the identified latent disease classes were observed with three perception-based health outcomes, namely poor self-rated health, poor quality of life and health score. To study the association between latent disease classes and perception-bases health outcomes chi-squared tests of significance were performed.

Data wrangling, analysis and visualization were performed using R studio Version 1.3.1093, (R Studio, Inc. PBC) and MS Excel. The r package 'poLCA' (2014) was used to conduct LCA [18]. All the estimates computed in this study are derived by applying appropriate sampling weights derived utilizing the surveys sampling plan.

Results

DESCRIPTION OF THE STUDY POPULATION

The background characteristics of the study participants is presented in Table I.

The prevalence of chronic diseases is presented in Figure 1. Our analysis suggests that 2.4% of the individuals in the working age-group were affected with multimorbidity. The findings suggest that among the working age population, skin disease (5.99%), hypertension (5.92%), arthritis (4.91%), acid peptic disorder (3.87%), diabetes (3.49%), and chronic back pain (1.76%) were the six most commonly occurring disease conditions.

Table II illustrates the findings from the latent model fits. For the present analysis four latent classes were well identified. Smallest values of AIC and BIC were utilized to identify the optimal number of latent classes. Findings suggest that latent class 2 has the lowest AIC (7605.7) and BIC (7826.8) values and therefore, two latent classes were identified from the study sample.

As shown in Table III, these classes were assigned labels on the basis of the item-response probabilities, which were 'low co morbidity' and 'Hypertension-Diabetes-Arthritis', respectively. Each of the study participant

 $\ensuremath{\text{Tab. I.}}$ Descriptive characteristics for working population (15-64 years).

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Variables	Frequency (N = 2912)	Percentage
Age group (in years)		
15-34	1371	51.72
35-49	940	31.61
50-64	601	16.67
Sex		
Male	1517	51.66
Female	1395	48.34
Ethnicity		
Aboriginal	1276	44.68
Non-aboriginal	1636	55.32
Schooling		
No	1031	34.49
Primary	862	29.41
Secondary and above	1019	36.10
Current marital status		
In union	2238	75.33
Not in union	674	24.67
Socio-economic Status		
Below poverty Line	1374	47.03
Above poverty Line	1538	52.97
Place of living		
Rural	812	28.39
Urban	2010	71.61
Health Insurance		
No	1711	61.25
Yes	1095	38.75
Facility		
Primary	430	15.28
Secondary	1902	65.53
Tertiary	580	19.19

was segregated into one of the two identified latent classes based on the highest item-response probability. Around sixty seven percent of the participants belonged to 'low comorbidity' class, whereas 32.89% belonged to 'Hypertension-Diabetes-Arthritis' group. The 'low comorbidity' group included those with low prevalence of all the assessed chronic diseases, whereas 'Hypertension-Diabetes-Arthritis' included individuals with high probabilities of diabetes, arthritis and hypertension, with latent class proportion of 50.60%, 50.20% and 46.10%, respectively.

Table IV provides the description of two latent classes identified in the present study. In the 'low co morbidity' group, 51.90% of the participants belonged in the age-group 15-34 years. Around 52% of the individuals in 'low co morbidity' group were males, 54.90% belonged to non-aboriginal ethnicity group, 36.04% had education level secondary and above, 74.68% were in a marital union, 52.82% reported to be above poverty line, 71.79% resided in urban areas, 61.13% had no health insurance, and 20.17% attended tertiary healthcare facility for curing their ailment. The 'Hypertension-Diabetes-Arthritis' group constituted 53.07% males, 66.99% of the non-aboriginal

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Number of latent classes	Number of observations	Number of parameters estimates	AIC	BIC	G^2	X^2	DF	LL
2	2912	37	7605.7	7826.8	120.8	333.5	2875	-3765.9
3	2912	56	7632.3	7966.9	109.4	265.4	2856	-3760.2
4	2912	75	7645.3	8093.59	84.5	226.1	2837	-3747.7
5	2912	94	7670.5	8232.32	71.7	369.4	2818	-3741.3

Tab. II. Fit statistics for latent class analyses.

L: Log Likelihood; BIC: Bayesian Information Criterion; AIC: Akaike Information Criterion.

Tab. III. Class Proportions and class-specific Probabilities from all Latent Class Model of Chronic Conditions.

Class	1	2
Assigned label	Low comorbidity	Hypertension-Diabetes-Arthritis
Class Proportion	67.11	32.89
Item-response probabilities		
Arthritis	0.039	0.502
Diabetes	0.005	0.506
Hypertension	0.001	0.461
Lung Disease	0.007	0.001
Acid Peptic disease	0.026	0.068
Back Pain	0.015	0.030
Heart Disease	0.004	0.003
Stroke	0.002	0.001
Vision	0.001	0.002
Deafness	0.001	0.001
Kidney Disease	0.003	0.001
Epilepsy	0.003	0.001
Thyroid Disease	0.008	0.001
Tuberculosis	0.008	0.001
Filariasis	0.002	0.001
Mental Disorder	0.001	0.001
Skin Disease	0.079	0.001
Osteoarthritis	0.002	0.001





Fig. 3. Boxplot depicting the distribution of health score between two latent disease classes (chi-squared p-value < 0.000) among older adults.



population, 38.83% not educated, 95.15% in marital union, 52.75% above the poverty line, 66.56% from urban areas, and 59.67% with no health insurance.

Binary logistic regression was adjusted for age, sex, ethnicity, education level, marital status, socio-economic status, residence, health insurance, and type of facility. The findings highlighted that age, ethnicity, and place of residence were found to be significantly associated with the being in one of the multimorbid groups. The findings suggest that with increasing age [(35-49 years: AOR = 9.69 (5.69,16.64); 50-64 years:10.80 (3.89, 15.77)] and belonging to a non-aboriginal ethnicity [AOR = 1.37 (1.02, 1.83)] increased the risk of being in the "Hypertension-Diabetes-Arthritis' group compared to 'low-co morbidity' group. Whereas, residing in urban

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areas [AOR = 0.72 (0.53, 0.98)] reduced the risk of being in the "Hypertension-Diabetes-Arthritis' group by compared to 'low co morbidity' group.

The findings suggest a statistically significant association between latent disease classes with self-rated health (p = 0.000), quality of life (p = 0.000) and health score (p = 0.000). Figure 2 highlighted that 49.96% of the individual in the 'Hypertension-Diabetes-Arthritis' group reported poor quality of life, whereas 30.19% reported poor self-rated health (SRH) compared to only 10.73% reporting poor SRH in the ''low comorbidity group''.

Additionally, the mean health score reported by the individuals in the 'Hypertension-Diabetes-Arthritis' group was 39.9 (scale 0-100) compared to 46.9 by their counterparts (Fig. 3).

Characteristics	Weighted percentage		Latent Class 2 <i>vs</i> Latent Class 1		
	Low comorbidity (N = 2603)	Hypertension- diabetes-arthritis (N = 309)	uOR (95% C.I.)	aOR (95% C.I.)	
Age group (in years)					
15-34 (Ref.)	51.90	6.47	1.00	1.00	
35-49	31.12	42.07	10.84*** (6.72, 17.49)	9.69***(5.64, 16.64)	
50-64	16.98	51.46	14.29***(5.07, 29.16)	10.80***(3.89, 15.77)	
Sex					
Male (Ref.)	51.98	53.07	1.00	1.00	
Female	48.02	46.93	0.95 (0.75, 1.21)	1.21 (0.91, 1.60)	
Ethnicity					
Aboriginal (Ref.)	45.10	33.01	1.00	1.00	
Non-aboriginal	54.90	66.99	1.67*** (1.29, 2.13)	1.37***(1.02, 1.83)	
Schooling					
No education (Ref.)	35.00	38.83	1.00	1.00	
Primary	28.97	34.95	1.09(0.82, 1.43)	1.25 (0.91, 1.72)	
Secondary and above	36.04		0.65**(0.48, 0.88)	0.99 (0.70, 1.41)	
Current marital status					
In union (Ref.)	74.68	95.15	1.00	1.00	
Not in union	25.32	4.85	0.15*** (0.08, 0.25)	0.97 (0.71, 1.32)	
Socio-economic status					
Below poverty line (Ref.)	47.18	47.25	1.00	1.00	
Above poverty line	52.82	52.75	0.99 (0.78, 1.26)	1.03(0.71, 1.31)	
Place of living					
Rural (Ref.)	28.21	33.44	1.00	1.00	
Urban	71.79	66.56	0.78* (0.61, 1.01)	0.72***(0.53, 0.98)	
Health insurance					
No (Ref.)	61.13	59.67	1.00	1.00	
Yes	38.87	40.33	1.06 (0.83, 1.35)	1.03 (0.77, 1.38)	
Facility					
Primary (Ref.)	14.56	16.50	1.00	1.00	
Secondary	5.27	65.70	0.88 (0.64, 1.23)	0.84 (0.58, 1.22)	
Tertiary	20.17	17.80	0.77 (0.52, 1.16)	0.67 (0.43, 1.06)	

Tab. IV. Bivariate and multivariable binary logistic regression results for covariates by latent disease class.

* p < 0.10, ** p < 0.05, *** p < 0.001. uOR: Unadjusted Odds Ratio; aOR: Adjusted Odds Ratio

Discussion

The study indicates the prevalence and patterns of multimorbidity among young working age group populations in primary care setting. The prevalence of multimorbidity was 2.4% in working age group and the most common conditions were skin diseases, hypertension, arthritis, acid peptic disorder, diabetes, and chronic back pain. Latent class analysis found two groups i.e., 'low comorbidity' and 'Hypertension-Diabetes-Arthritis'.

Similar to other studies from India increase in age is the most common risk factor for the higher morbidity group [18, 20, 21]. In contrast to most of studies from India where female gender is found to be predisposed for multimorbidity [11, 21, 22], in our study gender is not a risk factor for higher morbidity group. Hence, the relationship of multimorbidity with gender among the young adults does not seem similar to that in elderly and needs further assessment. We have found that chances of being in 'Hypertension-Diabetes-Arthritis' group is higher among rural population. Other studies from India have also highlighted the growing burden of multimorbidity among rural India. Growing burden of multimorbidity even among rural young's is a concern for Indian health system. Although there are auxiliary nurse midwifes (ANMs) and accredited social health activists (ASHAs) who are the main link between the community and health system i.e., Primary Health Care Centre (PHCs), there primary work is still oriented towards maternal and child care and they currently have very limited training in the field of non-communicable disease. In addition to this, there are paucity of qualified MBBS doctors (allopathic doctors) in rural India and PHCs are often managed by AYUSH (nonallopathic alternative system) physicians [23].

As different studies include different diseases for multimorbidity definition, comparing the pattern of multimorbidity from our study is unfeasible. Furthermore, there is lack of data on multimorbidity in productive age group. A recent community-based study from Kerala from productive age group found prevalence of multimorbidity to be 45%, reasons for high prevalence is that study are higher lower age limit cut off i.e., 30 years, whereas our

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study includes participants aged 15 years and above. Also, that study includes participants with higher blood pressure and blood sugar reading measured at the time of study as hypertension and diabetes whereas our study included only doctor diagnosed hypertensive and diabetic participants [24].

A multi-country study conducted on national databases from high and low middle-income countries among participants aged 50 years and above have found hypertension, cataract, and arthritis as the most prevalent co-morbid conditions. Most common patterns found in this study were "cardio respiratory" (angina, asthma, and chronic obstructive pulmonary disease), "metabolic" (diabetes, obesity, and hypertension), and "mental articular" (arthritis and depression) [22]. Studies from across the world and India also found these as common multimorbidity clusters [22, 25-28]. UK bio-bank study on participants aged 40 years and above has also highlighted that diabetes, hypertension and asthma and usually the common clusters found [29]. Another study from nationally representative data of Danish Adults aged 16 years and above had identified seven classes: 1) Relatively healthy; 2) hypertension; 3) Musculoskeletal Disorders; 4) Headache-Mental Disorders; 5) Asthma-Allergy; 6) Complex Cardio metabolic Disorders; and 7) Complex Respiratory Disorders. However, patterns can't be compared they have also identified poor healthrelated quality of life in patients with multimorbidity clusters in comparison to relative healthy. Other studies also shows poor health related health among patient with multimorbidity [8, 21].

From previous studies and our study finding we can postulate that hypertension, diabetes, asthma and arthritis are few of the most common co morbid conditions in the multimorbid people and affects patient's quality of life and the multidisciplinary approach targeting these diseases could be helpful for the management for patients with multimorbidity. The national programme for prevention and control of cancer, cardiovascular disease, diabetes and stroke (NPCDCS) in India have recently include Chronic Obstructive Pulmonary Disease (COPD), Chronic Kidney Disease (CKD), Non Alcoholic Fatty Liver (NAFLD) and TB program [30]. Integration of all these programs was important because of their common risk factors such as obesity, alcohol use, diabetes and will lead to holistic management of these disease in future. Despite arthritis being the part of most common disease combination, both is young and old population it is still not part of our national programme. Also, there is dearth of rheumatology specialist in India which leads to late diagnosis and mismanagement of patient with arthritis. Therefore, there is need for integration of arthritis management in NPCDCS program and capacity building of primary care physician for its diagnosis and management. Multimorbidity thus requires a multifaceted approach which can be well integrated and approached with ease.

Most of studies on multimorbidity in India are from the older population, anticipating the growing prevalence of multimorbidity among working age group studying the prevalence, patterns, and its health impact in working age population are pivotal. Also, to the best of our knowledge

this is first study from India, to identify the pattern of diseases using latent class analysis among working class group as most of the studies usually report most common dyad and triads. Although the data of chronic conditions are self-reported we have cross verified the medical records to confirm the diagnosis. Another limitation is association observed doesn't infer causality because of cross-sectional study design.

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Conclusions

'Hypertension-Diabetes-Arthritis' emerged as a recurrent disease group among the individuals in the working group. The findings hint towards sociodemographic inequality in the disease burden. Individuals in the disease group are more likely to be associated with poor perception-based health outcomes. Thus, interventions with equitable prevention approaches, ensuring improved physical and mental well-being, are vital to reducing the burden on the high-risk disease group. Study findings vary owing to the differential cut-off values used. There needs to be uniformity in deciding and defining where to start. Moreover, there is a shift in the causation of diseases, resulting in which preventive measures also need to be taken much prior. Similar studies based on a nationallyrepresentative sample are warranted.

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Ethical aproval

All the survey tools and documentations received an ethical approval from the Public Health Foundation of India (PHFI) research ethics committee. They were performed in accordance with the relevant guidelines and regulations. Additionally, all essential prior official permission was acquired to conduct the study at health facilities. An informed consent was obtained from all the study participants after disclosing the purpose and procedure of the study. Confidentiality and anonymity were maintained at all stages of data collection and dissemination.

Conflict of interest statement

The authors declare that they gave no competing interests.

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Authors' contribution

Conceptualization: SP. Methodology: SP, MP, MP, PP. Software: PP, PM, MP. Validation: PP, PM, MP. Formal analysis: PP, PM, MP. Data Curation: PP, PM, MP. Writing -Original Draft: SP, PP and PG. Writing - Review & Editing: SP, PP and PG. Visualization: PP, PM, MP. Supervision: SP. Project administration: SP.

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