Master of Public Health

Master de Santé Publique

THE MENTAL HEALTH IMPACT OF CARDIOMETABOLIC DISEASE AND ROLE OF DIAGNOSIS STATUS:

A COMPARATIVE ANALYSIS OF A 10-YEAR DEPRESSION INCIDENCE RATE IN DIAGNOSED AND UNDIAGNOSED HYPERTENSION/DIABETES IN RURAL INDIA

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List of acronyms

Abbreviation	Definition
APCAPS	Andhra Pradesh Children and Parents Study
BP	Blood pressure
CI	95% confidence intervals
DM	Diabetes Mellitus
FFQ	Food Frequency Questionnaire
HNT	Hyderabad Nutrition Trial
HPA	Hypothalamic-pituitary-adrenal
ICMR	Indian Council of Medical Research
NCDs	Non-communicable diseases
NFHS-2	National Family Health Survey (1998-1999)
NFHS-4	National Family Health Survey (2015-16)
NFHS-5	National Family Health Survey (2019-21)
OR	Odds ratios
PHQ-9	Patient Health Questionnaire-9
RSSDI	Research Society for the Study of Diabetes in India
SLI	Standard of Living Index

Abstract in English

Background: Understanding the impact of cardiometabolic diseases and diagnosis status on mental health in rural India is crucial for estimating the burden of such conditions. This research will explore the relationship between cardiometabolic diseases on whether the risk of developing depression is affected by diagnosis status. We hypothesise that people with the diagnosed cardiometabolic disease have a higher incidence of depression compared to those with the disease based on screening or without either condition.

Methods: We analysed data on 3233 participants from Andhra Pradesh Children and Parents Study, a prospective inter-generational ongoing cohort research, from the 3rd (2012-12) and 4th follow-up (2020-22) waves. The incidence risk of depression in different diagnosis status groups was calculated. Logistic regression analysis examined the association between diagnosis status and the risk of developing depression while controlling for potential confounders.

Results: The incidence risk of all participants with depression was 13.07%. Individuals who screened positive for cardiometabolic disease but did not report a previous diagnosis had a lower risk, 10.13%. Participants who were classified as undiagnosed in the diagnosis status of cardiometabolic disease had a 31% (OR: 0.69 95% CI: 0.50, 0.94) lower odds of having depression compared to those who had no previous diagnosis and did not screen positive after adjusting for all aforementioned covariates and also behavioural one, including smoke and alcohol consumption, sleeping habits and dietary habits (food and vegetables daily intake). Although no strong evidence of an association between previous diagnosis status and the odds of depression (OR: 1.17 95% CI: 0.80, 1.67).

Conclusion: The results suggest that there might be some psychological impact that comes with receiving a diagnosis of cardiometabolic disease and depression. Thus, a holistic healthcare strategy is needed to prioritise the physical and mental well-being of individuals affected by these conditions. Further research is required in order to explore the underlying mechanisms linking disease diagnosis and depression and evaluate the effectiveness of interventions aimed at improving mental health outcomes in this population.

Keywords: cardiometabolic disease, depression, diagnosis status, APCAPS

Abstract in French

Contexte : Comprendre l'impact des maladies cardiometaboliques et du statut de diagnostic sur la santé mentale dans les zones rurales de l'Inde est crucial pour estimer le fardeau de ces maladies. Cette recherche explorera la relation entre les maladies cardiometaboliques et l'incidence de développer une dépression en fonction du statut de diagnostic. Nous formulons l'hypothèse que les personnes atteintes de maladies cardiometaboliques diagnostiquées ont une incidence plus élevée de dépression par rapport à celles ayant une maladie basée sur le dépistage ou aucune des deux conditions.

Méthodes : Nous avons analysé les données de 3233 participants de l'étude en cours prospective intergénérationnelle "Andhra Pradesh Children and Parents Study", à partir des 3ème (2012-12) et 4ème (2020-22) vagues de suivi. Le risque d'incidence de la dépression dans différents groupes de statuts de diagnostic a été calculé. Une analyse de régression logistique a été réalisée pour examiner l'association entre le statut de diagnostic et le risque de développer une dépression, tout en contrôlant les facteurs de confusion potentiels.

Résultats : Le risque d'incidence de la dépression pour l'ensemble des participants était de 13,07 %. Les personnes ayant un dépistage positif pour une maladie cardiometabolique mais n'ayant pas signalé de diagnostic antérieur présentaient un risque plus faible, soit 10,13 %. Les participants classés comme non diagnostiqués dans le statut de diagnostic des maladies cardiometaboliques avaient une probabilité inférieure de 31 % (OR : 0,69, IC à 95 % : 0,50, 0,94) d'avoir une dépression par rapport à ceux qui n'avaient pas de diagnostic antérieur et n'avaient pas un dépistage positif après ajustement pour tous les covariables précédents et comportementaux, y compris la consommation de tabac et d'alcool, les habitudes de sommeil et les habitudes alimentaires (consommation quotidienne de fruits et légumes). Bien qu'il n'y ait pas de preuve solide d'association entre le statut de diagnostic antérieur et la probabilité de dépression (OR : 1,17, IC à 95 % : 0,80, 1,67).

Conclusion : Les résultats suggèrent qu'il pourrait y avoir un impact psychologique lié au fait de recevoir un diagnostic de maladie cardiometabolique et de dépression. Ainsi, il est nécessaire de mettre en place une stratégie de soins de santé holistique qui priorise le bien-être physique et mental des personnes touchées par ces conditions. Des recherches supplémentaires sont nécessaires pour explorer les mécanismes sous-jacents liant le diagnostic de la maladie et la dépression, ainsi que pour évaluer l'efficacité des interventions visant à améliorer les résultats de santé mentale dans cette population.

Mots clés : maladie cardiometabolique, dépression, statut de diagnostic, APCAPS

Introduction

India and the burden of non-communicable diseases

Non-communicable diseases (NCDs) include a diverse range of conditions, including cardiovascular diseases, cancer, diabetes, and chronic respiratory diseases. [i] These NCDs are responsible for a significant proportion of global mortality, accounting for approximately 55 million deaths (nearly 71% of total deaths) worldwide.[ii iii] The majority of NCDs fatalities occur in low and middle-income countries, such as India, which are currently experiencing an epidemiological health transition as a result of rapid urbanisation, population ageing, limited availability of healthcare resources and inadequate infrastructure for disease management.[ivv] In India, approximately 5.87 million deaths (60% of total deaths) are attributed to NCDs.[vi]

Changes in lifestyle and dietary habits, including increased consumption of processed foods, sedentary behaviour, and decreased physical activity, have led to an increase in the incidence of cardiometabolic diseases such as hypertension and diabetes, which are major contributors to morbidity and mortality, not just in India, but in the world.[vii]

Cardiometabolic risk factors can develop into cardiometabolic diseases, playing a significant role in increasing the risk of NCDs. [viii] Among these, hypertension, or elevated blood pressure, is the leading global contributor to attributable deaths, accounting for 19% of global deaths. It is followed by diabetes, raised blood glucose levels, and overweight/obesity in terms of their impact on mortality rates. [ix] Other behavioural and biological risk factors contribute to the predisposition for developing NCDs, including tobacco and alcohol use, decreased physical inactivity, excessive fat and sodium intake, and inadequate fruit and vegetable consumption. [xxi]

Hypertension and Diabetes in India

In India, hypertension and diabetes are two of the most prevalent cardiometabolic diseases. [xii] The prevalence of diabetes mellitus (DM) in India is alarmingly high, with around 15% of the general adult population being affected by either diabetes or pre-diabetes. [xiiixiv] Additionally, the prevalence of hypertension among men and women has risen from 19% and 17%, respectively, as reported in the previous round of the National Family Health Survey (NFHS-5) conducted in 2015-2016, to 24% in men and 21% in women in the latest survey conducted during 2019-2020.[xv] These risk factors are considered potentially modifiable, except for age and gender.[xvi]

Hypertension is particularly significant in India as a risk factor for disability and mortality, given its strong association with CVDs.[xvii] A study by the Indian Council of Medical Research (ICMR) reported a hypertension prevalence of 25% in 2017, highlighting that hypertension increases with age.[xviiixix]

The high prevalence of hypertension and diabetes in India poses a substantial public health burden, and preventive measures are essential to reduce their burden on individuals, families, and society.[xx] Factors such as poor access to healthcare, limited education, poverty, and a lack of awareness about these diseases contribute to the high prevalence of hypertension and diabetes in rural India.[xxi]

Undiagnosed Hypertension and Diabetes in India

These conditions often go undiagnosed, particularly in rural areas with low health awareness, limited access to health or inadequate healthcare infrastructure, and limited availability of healthcare professionals or low quality of medical care attention.[xxiixxiii] A recent study suggests that the prevalence rate of undiagnosed hypertension among older adults in India was 42.3%. In the context of rural India, it's essential to understand the disparities between urban and rural areas.[xxiv] The same study revealed that the prevalence of undiagnosed hypertension was higher in rural areas by 12.4%. Socioeconomic and lifestyle factors appear to play a significant role in this disparity.[xxvxxvi]

Despite remarkable progress in awareness and treatment rates for hypertension, undiagnosed and untreated cases continue to be a significant public health concern. This might be because it lacks early symptoms, and why it is commonly referred to as the "silent killer".[xxvii]

A study of the National Family Health Survey (NFHS-4)/Demographic Health Survey 2015–2016 suggests that a substantial proportion, around 42%, of the diabetes population in India remains unaware of their diabetes condition. [xxviii] On the other hand, in 2019, the prevalence of diabetes in India was estimated to be 77 million individuals. Alarmingly, around 57% remain undiagnosed.[xxix] Another study suggested that the prevalence of undiagnosed diabetes followed a similar trend as undiagnosed hypertension, which is higher in rural areas compared to urban areas.[xxx]

Previous studies have suggested a strong correlation between undetected, untreated, or uncontrolled hypertension or diabetes and lower socio-economic status, including living in rural areas, lower education levels, and limited income, as well as age and gender.[xxxi]

This highlights the need for improved prevention, diagnosis, and management of cardiometabolic diseases in India. [xxxiixxxiii] Undiagnosed cases of these conditions have significant consequences for individuals and the healthcare system.[xxxiv] When left undiagnosed, cardiometabolic diseases can progress silently, leading to severe complications such as heart attacks, strokes, kidney disease, and vision loss.[xxxv] However, with accurate diagnosis, timely management, and appropriate treatment, the health outcomes and quality of life for individuals with these conditions can be significantly improved.[xxxvi] Early detection allows for the implementation of lifestyle modifications, medication adherence, and regular monitoring, reducing the risk of complications and enabling individuals to lead healthier lives.[xxxvii] Moreover, effective management of hypertension and diabetes can also alleviate the burden on the healthcare system by preventing costly emergency interventions and hospitalisations.[xxxviii]

Relationship between chronic disease and depression

The mental health impact of cardiometabolic diseases cannot be underestimated.[xxxix] Mental health conditions also contribute to the global burden of disease.[xl] According to the Global Burden of Disease study, mental disorders account for approximately 15% of years of life lost, making them one of the leading contributors to global disability.[xli] Depression is a leading cause of disability worldwide and a significant public health issue in India.[xlii], The prevalence of chronic and mental conditions has increased in recent years, leading to concerns about the physical and mental health of those living with such conditions.[xliii]

In India, there is a significant burden of depression that often goes undiagnosed and is closely associated with adverse health and well-being outcomes. [xliv]Similarly, depression has a significant impact on an individual's quality of life and productivity.[xlv] A study conducted in India found that individuals with depression had lower levels of physical, social, and occupational functioning compared to those without depression.[xlvi] Moreover, depression has been associated with an increased mortality risk among individuals with chronic diseases such as hypertension and diabetes.[xlvii]

In addition to its impact on quality of life and productivity, depression has been found to have a higher prevalence in individuals with cardiometabolic diseases.[xlviii] Various potential mechanisms contribute to the increased risk of depression among individuals with hypertension or diabetes. Firstly, the physiological consequences of these diseases are similar, including chronic inflammation, oxidative stress, and dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, which can directly affect brain function and neurotransmitter systems implicated in mood regulation.[xlixl]

Moreover, the psychological and emotional burden associated with the diagnosis and management of these chronic diseases can significantly impact an individual's mental health. [li] The experience of living with a chronic condition often entails lifestyle modifications, medication adherence, and regular monitoring, which can lead to feelings of stress, frustration, and even self-blame. [lii]Additionally, potential complications and social stigma can further contribute to psychological distress and increase the risk of depression.

The diagnosis status, whether hypertension or diabetes is diagnosed or undiagnosed, may also play a role in the development of depression. Undiagnosed conditions, in particular, can generate uncertainty and anxiety, as individuals may experience symptoms without a clear understanding of their underlying cause. [liii] On the other hand, the awareness of a diagnosed condition may bring about additional psychological challenges, such as fear of disease progression, concerns about medication side effects, or the perceived stigma associated with having a chronic illness. [liv]

Few research studies have directly compared the long-term consequences of chronic illnesses and depression. Even fewer studies, particularly small cross-sectional ones, in the world have examined the likelihood of developing depression after the diagnosis of a chronic illness within the same cohort.[lvlvi]. The longitudinal design of the APCAPS data will allow the use of a single cohort through time. Studying the impact of cardiometabolic diseases and the role of diagnosis status on mental health in rural India is crucial for estimating the burden of cardiometabolic diseases in rural India.

Aim and objectives:

This research will explore the relationship between cardiometabolic diseases and mental health conditions, specifically focusing on whether the risk of developing depression is affected by having diagnosed or undiagnosed hypertension or diabetes. By understanding this relationship, we could

also explore potential causal mechanisms. Similarly, healthcare professionals and policymakers will be able to develop better strategies to address the mental health needs of those living with chronic diseases.

This research will include the following objectives:

Objectives

1. To determine and compare the incidence of depression among individuals.
    a. Diagnosed with cardiometabolic disease (hypertension and/or diabetes).
    b. Undiagnosed with cardiometabolic disease (hypertension and/or diabetes) but screening positive.
    c. Not diagnosed nor screened positive for cardiometabolic disease (hypertension and/or diabetes).
2. To examine the association between having diagnosed or undiagnosed hypertension/diabetes compared with being healthy on the risk of developing depression while controlling for confounding variables such as age, gender, education, lifestyle, and socioeconomic status.

Hypothesis:

People with a diagnosed cardiometabolic disease (hypertension or diabetes) are at higher risk of depression compared to those with a cardiometabolic disease based on screening and those without either, which may be due to both symptoms associated with their cardiometabolic condition, as well as negative impacts of disease diagnosis and management (stress, healthcare costs, stigma etc).

Methods:

Population and settings

The APCAPS is a prospective inter-generational ongoing cohort research project in Southern India. It began with the long-term follow-up of the Hyderabad Nutrition Trial (HNT) 1987-90 conducted in 29 villages (Ranga Reddy district) in the south Indian state of Telangana. It evaluated a national community outreach program providing daily food supplements to pregnant women and young children.[lvii]

In 2003-05, mothers who referred having at least one child born during the trial period and still alive became the APCAPS prospective cohort index children. A third follow-up was carried out between 2010 and 2012 when their siblings and parents were also examined. In 2020-2022, a fourth APCAPS survey wave included all available HNT index children, their parents, and siblings.[lviii]

Inclusion and exclusion criteria

The study population included all who consented to the third and fourth follow-up waves of the APCAPS survey. Likewise, those who had participated in both follow-up surveys underwent a physical examination for blood pressure, gave a blood sample for fasting plasma glucose in the third follow-up, and completed the Patient Health Questionnaire-9 (PHQ-9) in the fourth follow-up wave. Exclusion criteria consisted of individuals who did not participate in the data collection, including blood samples and blood pressure measurement in the third follow-up wave, as well as those who did not complete the PHQ-9 diagnostic tool for depression in the fourth follow-up wave. Participants with any missing data in the covariates studied were excluded from this study. Similarly, those who reported a previous diagnosis of depression in the third follow-up were excluded from the study population.

Ethical review

The study has received ethical approval from the University of Sheffield, ensuring that the research is conducted ethically and responsibly. Using secondary data collected by the APCAPS group allows us to address the research question while upholding ethical standards and principles. The approval process involved a rigorous review of the study design, data collection methods, and the potential risks and benefits to participants. The approval granted by the University of Sheffield also ensures that the use of the data complies with relevant laws and regulations related to data protection and privacy. The study team will ensure that all data is kept secure and confidential and that the study results are reported in a way that protects the privacy and confidentiality of the participants.

Source of Data and Data collection

The research will be based on secondary data from participants, using a self-reported questionnaire, through an interviewer-administered in the local language, which was previously collected through a longitudinal study in the third (2010-2012) and fourth follow-up wave (2020-2022). It included socioeconomic and demographic details, lifestyle habits (such as diet, exercise, tobacco and alcohol consumption, and sleep patterns), as well as a physical examination. The aforementioned, along with occupation, marital status and education level, were considered covariates.

The questionnaire started by asking about personal data, where age and gender were taken from. To determine the standard of living, the NFHS developed a Standard of Living Index (SLI) in 2000 with data collected by the National Family Health Survey (NFHS-2) 1998-1999; a subset of questions about socioeconomic position was used, 27 items such as consumer goods, agricultural equipment, housing quality, and access to essential services such as water, electricity, and fuel.

The single Food Frequency Questionnaire (FFQ) was designed and conducted using a validated interviewer-administered semi-quantitative food frequency questionnaire, which collected information on portion sizes and frequencies of 184 commonly consumed food items over the last year. Visual aids were used to record standard portion size and frequency.[lix]

On the other hand, tobacco was assessed with the question “If ever smoked tobacco on regular basis” and alcohol consumption was asked as frequency intake of beer, wine, and local and branded spirits. Lastly, sleeping habits was inquired as average hours of sleep on a working day.

During the physical examination in the third wave, the participant's blood pressure was measured using a validated oscillometric device (Omron M5-I model) with an appropriate-sized cuff on the right upper arm, in a sitting position. After resting for 5 minutes, three consecutive readings were taken 1 min apart from each other. Similarly, participants were asked to fast overnight (at least 8 hours) and rest quietly for 10 minutes before venous blood samples (up to 20ml) were collected from their preferred arm by a trained phlebotomist. Blood was collected into vacutainers and processed (centrifuged and aliquoted) for the fasting plasma glucose sample.

The PHQ-9 was used as a screening tool for depression, which is a short questionnaire consisting of nine questions relating to depression symptoms, facilitating a criterion-based diagnosis of depression.

Data analysis

The exposure variables and covariates were only chosen from the third follow-up wave, including age, gender, occupation, education, marital status, standard of living, alcohol and tobacco consumption, sleeping patterns, and dietary habits. On the other hand, the outcome variable of depression was taken from the fourth follow-up wave.

Occupation was categorised as student/training, housework, employed and unemployed. Socioeconomic status, was grouped into tertiles using the Standard of Living Index. Education level was divided into none (no formal education and illiterate), primary, secondary, and higher education. Lastly, marital status was categorised as never married, currently married, and widowed/divorced or separated.

Tobacco and alcohol consumption were created as binary; the latter was created by combining frequency intake of beer, wine, and local and branded spirits considering if ever they had as positive. On the other hand, tobacco was assessed as if ever having smoked tobacco on a regular basis (at least weekly); former (<6 months) and current were categorised as yes and never as no. Sleeping habits were categorised by how many hours a day they slept on average, <6, 6-8 or >8 hours.

This research used only portions of fruits and vegetables to indicate an adequate diet. We used average consumption, portion frequency, and frequency of consumption per every fruit and vegetable in the FFQ. We focused on the 16 types of fruits and 14 vegetables included in the questionnaire to determine the portions per day for each. We then proceeded to add the total amount and see if it was above or below five daily portions.

As for high blood pressure, for purposes, and in accordance with guidelines, the last two readings of systolic and diastolic blood pressure were used to determine the average reading for recording purposes. The cut-off points were an average systolic blood pressure of ≥140 mmHg or an average diastolic blood pressure of ≥90 mmHg at the time of the interview. As for a high fasting plasma glucose, the criterion of ≥125 mg/dl was used as part of the guidelines of the Research Society for the Study of Diabetes in India (RSSDI).[lx]

Regarding PHQ-9, each question is assigned a score ranging from zero (not at all) to three (nearly every day), enabling a minimum score of zero and a maximum score of 27, with higher scores indicating greater severity of depression. Among Indians, a cut-off score of 10 has a sensitivity of 87.1% and a specificity of 79.7% for detecting depression.[lxi]

The data was analysed using a quantitative approach to address the research question and objectives using R as a technological tool.

Definition of cardiometabolic disease as exposure categorical variable, diagnosis status.

- *Diagnosed:* Participants in both the third and fourth wave follow-up who self-reported having previously been diagnosed with hypertension or diabetes in the third follow-up wave.

- *Undiagnosed:* Participants that were in the third and fourth wave follow-up who did not self-report having previously been diagnosed with hypertension or diabetes but that had an average systolic or diastolic blood pressure of ≥140 or 90 mmHg respectively, or ≥126 mg/dl of fasting plasma glucose in the third follow-up wave.

- *Without diagnosis or screening positive:* participants that partook in both the third and fourth follow-up waves, who did not refer ever been diagnosed with hypertension or diabetes and did not have an average systolic or diastolic blood pressure of ≥140 or 90 mmHg respectively, and ≥126 mg/dl of fasting plasma glucose in the third follow-up wave.

Definition of depression as outcome binary variable

- Participants who had a score ≥ 10 on the PHQ-9 Depression Test questionnaire were considered as positive.

Statistical analysis

Description of how the study population was created, including those who were not included and why. Followed by descriptive statistics, such as frequency distributions, of the complete case study population, with an overall view and divided by diagnosis status and the exposure variable.

The cumulative incidence of depression among three groups of participants based on their health status: a) those diagnosed with hypertension and/or diabetes, b) those with hypertension and/or diabetes (based on screening tests) but without a diagnosis for either, and c) healthy individuals without hypertension or diabetes will be obtained. The incidence risk of depression will be calculated for each group, which is the proportion of individuals who developed depression from the third follow-up wave to the fourth follow-up wave of those without depression in the third follow-up wave.

Regression analysis

To investigate the association between health status (diagnosed or undiagnosed hypertension/diabetes, or without hypertension or diabetes) and the risk of developing depression while controlling for potential confounding variables, a logistic regression analysis will be conducted.

The dependent variable will be the presence or absence of depression, and the independent variables will include the participants' health status (diagnosed or undiagnosed hypertension/diabetes, or healthy without hypertension or diabetes), as well as, gender, lifestyle factors (e.g., smoking, dietary habits, sleeping habits, alcohol consumption, etc.), socioeconomic status (measured in tertiles of the Standard Living Index), education level, and marital status.

Odds ratios (OR) with corresponding 95% confidence intervals (CI) will be used to estimate the strength and direction of the association between each independent variable (10) and the dependent variable. The results will be interpreted to determine the extent to which having diagnosed or undiagnosed hypertension/diabetes is associated with an increased risk of depression, after controlling for other factors.

Results

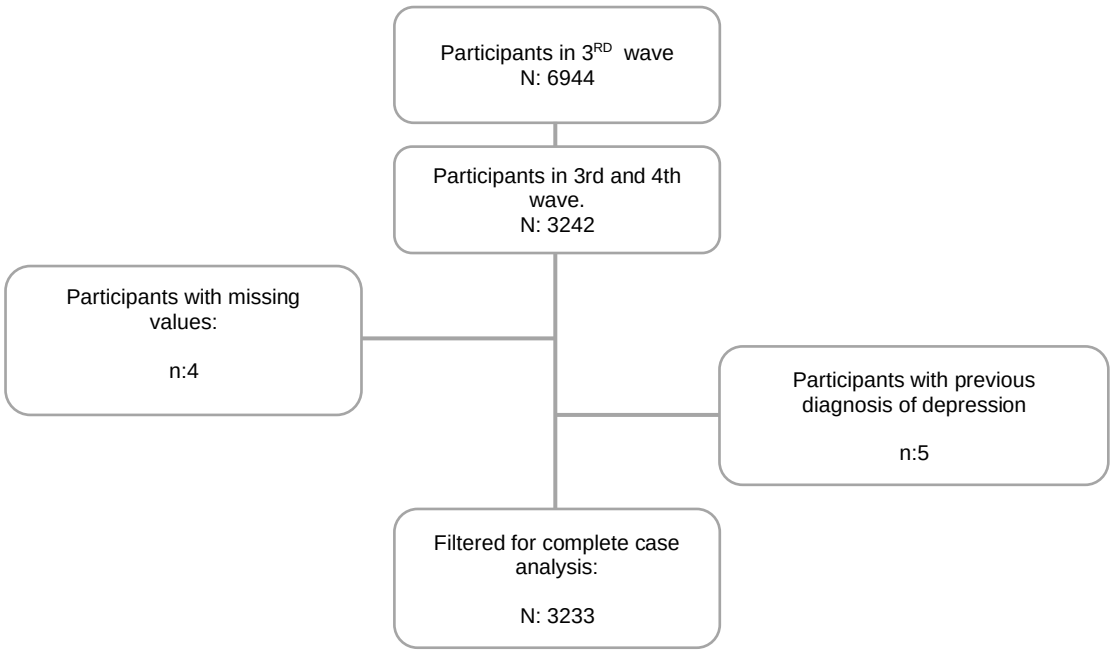

Figure 1. Schematic representation of the construction of the study's cohort

Figure 1. shows how the final cohort was constructed. Out of 6944 participants in the third follow-up, only 3242 had data in the fourth follow-up. Therefore, a complete case analysis was performed, removing those who had at least one variable used in the research, including covariates (gender, age group, occupation, occupation, education level, marital status, alcohol and tobacco consumption and dietary habits) with missing information. The final population, with the exposure and outcome and no missing data in the covariates considered for this research, was 3233 participants.

Table 1 Sociodemographic characteristics of the population by diagnosis status

Characteristics	Overall N = 3,233	Previously diagnosed with cardiometabolic disease. N = 241[1]	Presence of undiagnosed cardiometabolic disease N = 518[1]	Current presence of cardiometabolic disease (previous diagnosis and screening) N = 759 [1]	Neither, not diagnosed or screened for cardiometabolic disease. N = 2,474[1]
Gender					
Female	1,496 (46)	121 (50)	200 (39)	321 (42.3)	1,175 (47)
Male	1,737 (54)	120 (50)	318 (61)	438 (57.7)	1,299 (53)
Age group					
18-44	1,261 (39)	7 (2.9)	105 (20)	112 (14.7)	1,149 (46)
45-64	1,536 (48)	172 (71)	317 (61)	489 (64.4)	1,047 (42)
65+	436 (13)	62 (26)	96 (19)	158 (20.8)	278 (11)
Marital Status					

Currently married	2,282 (71)	213 (88)	439 (85)	652 (85.9)	1,630 (65.8)
Never married	766 (24)	1 (0.4)	52 (10)	53 (7.0)	713 (29)
Widowed/Divorced/Separated	185 (5.7)	27 (11)	27 (5.2)	54 (7.1)	131 (5.3)
Occupation					
Employed	2,516 (78)	189 (78)	461 (89)	650 (85.6)	1,866 (75)
Housework	340 (11)	39 (16)	41 (7.9)	80 (10.5)	260 (11)
Student/training	313 (9.7)	1 (0.4)	9 (1.7)	10 (1.3)	303 (12)
Unemployed	64 (2.0)	12 (5.0)	7 (1.4)	19 (2.5)	45 (1.8)
Education level					
None	1,856 (57)	185 (77)	360 (69)	545 (71.8)	1,311 (53)
Primary	431 (13)	44 (18)	74 (14)	118 (15.5)	313 (13)
Secondary	791 (24)	11 (4.6)	69 (13)	80 (10.5)	711 (29)
Higher	155 (4.8)	1 (0.4)	15 (2.9)	16 (2.1)	139 (5.6)
Standard of Living Index					
One	139 (4.3)	6 (2.5)	27 (5.2)	33 (4.3)	106 (4.3)
Two	816 (25)	59 (24)	121 (23)	180 (23.7)	636 (26)
Three	2,278 (70)	176 (73)	370 (71)	546 (71.9)	1,732 (70)
Smoking					
Yes	538 (17)	60 (25)	133 (26)	193 (25.4)	345 (14)
No	2695 (83)	181 (75)	385 (74)	566 (74.6)	2129 (86)
Sleeping habits					
<6 hours	266 (8.2)	14 (5.8)	47 (9.1)	61 (8.0)	205 (8.3)
6-8 hours	2,233 (69)	176 (73)	350 (68)	526 (69.3)	1,707 (69)
>8 hours	734 (23)	51 (21)	121 (23)	172 (22.6)	562 (23)
Alcohol consumption					
Yes	2,237 (69)	166 (69)	412 (80)	578 (76.1)	1,659 (67)
No	996 (31)	75 (31)	106 (20)	181 (23.8)	815 (33)
Diet: fruits and vegetables					
<5 portions per day	1,565 (48)	132 (55)	249 (48)	381 (50.2)	1,184 (48)
>5 portions pr day	1,668 (52)	109 (45)	269 (52)	378 (49.8)	1,290 (52)

[1] n (%)

Table 1. represents the sociodemographic features of the 3233 participants, according to their diagnosis status. Overall, approximately 54% self-reported as men and 46% as women. Only in the diagnosed group the prevalence of females was higher than men.

On the other hand, in age groups, in all disease present groups (previous diagnosis, no previous diagnosis but screening positive and the combination of the two), the prevalence was higher between 45-64. Whereas in the no previous diagnosis, no screening positive for cardiometabolic disease, the predominant age group was 18-44.

Regarding marital status, most participants (71%) reported being currently married and followed similar trends within each diagnosis status; at least 2/3 self-reported being currently married. Only one participant self-reported never being married within the diagnosed group (previous diagnosis). Similar proportions were seen in those with a current presence of cardiometabolic disease (previous diagnosis or no previous diagnosis but screening positive), between

widowed/divorced or separated ad never being married, with 7.1 and 7.0%, respectively. It was even higher within the diagnosed group (88%).

The majority, within each diagnosis status group, reported currently being employed. Whereas housework was more predominant in the diagnosed group. Unemployment was only reported in less than 5% of all of the diagnosis status groups. On the other hand, no formal education was reported in every diagnosis status group, with more than 50%. The second highest proportion within the overall population was secondary school, with 24%. However, only those who did not report a previous diagnosis and did not screen positive followed the same trend, all the other diagnosis statuses had primary as their second-highest education level. Regarding the Standard of Living Index, 70% of the overall population was found in the third tertile, followed by the second and the third. The same trend was seen in all diagnosis categories.

Regarding health-related behaviours, 17% of the overall sample had or were current smokers, compared to those that never had. However, it was slightly higher in those who did not report a previous diagnosis of cardiometabolic disease but screened positive for it compared to those that reported a previous diagnosis of cardiometabolic disease, with 26% and 25%, respectively.

Likewise, concerning sleeping habits, most of the overall population was within the range of sleeping 6 to 8 hours a day, followed by more than 8 hours. Similar trends were seen in al diagnosis status groups. On the other hand, alcohol consumption was present in 69% of the population. However, the highest proportion was found in those who did not refer a previous cardiometabolic disease but screened positive, with 80%. The lowest was found in those who had not been ever diagnosed and had not screened positive for any cardiometabolic disease, with 67%. Lastly, regarding dietary habits, 52% of the population eats more than five portions of fruits and vegetables daily. However, in the diagnosed group, the proportion was less, with the majority, 55% consuming less than five portions a day.

Table 2 Clinical characteristics of participants by diagnosis status and depression

Clinical Characteristic	N = 3,233	Yes N = 422[1]
Previously been diagnosed with Diabetes	60 (1.9)	13 (21.67)
Previously been diagnosed with Hypertension	197 (6.1)	35 (17.77)
Previously been diagnosed with Diabetes or Hypertension	241 (7.5)	43 (17.84)
Screened positive for Hypertension without previous diagnosis	475 (15)	49 (10.32)

Screened positive for Diabetes without previous diagnosis	68 (2.1)	6 (8.82)
Screened positive for Diabetes or Hypertension without previous diagnosis	518 (16)	52 (10.04)
No previous diagnosis and no screening for Diabetes and Hypertension	2,474 (77)	327 (13.22)
Previous diagnosis and screened positive for hypertension or diabetes	759 (23)	95 (12.52)
Total population in study cohort	3233 (100)	422 (13.05)

[1] n (%)

In *Table 2.* We can observe that there were 518 participants who did not previously report a diagnosis of a cardiometabolic disease but had high blood pressure or high fasting plasma glucose. However, within that group, the majority were from those who did not refer previous hypertension but had an average blood pressure of ≥140/90 mmHg during the physical examination (475 participants) compared to those who did not refer a previous diagnosis of diabetes but had ≥126 fasting plasma glucose (68 participants). Within this group, 25 did not report a previous cardiometabolic disease but screened positive for both, thus the difference. On the other hand, only 241 referred a previous cardiometabolic diagnosis. Similarly to the undiagnosed group, 16 participants had comorbidity (hypertension and diabetes) when asked if previously diagnosed and thus were only counted once. A total of 759 participants currently had cardiometabolic disease. On the other hand, 2474 did not refer to ever being diagnosed with hypertension or diabetes and did not screen positive during the physical examination.

The outcome, depression, was measured in the fourth follow-up wave. In contrast, the exposure of cardiometabolic disease as diagnosis status was measured in the third follow-up wave, giving us ten years between the exposure and the outcome. However, during the self-report questionnaire, five people reported a previous diagnosis of depression. Thus, for this analysis, the 5 participants were excluded in order to obtain the incidence risk estimate for depression in each health status category.

In the second and third columns of *Table 2.* we can observe the participants by diagnosis status and depression. Depression was present in 13.05% of participants, 422 out of 3228. Previous diagnosis of hypertension and previous diagnosis of hypertension or diabetes had similar risks for developing depression, 17.77% and 17.84%, accordingly in the 10-year difference in follow-up waves. On the other hand, when compared to those who did not report having a previous diagnosis but screened positive (high blood pressure or high fasting plasma glucose), only 10.04% developed depression in the time period.

Table 3. Univariate analysis to evaluate the impact of potential confounders on the outcome of depression with OR, 95% CI and p-values. (N = 3233)

Potential confounders	OR [1]	95% CI [1]	p-value
Gender			
Female	1	1	
Male	0.45	0.36, 0.55	<0.001
Age Groups			
18-44	1	1	
45-64	1.96	1.55, 2.49	<0.001
65+	1.76	1.27, 2.44	<0.001
Marital Status			
Currently married	1	1	
Never married	0.5	0.37, 0.67	<0.001
Widowed/Divorced/Separated	1.61	1.10, 2.32	0.012
Occupation			
Employed	1	1	
Housework	1.27	0.92, 1.71	0.14
Student/training	0.45	0.27, 0.70	<0.001
Unemployed	1.84	0.97, 3.27	0.049
Education level			
Higher	1	1	
None	2.8	1.53, 5.73	0.002
Primary	1.65	0.84, 3.55	0.2
Secondary	1.36	0.72, 2.88	0.4
Standard of Living Index			
One	1	1	
Two	0.76	0.48, 1.26	0.3
Three	0.69	0.44, 1.11	0.11
Sleeping habits			
<6 hours	1	1	
6-8 hours	0.75	0.54, 1.07	0.1
>8 hours	0.7	0.47, 1.04	0.07
Alcohol consumption			
No	1	1	
Yes	0.96	0.77, 1.20	0.7
Smoking			
No	1	1	
Yes	0.62	0.45, 0.85	0.003
Diet: fruits and vegetables			
<5 portions per day	1	1	
>5 portions per day	0.97	0.79, 1.19	0.8

Table 3. presents the results of the univariate analysis exploring the relationship between the potential covariates and the odds of experiencing depression. This univariate analysis provides preliminary insights into the potential associations between various characteristics and the odds of experiencing depression. These findings can help identify potential confounding variables that may need to be considered in multivariate analysis to assess the independent effects of these characteristics on depression.

Regarding gender, being male was associated with significantly lower odds of depression compared to females (OR: 0.45, 95% CI: 0.36-0.55, p < 0.001). However, the odds of depression were significantly higher for individuals in the 45-64 age group (OR: 1.96, 95% CI: 1.55-2.49, p < 0.001) and the 65+ age group (OR: 1.76, 95% CI: 1.27-2.44, p < 0.001) compared to the 18-44 age group.

Among the potential sociodemographic covariates, marital status was also associated with depression. However, being never married was associated with significantly lower odds of depression (OR: 0.5, 95% CI: 0.37-0.67, p < 0.001). In comparison, being widowed/divorced/separated showed significantly higher odds (OR: 1.61, 95% CI: 1.10-2.32, p = 0.012).

Among occupation categories, being a student/training was associated with significantly lower odds of depression (OR: 0.45, 95% CI: 0.27-0.70, p < 0.001) compared to being employed. Whereas being unemployed showed higher odds (OR: 1.84, 95% CI: 0.97-3.27, p-value= 0.049). On the other hand, in terms of education level, participants with no formal education had significantly higher odds of depression (OR: 2.8, 95% CI: 1.53-5.73, p-value= 0.002)

Within the behavioural characteristics, only smoking was associated with significantly lower odds of depression (OR: 0.62, 95% CI: 0.45-0.85, p = 0.003), while alcohol consumption, sleeping habits, and dietary habits (fruits and vegetables daily intake) did not show significant associations with depression.

Table 4 Logistic regression analysis with depression as the outcome variable, with Odds ratio (OR), Confidence Interval (CI) and p-value

		Model 1		**Model 2**		**Model 3**		**Model 4**	
		OR (95% CI)	*p value*	*OR (95% CI)*	*p value*	*OR (95% CI)*	*p value*	*OR (95% CI)*	*p value*
Diagnosis status	*Intercept*	0.15 (0.14, 0.17)	0.000 ***	0.16 (0.12, 0.20)	0.000 ***	0.14 (0.06, 0.34)	0.000***	0.19 (0.07, 0.49)	0.000***
	Undiagnosed	0.73 (0.53, 0.99)	0.049 *	0.69 (0.50, 0.95)	0.024 *	0.69 (0.49, 0.94)	0.021*	0.69 (0.50, 0.94)	0.024
	Diagnosed	1.43 (0.99, 2.00)	0.047 *	1.18 (0.81, 1.68)	0.374	1.14 (0.78, 1.64)	0.474	1.17 (0.80, 1.67)	0.414
Age /Gender	*Age Group 18-44*			1		1		1	
	Age Groups 45-64			1.55 (1.19, 2.01)	0.001 **	1.28 (0.87, 1.91)	0.207	1.30 (0.89, 1.94)	0.186
	Age Group 65+			1.82	0.001 ***	1.42	0.140	1.46	0.110

		(1.29, 2.54)		(0.89, 2.26)		(0.92, 2.34)	
	Female	1		1		1	
	Male	0.50 (0.40, 0.63)	0.000***	0.52 (0.40, 0.68)	0.000***	0.57 (0.42, 0.78)	0.000 ***
SLI	*One*			1		1	
	Two			0.86 (0.53, 1.43)	0.547	0.83 (0.52, 1.39)	0.467
	Three			0.85 (0.54, 1.38)	0.490	0.80 (0.51, 1.32)	0.370
Education level	*Higher*			1		1	
	None			1.55 (0.74, 3.50)	0.265	1.62 (0.78, 3.68)	0.219
	Primary			1.30 (0.63, 2.93)	0.495	1.34 (0.64, 3.01)	0.457
	Secondary			1.23 (0.64, 2.63)	0.561	1.25 (0.64, 2.67)	0.534
Occupation	*Employed*			1		1	
	Housework			1.00 (0.70, 1.40)	0.996	1.00 (0.70, 1.41)	0.995
	Student/training			0.76 (0.42, 1.33)	0.343	0.76 (0.42, 1.34)	0.345
	Unemployed			2.37 (1.22, 4.39)	0.008 **	2.40 (1.23, 4.45)	0.007 **
Marital status	*Never married*			1		1	
	Married			1.03 (0.64, 1.66)	0.898	1.00 (0.62, 1.62)	0.986
	Widowed/ Divorced/Separated			1.13 (0.76, 1.66)	0.525	1.13 (0.76, 1.65)	0.545
Smoking	*No*					1	
	Yes					0.76 (0.52, 1.11)	0.166
Alcohol	*No*					1	
	Yes					0.95 (0.75, 1.22)	0.713
Diet	*<5 portions per day*					1	
	>5 portions per day					1.10 (0.89 1.36)	0.391
Sleeping habits	*<6 hours*						
	6-8 hours					0.72 (0.51, 1.03)	0.038 *
	>8 hours					0.65 (0.44, 0.98)	0.068

A stepwise approach was used to assess the association between diagnosis status and depression. Model 1, the crude associations, Model 2; was adjusted for age groups and gender, Model 3 adjusted for age groups, gender, and sociodemographic variables (Standard of living index, occupation, education level and marital status); and Model 4 further adjusted for behavioural variables such as smoking habits, alcohol consumption, sleep habits and daily intake of fruits and vegetables.

In Model 1 of *Table 4.* the logistic regression analysis was performed to assess the relationship between the diagnosis status of cardiometabolic disease (diagnosed, undiagnosed and neither) and the likelihood of experiencing depression. The crude odds ratio for undiagnosed status was 0.73, suggesting 27% (95% CI: 0.53, 0.99), lower odds of depression compared to the reference group (no previous diagnosis and not screening positive for cardiometabolic disease). The crude odds ratio for diagnosed status was 1.43, indicating 43% (95% CI: 0.99, 2.00) higher odds of depression compared to the reference group.

Model 2 revealed that participants with undiagnosed status, within the diagnosis status for cardiometabolic disease categories, had approximately 30.6% (OR: 0.69 95% CI: 0.50, 0.95) lower odds of experiencing depression compared to the reference group (neither). At the same time, there was no strong evidence of an association between diagnosed status and the odds of depression (the CI does not cross the null) when adjusting for age and gender. On the other hand, participants in the age group 45-64 had approximately 55% (OR: 1.55 95% CI: 1.19, 2.01) higher odds of experiencing depression, and individuals in the age group 65+ had approximately 82% (OR: 1.82 95% CI: 1.29, 2.54) higher odds compared to the reference group (18-44). Males had approximately 49.8% (OR: 0.50 95% CI: 0.40, 0.63) lower odds of experiencing depression compared to females.

In Model 3, participants in the undiagnosed category of the diagnosis status for cardiometabolic disease variable had approximately 31% lower odds of experiencing depression (OR: 0.69, 95% CI: 0.49, 0.94) compared to the reference group (neither) with no strong evidence of an association between previous diagnosis status and the odds of depression (as the confidence interval includes the null) after adjusting for age, gender, the standard of living index, education level, occupation and marital status. On the other hand, the age group 45-64 had approximately 28% higher odds of experiencing depression (OR: 1.28, 95% CI: 0.87, 1.91). Males had approximately 48% lower odds of experiencing depression compared to females (OR: 0.52, 95% CI: 0.40, 0.68), as in previous models.

In Model 4, participants who were classified as undiagnosed in the diagnosis status of cardiometabolic disease had a 31% (OR: 0.69 95% CI: 0.50, 0.94) lower odds of having depression compared to those who had no previous diagnosis and did not screen positive; and male participants continued to show lower odds of having depression, 43% (OR: 0.57 95% CI:

0.42, 0.78) compared to female participants after adjusting for all previous covariates and also behavioural one, including smoke and alcohol consumption, sleeping habits and dietary habits (food and vegetables daily intake).

Discussion

The regression models assessed the association between cardiometabolic disease status and depression risk. The results revealed that individuals with undiagnosed cardiometabolic disease had lower odds of depression compared to those who did not refer previous diagnosis or screened positive for cardiometabolic disease while controlling for age, gender, and other lifestyle confounders. In contrast, the diagnosed group did not show conclusive evidence of a higher risk of depression compared to the control group while controlling for confounders, as the confidence intervals crossed the null, even if the effect estimates followed a similar trend as in the crude model, which might suggest a potential association between diagnosed status and increased risk of depression.

This potential association suggests that disease diagnosis itself may be a crucial factor contributing to the increased risk of depression observed in individuals with cardiometabolic diseases. It suggests that factors related to disease diagnoses, such as the psychological and emotional impact, healthcare costs, or stigma, may play a more substantial role in the development of depression than the physiological symptoms associated with these conditions alone.[lxii lxiii]

These findings might also suggest that the awareness of having a cardiometabolic disease may contribute to increased psychological distress and consequently elevate the risk of developing depression. This finding would be consistent with previous studies highlighting the psychological impact of chronic diseases. [lxiv] Likewise, these results align with previous research, indicating that chronic illnesses, including cardiometabolic conditions, can have a significant impact on mental health outcomes..[lxv] Similarly, it emphasises the importance of considering the psychological well-being of individuals with cardiometabolic disease and implementing appropriate mental health screening and support services within clinical settings.

Furthermore, the incidence risk of depression was higher in those with a previous diagnosis of hypertension (17.77%) compared to those with no previous diagnosis but screened positive

during the examination (10.32%), further supporting the potential association between diagnosis status and an increased risk of depression. By identifying and diagnosing individuals with hypertension and diabetes, healthcare providers can implement preventive measures and interventions to mitigate the risk of complications and reduce the burden on the healthcare system. [lxvi]

While some association between previously diagnosed cardiometabolic disease and increased risk of depression was observed, the specific contributions of symptoms and disease management factors were not directly assessed. The findings of this study support the hypothesis to some extent. They suggest the importance of psychological support and interventions for individuals diagnosed with cardiometabolic disease.

However, it is interesting to note that including these covariates did not have a statistically significant result regarding their individual associations with depression risk. The confidence intervals for variables such as age, education level, marital status, Standard of Living Index, alcohol and tobacco consumption, sleeping habits, and dietary habits crossed the null, suggesting no significant independent effect on the outcome of depression. This may be attributed to decreased statistical power or the possibility that these lifestyle factors partially explain the association between cardiometabolic disease status and depression. As seen in the univariate analysis, marital status, education level, and occupation were associated with the odds of depression. [lxviilxviiilxixlxxlxxi]

These findings indicate that, while these covariates may have some influence on the overall relationship, their impact on the diagnosis status and its association with depression is relatively less important. Even though the effect estimate for those with a diagnosed status maintains a similar trend in all models.

However, it is important to acknowledge some limitations of the study. The study relied on self-reporting for both the diagnosis of cardiometabolic diseases and the assessment of depression. This reliance on self-reporting introduces the potential for recall bias or misclassification, which may have influenced the results, either overestimating or underestimating the association. Likewise, depression was also measured by self-report rather than screening, so some people likely had depression in the third follow-up wave. Similarly, a potential for false positives during the physical examination for hypertension and/or diabetes might have occurred.

Similarly, another limitation of the study is regarding the confidence intervals for the diagnosed group, which crossed the null in the adjusted models. This observation could be attributed to small sample sizes within the diagnosed group, which may result from high levels of underdiagnosis in the population. The limited number of participants in the diagnosed group could have impacted the precision and statistical power of the analysis, potentially leading to inconclusive results regarding the association between diagnosed status and depression.

It is important to highlight that the National Standard of Living Index was created in 2000. The NFHS produces updated national reference values every 10 years related to other Indian states, not just Telangana. Therefore, the reason why most of the participants were in the third tertile might be due to urbanisation and modernisation. It might be recommended to create variation within this specific population and thus generate new tertiles among the participants only. Therefore, developing new tertiles among the participants only to assess the socioeconomic level within this population might give a better insight into the current socioeconomic status of this population.

One important strength of our study is the longitudinal design. This longitudinal approach allowed us to examine the relationship between cardiometabolic diseases and the risk of developing depression over ten years, providing valuable insights into the long-term associations. Similarly, as we excluded those who referred previous diagnosis of depression in the third follow-up, we were able to reduce the percentage of reverse causation. Similarly, the use of validated measures to assess depression and rigorous diagnostic criteria for cardiometabolic diseases are important strengths of our study. The inclusion of established and widely recognised assessment tools (PHQ-9) and cut-off points (≥140/90 mmHg and ≥126 mg/dl) for evaluating depression and cardiometabolic disease enhances the reliability and accuracy of the data collected as well as the validity of its findings. It facilitates meaningful comparisons with other research studies in the field.

The research was conducted in a rural Indian setting with low health literacy and high out-of-pocket healthcare costs. These contextual factors may limit the generalizability of the findings to other populations with different healthcare systems and cultural contexts. This study contributes valuable knowledge within its specific setting; caution should be exercised when extrapolating the results to other populations.

Conclusion

In conclusion, our study suggests an association between cardiometabolic disease diagnosis and depression. All effect estimates from the regression model from participants with a previous diagnosis of cardiometabolic disease showed a higher risk of developing depression compared to those who did not refer a previous diagnosis and did not screen positive for cardiometabolic disease. However, the evidence was not conclusive as the confidence intervals crossed the null. Nevertheless, the results suggest that there might be some psychological impact that comes with receiving a diagnosis of cardiometabolic disease and depression. Thus, the need for a holistic healthcare strategy that prioritises the physical and mental well-being of individuals affected by these conditions.

By acknowledging and addressing the psychological consequences of disease diagnosis, healthcare professionals have the opportunity to offer tailored support and interventions that can enhance the overall quality of life for those living with cardiometabolic diseases.

Further research, and in a larger sample size, is needed to explore the underlying mechanisms linking disease diagnosis and depression, as well as to evaluate the effectiveness of interventions aimed at improving mental health outcomes in this population.

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