IMPACT OF AGE ON METABOLIC AND GENETIC DETERMINANTS OF DIABETES AND HYPERTENSION IN INDIAN ADULTS: INSIGHTS FROM LONGITUDINAL AGEING STUDY IN INDIA

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Introduction

India is currently experiencing a demographic and epidemiological shift, marked by rising life expectancy and a growing burden of non-communicable diseases (NCDs) such as diabetes and hypertension. These two conditions are among the most prevalent NCDs worldwide, significantly affect the health and functional capacity of older adults. In India, the burden is particularly severe due to delayed diagnoses, low health awareness, and disparities in healthcare access(Anjana et al., 2017; Geldsetzer et al., 2018). These diseases contribute significantly to premature mortality, morbidity, and healthcare costs, underscoring an urgent need for identifying modifiable and non-modifiable risk factors that evolve across the life course(Hacker, 2024; Olufunke Omotayo et al., 2024).

A key dimension of this public health challenge is the role of metabolic and genetic determinants in shaping the trajectory of diabetes and hypertension. Metabolic risk factors such as elevated body mass index (BMI), abdominal adiposity, and poor sleep quality have been consistently associated with increased odds of metabolic syndrome and cardiovascular conditions(Knutson, 2010; Koren et al., 2016; Rexrode et al., 2001) Similarly, genetic predisposition, especially a family history of diabetes or hypertension, has long been recognized as a critical non-modifiable risk factor that interacts with environmental and behavioural influences to increase disease susceptibility(Arokiasamy et al., 2016; Barlassina et al., 2002; Jabbar et al., 2023). Sex-based differences in disease expression further complicate the risk profile, as women often show higher prevalence of hypertension post-menopause, while men may have a greater tendency toward earlier-onset diabetes(Ong et al., 2008).

Most existing studies in India have utilized either clinic-based samples or national surveys that do not include biomarkers or detailed age stratification(Corsi & Subramanian, 2019; Khobragade et al., 2025; Shah & Afzal, 2013; Shriraam et al., 2021). Consequently, the interplay between age and metabolic and genetic risk factors remains underexplored, particularly in nationally representative datasets. In this context, the cumulative disadvantage theory(Dannefer, 2003) provides a compelling framework to investigate whether age amplifies the effects of metabolic and genetic risk factors on health outcomes.

Within this framework, the study also incorporates the conceptual debate on whether the effect of risk factors diverges or converges with age. The divergence hypothesis posits that the influence of metabolic and genetic risk factors may become more pronounced with increasing age, as biological wear and tear and accumulated exposures amplify health risks. In contrast, the convergence hypothesis suggests that age-related biological processes and selective survival may attenuate these differences, resulting in a levelling of risk across older age groups. These opposing perspectives highlight the need to empirically examine how age modifies the relationship between metabolic and genetic risk factors and chronic disease outcomes.

Data and Methods

Data Source

This Study uses the wave I data from Longitudinal Aging study in India (LASI), a survey conducted by International Institute for Population Science (IIPS) and the Harvard T.H. Chan School of Public Health that collects information on aging, health and well-being among older Indians. LASI employs a multistage stratified area probability cluster sampling design, targeting individuals aged 45 and above along with their spouses irrespective of age. The data is gathered via face-to-face interviews, physical measurements, and biomarker assessments covering demographics, chronic diseases, cognitive and mental health, social support, healthcare utilization and socio-economic factors.

The analytical sample for this study comprises 60,624 respondents with complete information on self-reported diagnoses of diabetes and hypertension, as well as on key explanatory variables including metabolic and genetic risk factors. The primary metabolic indicators include Body Mass Index (BMI) categories, sleep disturbances, and presence of comorbid diabetes or hypertension, while the genetic risk profile is captured through family history of diabetes or hypertension and sex. The sociodemographic variables used as potential confounders include sector of residence (rural/urban), religion, social group (Scheduled Tribes, Scheduled Castes, Other Backward Classes, and others), current marital status, current work status, and region of residence. The extent of

information available in LASI allows for a rich examination of health risks across India's diverse population.

Methods

To assess the association between metabolic and genetic risk factors and the likelihood of self-reported diabetes and hypertension, we employed multivariate logistic regression models, separately for each health outcome. All models were adjusted for relevant confounders to reduce bias and ensure robust estimation. Odds ratios (ORs) and p-values were computed to quantify the relative effect of each explanatory variable. In addition to baseline estimation, predicted probabilities were derived using post-estimation margins to capture age-specific gradients in the risk of diseases (diabetes or hypertension) across different subgroups. Further, marginal effects were estimated by age-groups to capture the change in the predicted probability of the outcome (diabetes or hypertension) associated with a change from the reference category. This approach offers a more intuitive interpretation of effect sizes, allowing for clearer comparisons of their relative importance.

Results

Table 1: Sample characteristic of data

Variables	**Sample (n)**	**percentage (weighted)**
Metabolic factors		
Body mass index (missing sample=725)		
Underweight	10,992	21.37
Normal	31,335	51.53
Overweight	13,133	20.29
Obese	4,439	6.81
Sleep problem (missing sample=9)		
No	53,457	87.07
Yes	7,158	12.93
Diabetes (missing sample=0)		
No	52,883	88.09
Yes	7,741	11.91
Hypertension (missing sample=0)		
No	43,528	73.54
Yes	17,096	26.46
Genetic Factors		
Family history of diabetes (missing sample=214)		
No	50,808	84.85
Yes	9,602	15.15
Family history of hypertension (missing sample=209)		

No	46,661	78.45
Yes	13,754	21.55
sex (missing sample=0)		
Men	28,127	45.86
Women	32,497	54.14
Confounding factors		
Sector (missing sample=0)		
Rural	39,799	69.89
Urban	20,825	30.11
Religion (missing sample=0)		
Hindu	44,288	82.50
Muslim	7,101	11.03
Christian	6,117	2.97
Others	3,118	3.49
Social group (missing sample=0)		
ST	10,869	8.60
SC	10,091	19.40
OBC	22,991	45.66
None of them	16,673	26.33
Current marital status (missing sample=0)		
Currently married	45,306	73.68
Widowed	13,337	23.49
Divorced, Separated, Deserted or Others	1,981	2.83
Working status (missing sample=0)		
Never worked	16,869	26.15
Currently working	29,767	50.06
Worked in the past but currently not working	13,933	23.78
Region (missing sample=0)		
North	10,988	12.64
Central	8,187	20.99
East	10,742	23.72
Northeast	8,676	3.47
West	7,856	15.82
South	14,175	23.37

Note: The results are based on LASI survey, 2017-18

Table 1 presents the weighted sample characteristics of the study population aged 45 years and above from the LASI Wave 1 dataset, highlighting key metabolic, genetic, and socio-demographic variables. For metabolic factors, a majority of individuals were classified as having a normal Body Mass Index (51.53%), while 21.37% were underweight, 20.29% overweight, and 6.81% obese. Further, 12.93% of older adults reported experiencing sleep problems, an indicator known to be associated with chronic conditions such as diabetes and hypertension. The burden of non-communicable diseases appears prominently in the sample. The prevalence of self-reported diabetes is 11.91%, whereas hypertension is significantly higher, affecting 26.46% of the study population. In

terms of genetic factors, 15.15% of individuals reported a family history of diabetes, while 21.55% reported a family history of hypertension. The sample comprises a slightly higher proportion of women (54.14%) compared to men (45.86%).

A significant proportion of the population resides in rural areas (69.89%). Religious affiliation is predominantly Hindu (82.50%), with Muslims (11.03%), Christians (2.97%), and others (3.49%) comprising the remaining segments. In terms of social group composition, Other Backwards Classes (OBCs) represent the largest category (45.66%), followed by Scheduled Castes (19.40%), Scheduled Tribes (8.60%), and those not belonging to any of these categories (26.33%). Marital status data reveal that 73.68% of respondents are currently married, while 23.49% are widowed. Regarding work status, 50.06% of respondents are currently working, while 26.15% have never worked, and 23.78% worked previously but are no longer employee. Finally, regional distribution shows that the largest shares of the sample are from the eastern (23.72%), southern (23.37%), and central (20.99%) regions, followed by western (15.82%), northern (12.64%), and northeastern (3.47%) India.

Table 2: Prevalence of diabetes and hypertension across various metabolic and genetic risk factors

			Diabetes	**Hypertension**
Metabolic factors	Body mass index	Underweight	3.54	14.73
		Normal	10.2	23.41
		Overweight	19.63	37.72
		Obese	27.46	50.81
	Sleep problem	No	11.81	25.57
		Yes	12.54	32.40
	Hypertension/Diabetes	No	6.09	21.6
		Yes	28.07	62.36
Genetic factors	Family history of Diabetes/ Hypertension	No	9.13	22.97
		Yes	27.46	39.07
	Sex	Men	11.89	22.3
		Women	11.92	29.97

Note: The estimates are based on LASI survey, 2017-18

Table 2 presents the prevalence of diabetes and hypertension across key metabolic and genetic risk factors among adults aged 45 years and above**.** A distinct incline is observed in the prevalence of both conditions across body mass index (BMI). The proportion of individuals diagnosed with diabetes rises sharply from 3.54% among the underweight to 27.46% among the obese, while hypertension prevalence follows a similar trajectory from 14.73% in underweight individuals to 50.81% among the

obese**.** These findings affirm the strong positive association between higher BMI and the risk of non-communicable diseases. The increasing burden of both diabetes and hypertension with rising adiposity highlights the role of excess body weight as a critical metabolic risk factor among older adults. Sleep problems also exhibit a clear association with both conditions. Among those reporting sleep problems, 12.54% have diabetes and 32.40% have hypertension, compared to 11.81% and 25.57%**,** respectively, among those without sleep disturbances. While the difference in diabetes prevalence is modest, the higher prevalence of hypertension among individuals with sleep issues underscores the potential link between sleep disruption and elevated blood pressure. A particularly stark contrast is observed in comorbid prevalence. Among individuals who do not report hypertension, the prevalence of diabetes is only 6.09%**,** whereas it increases substantially to 28.07% among those with hypertension. Similarly, 21.6% of non-diabetic individuals report hypertension, compared to 62.36% among those with diabetes. These findings suggest a bidirectional and comorbid relationship between diabetes and hypertension, strengthening the need to examine these conditions not in isolation but as interlinked health outcomes that may share common biological and behavioural pathways.

Genetic predisposition also appears to play a significant role in disease occurrence. The prevalence of diabetes and hypertension are 9.13% and 22.97% among those without a family history of the disease, compared to 27.46% and 39.07% among those with a positive family history. This indicates that a familial predisposition substantially increases the likelihood of developing these conditions. Sex differentials reveal that the prevalence of diabetes is nearly identical among men and women (11.89% vs. 11.92%). However, women exhibit a higher prevalence of hypertension (29.97%) compared to men (22.3%). This finding may be partly attributable to physiological changes post-menopause, longer life expectancy, and possible differences in health-seeking behaviour or diagnosis rates among older women.

Table 3: Odds ratios for understanding the effect of metabolic and genetic factors on diabetes and hypertension

Diabetes					**Hypertension**			
Variables	**Odds Ratio**	**Standard Error**	**P-value**		**Variables**	**Odds Ratio**	**Standard Error**	**P-value**
Metabolic factors					**Metabolic factors**			
Body mass index					***Body mass index***			
Underweight®	1.00				Underweight®	1.00		
Normal	2.25	0.125	0.000		Normal	1.68	0.053	0.000
Overweight	3.37	0.198	0.000		Overweight	2.77	0.099	0.000
Obese	3.61	0.243	0.000		Obese	3.82	0.173	0.000

Sleep problem					***Sleep problem***			
No®	1.00				No®	1.00		
Yes	1.13	0.045	0.003		Yes	1.38	0.041	0.000
Hypertension					***Diabetes***			
No®					No®	1.00		
Yes	3.72	0.104	0.000		Yes	3.68	0.102	0.000
Genetic Factors					**Genetic Factors**			
Family history of diabetes					***Family history of hypertension***			
No®	1.00				No®	1.00		
Yes	2.74	0.083	0.000		Yes	2.00	0.046	0.000
Sex					***Sex***			
Men®	1.00				Men®	1.00		
Women	0.67	0.024	0.000		Women	1.27	0.032	0.000
Confounding factors					**Confounding factors**			
Sector					***Sector***			
Rural®	1.00				Rural®	1.00		
Urban	1.63	0.046	0.000		Urban	1.19	0.026	0.000
Religion					***Religion***			
Hindu®	1.00				Hindu®	1.00		
Muslim	1.03	0.042	0.516		Muslim	1.16	0.036	0.000
Christian	1.20	0.065	0.001		Christian	0.97	0.041	0.478
Others	1.16	0.073	0.017		Others	1.16	0.053	0.001
Social group					***Social group***			
ST®	1.00				ST®	1.00		
SC	1.30	0.078	0.000		SC	1.31	0.053	0.000
OBC	1.37	0.071	0.000		OBC	1.29	0.047	0.000
None of them	1.48	0.078	0.000		None of them	1.40	0.052	0.000
Current marital status					***Current marital status***			
Currently married®	1.00				Currently married®	1.00		
Widowed	0.80	0.030	0.000		Widowed	1.19	0.031	0.000
Divorced, Separated, deserted or Others	0.74	0.059	0.000		Divorced, Separated, deserted or Others	0.92	0.054	0.183
Working status					***Working status***			
Never worked®	1.00				Never worked®	1.00		
Currently working	0.68	0.028	0.000		Currently working	0.78	0.022	0.000

Worked in the past but currently not working	0.97	0.039	0.392		Worked in the past but currently not working	1.06	0.031	0.037
Region					***Region***	1.00		
North®	1.00				North®	0.69	0.027	0.000
Central	0.97	0.056	0.584		Central	0.83	0.028	0.000
East	1.14	0.056	0.007		East	1.09	0.044	0.037
Northeast	0.92	0.057	0.189		Northeast	0.86	0.031	0.000
West	1.41	0.069	0.000		West	0.89	0.029	0.001
South	1.91	0.083	0.000		South			
Age	1.02	0.002	0.000		Age	1.03	0.001	0.000

Note: The estimates are based on LASI survey, 2017-18

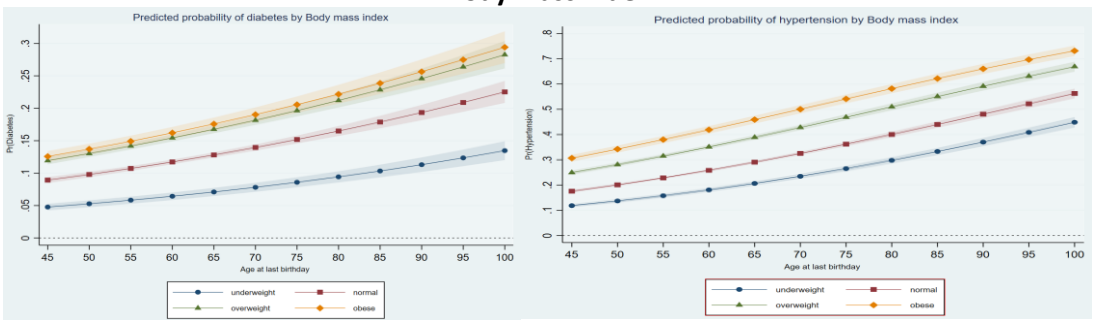
Table 3 reveals strong and significant associations between metabolic factors and the risk of diabetes and hypertension among older adults. Compared to underweight individuals, those with normal BMI had 2.25 times higher odds of having diabetes ($p<0.001$), and those categorized as overweight and obese had even greater odds, at 3.37 and 3.61, respectively. A similar gradient is observed for hypertension, normal BMI was associated with 1.68 times higher odds, overweight with 2.77, and obesity with 3.82 times higher odds (all $p<0.001$). These findings clearly demonstrate a positive and significant relationship between body weight and chronic disease risk. Sleep problems also show a significant, though more modest, association with both conditions. Individuals reporting sleep issues had 0.13 times higher odds of diabetes and 0.38 times higher odds of hypertension than those without sleep problems, suggesting that poor sleep may exacerbate metabolic and cardiovascular risks, especially in older populations. The results strongly confirm the comorbid and bidirectional nature of diabetes and hypertension. Individuals with hypertension were 3.72 times more likely to have diabetes, and those with diabetes were 3.68 times more likely to have hypertension (both $p<0.001$), indicating a mutually reinforcing relationship.

Genetic predisposition emerges as a potent risk factor. Respondents with a family history of diabetes had 2.74 times higher odds of developing the condition themselves, and those with a family history of hypertension had twice the odds of suffering from the condition. These associations validate the role of inherited risk in disease manifestation and highlight the need for early screening among individuals with known family history. Sex differentials in chronic disease risk are observed. While women had significantly lower odds of diabetes (OR = 0.67, $p<0.001$) compared to men, they had higher odds of hypertension (OR = 1.27, $p<0.001$).

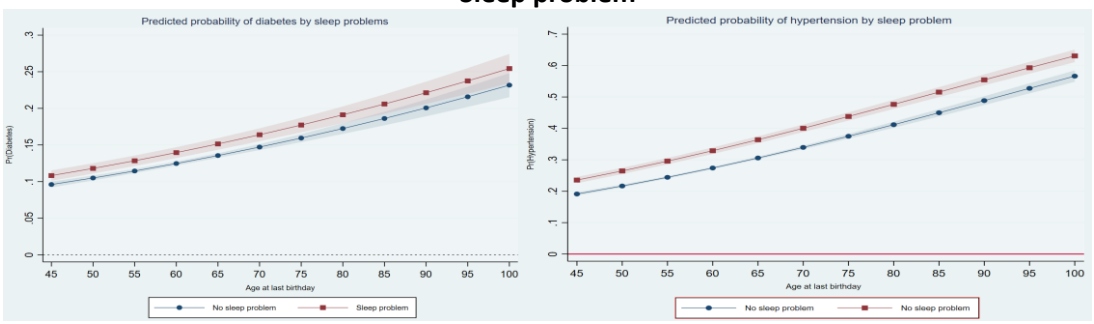
Among confounding factors, urban residence was associated with a higher likelihood of both diabetes and hypertension. Religious differences were more evident for diabetes than hypertension,

while caste-based disparities showed that socially advantaged groups were more likely to report both conditions although not much significant. Marital status and employment also influenced disease risk, with working individuals showing lower odds of both diseases. Regional patterns indicated a higher diabetes burden in the South and West, while hypertension showed more variation. Age emerged as a strong predictor, reinforcing the cumulative nature of chronic disease risk over time.

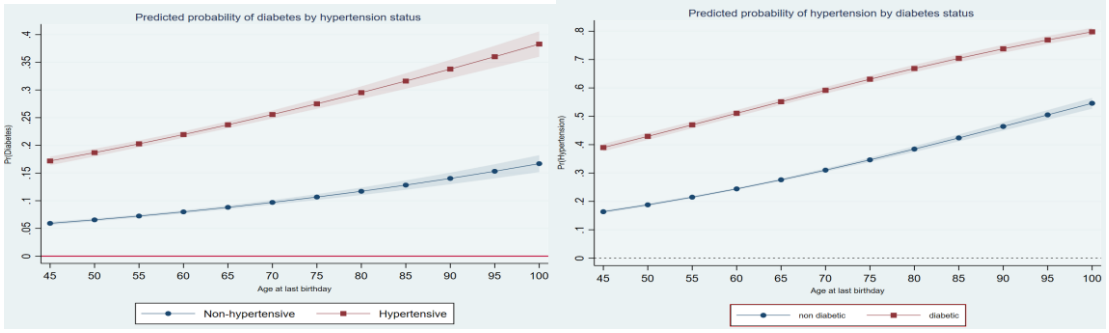
Body mass index



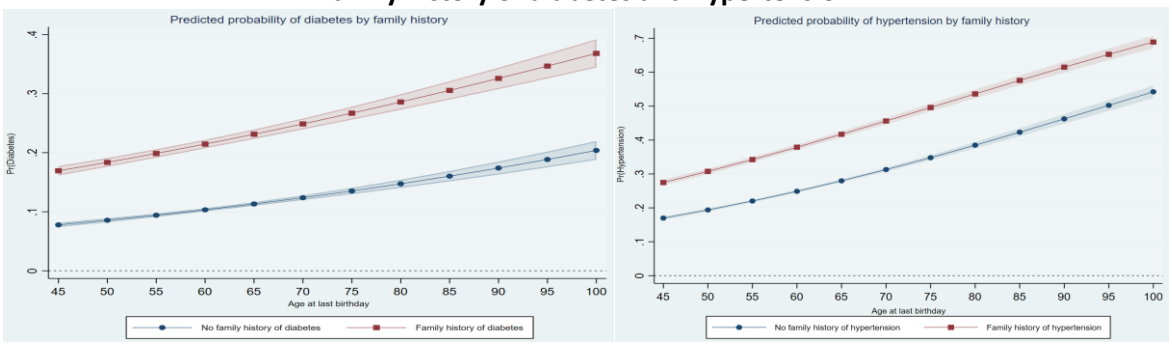
Sleep problem



Diagnosed for Hypertension/Diabetes



Family history of diabetes and hypertension



Sex

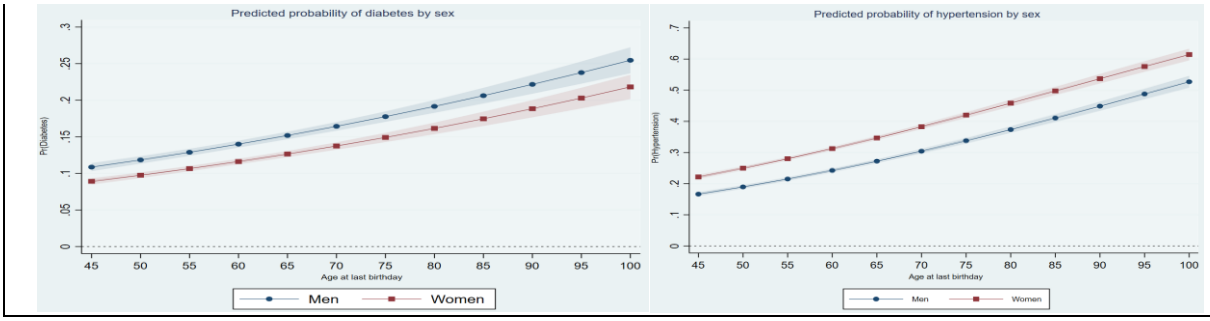


Figure1: Predicted probabilities of diabetes and hypertension by age, metabolic and genetic factors

Figure 1 illustrates the predicted probabilities of diabetes and hypertension across age groups for various metabolic and genetic risk factors. A clear and consistent pattern emerges with respect to body mass index (BMI), where the predicted probability of both diabetes and hypertension increases progressively with age across all BMI categories. Notably, individuals classified as obese and overweight show substantially higher predicted probabilities compared to those who are underweight or have normal BMI. This difference becomes more pronounced in the older age groups, suggesting that the adverse impact of excess weight accumulates over the life course, elevating chronic disease risk in later years.

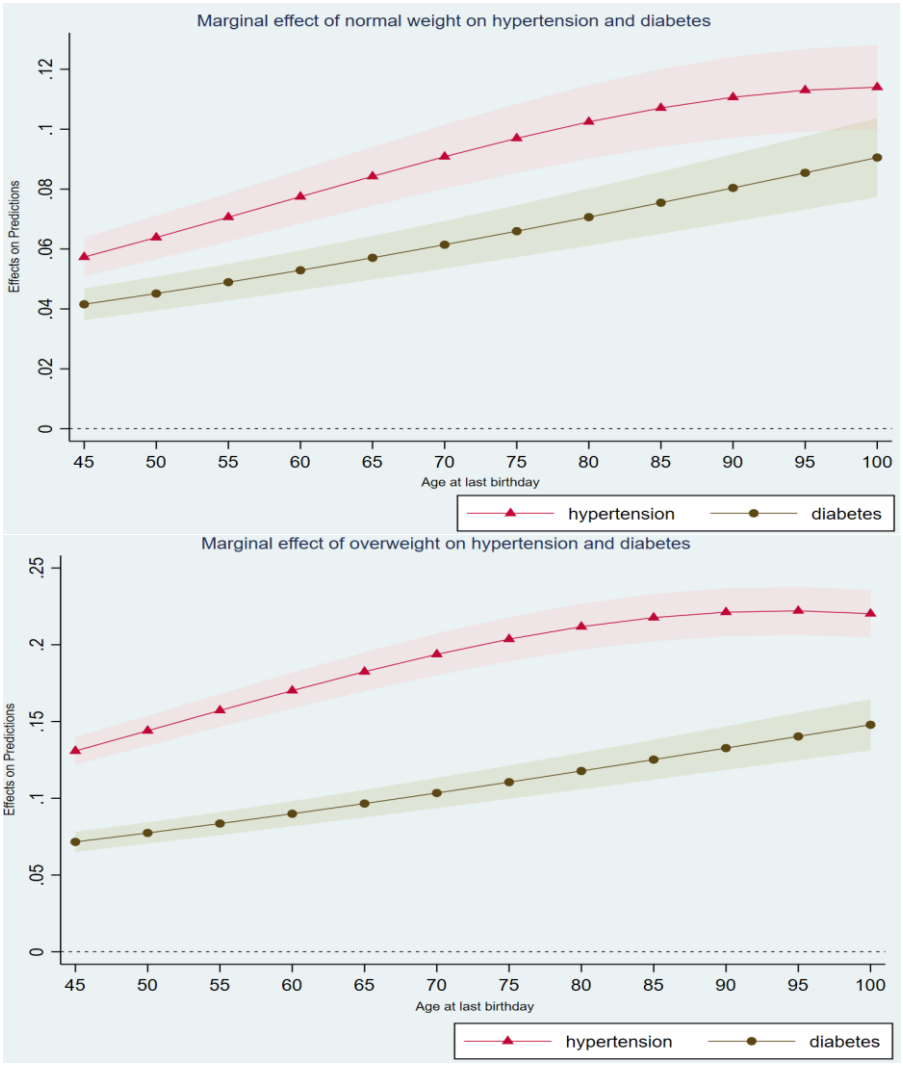
Among those with sleep problems, the predicted probability of both diabetes and hypertension is higher than among those without sleep issues. This disparity is especially prominent in the case of hypertension, where the gap widens with age. The findings strengthen the role of sleep quality as an important behavioural determinant of cardiovascular and metabolic health, particularly among older adults. Similarly, individuals with a pre-existing diagnosis of hypertension demonstrate significantly higher predicted probabilities of diabetes, and vice versa, across all ages. This mutual reinforcement between the two conditions intensifies with age, emphasizing the comorbid and interdependent nature of these lifestyle diseases. The presence of a family history of diabetes or hypertension is associated with a consistently higher probability of disease, and this gap remains stable or widens slightly with age. This points to the lifelong influence of genetic predisposition on disease risk. When disaggregated by sex, women tend to have higher predicted probabilities of hypertension, while diabetes probabilities appear largely among men. This suggests that women may be more vulnerable to age-related increases in blood pressure.

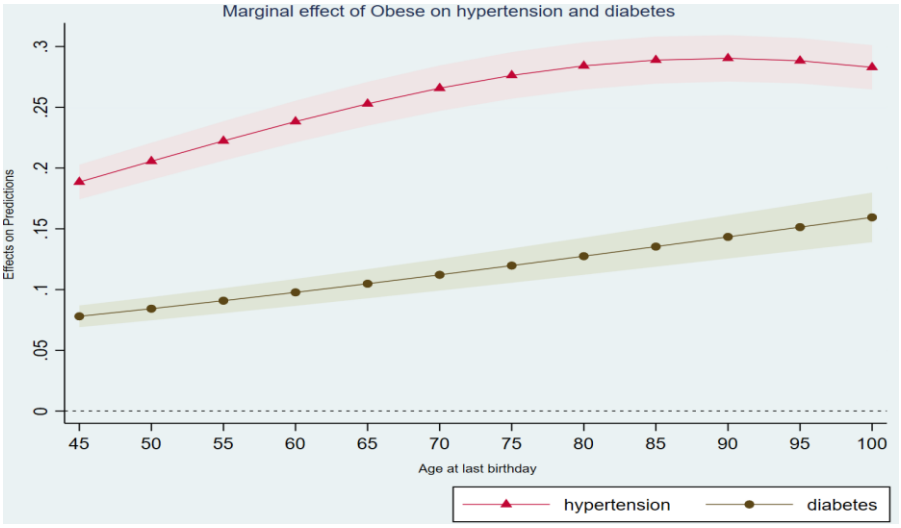
Figure 2 presents the marginal effects of metabolic and genetic risk factors on diabetes and hypertension across different age groups, highlighting the change in predicted probability compared to a reference category. The marginal effect of BMI is most substantial, particularly for those in the obese and overweight categories. As age increases, the marginal difference in disease probability between obese individuals and those with normal or underweight BMI becomes more pronounced, with the steepest effect observed for diabetes among individuals above age 50 whereas attenuates

for hypertension. This reinforces the notion that the burden of adiposity-related diseases increases substantially with age for diabetes, placing older obese adults at significantly elevated risk. The marginal impact of sleep problems also reveals a rising pattern across age for both conditions, but more so for hypertension. This trend suggests that sleep disturbances may contribute cumulatively to elevated blood pressure as individuals age. Furthermore, individuals with a prior diagnosis of hypertension or diabetes exhibit the highest marginal effects which attenuates with age for hypertension and increases for diabetes.

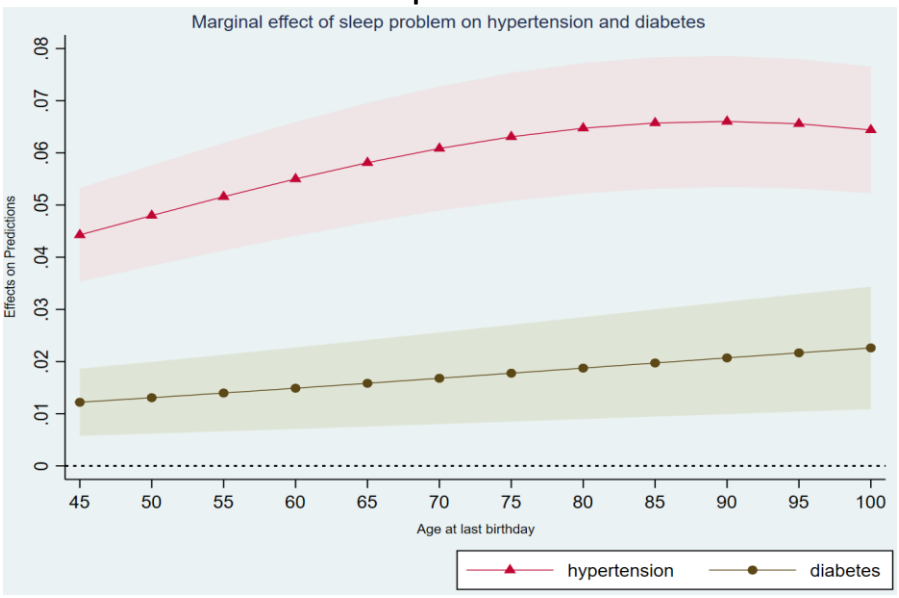
A family history of diabetes or hypertension exerts its highest marginal influence in the younger-old age group (45–80 years), with the effect for hypertension gradually stabilizing in older age. This implies that genetic predisposition may have a stronger impact earlier in the aging trajectory. Lastly, the marginal effect of being female is negligible for diabetes but positive for hypertension, especially after age 55. This suggests gender-specific patterns in the development of hypertension among older adults, possibly influenced by hormonal transitions, health behaviour, and access to care.

BMI

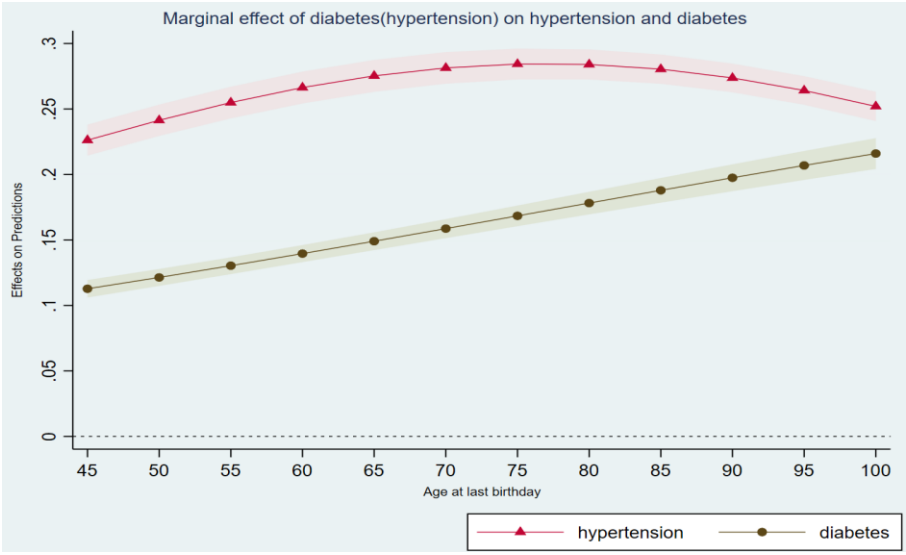




Sleep Problem



Diagnosed for Hypertension/Diabetes



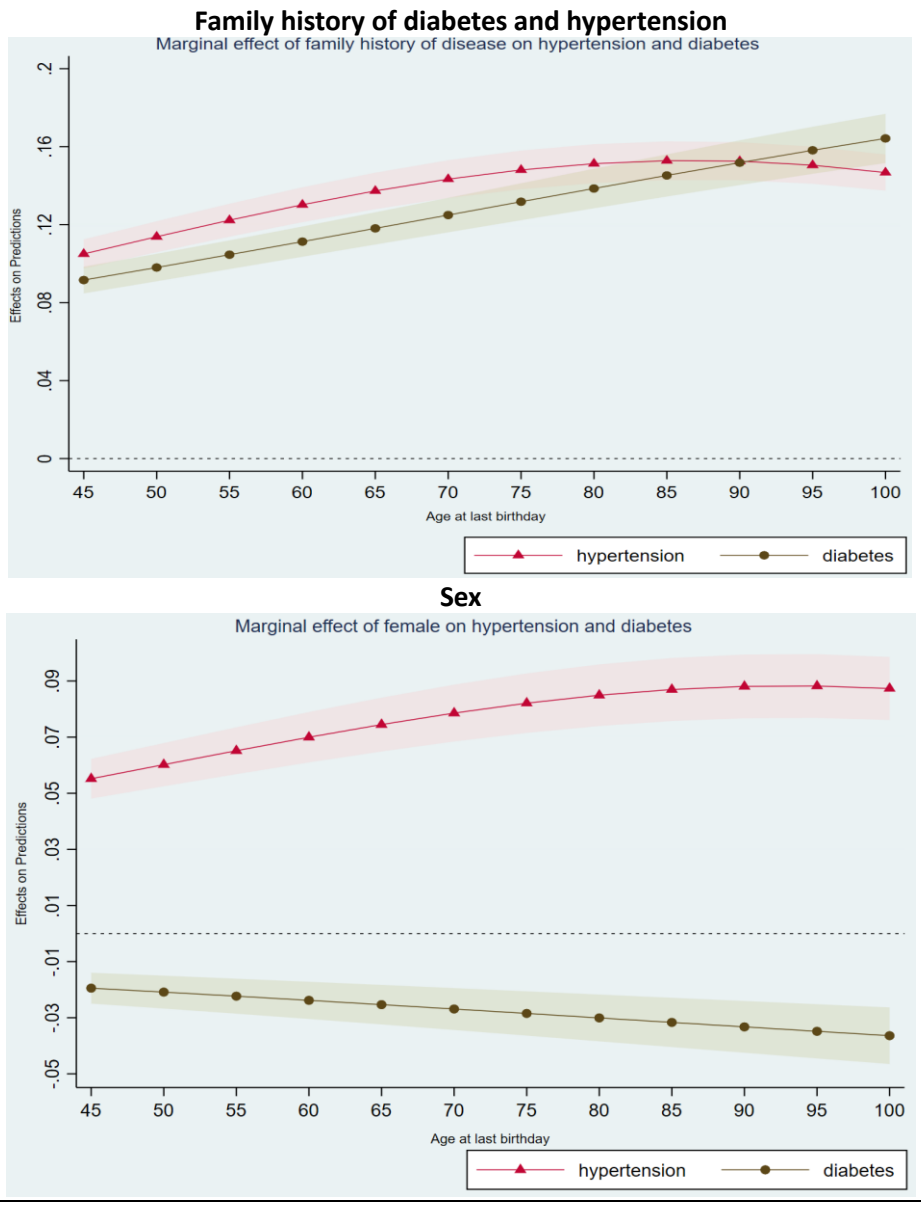


Figure2: Marginal effects on diabetes and hypertension by age and between the reference category and other levels of metabolic and genetic factors

Conclusion and Discussion

Discussion

This study underscores the significant role that metabolic and genetic risk factors play in shaping the likelihood of diabetes and hypertension among older Indian adults, with these associations showing notable variation by age. Body Mass Index (BMI) emerged as a key predictor, with the risk of both diseases escalating considerably among overweight and obese individuals. These effects intensified with age, reflecting the accumulation of metabolic stress and aligning with the cumulative disadvantage hypothesis, which posits that early disadvantages amplify over time(Dannefer, 2003). The findings are consistent with previous studies linking adiposity to cardiovascular and metabolic

risk (Gupta et al., 2012; Nakamura et al., 2014; Rexrode et al., 2001). Sleep disturbances also showed a significant positive association with both conditions, particularly with hypertension, and the marginal effects increased with age initially and the becomes modest. This suggests that poor sleep is a cumulative behavioural risk factor that may exacerbate cardiovascular strain in older age groups(Koren et al., 2016). Moreover, the comorbidity of diabetes and hypertension was pronounced. Individuals diagnosed with one condition had significantly higher odds of having the other, confirming their shared pathophysiological mechanisms and underscoring the need for integrated disease management approaches in public health strategies(Libianto et al., 2018).

Genetic predisposition measured through family history was another strong determinant. However, marginal effect patterns indicated that its influence was more pronounced in midlife and early old age, potentially weakening in advanced age due to survival selection or competing health risks, mostly for hypertension(Ahmed, 2024; Fields & Johnston, 2018). This may reflect a convergence effect with aging, whereby genetic risk exerts diminishing influence. Sex-based patterns also emerged, while women were less likely to report diabetes, they had a higher risk of hypertension, especially post-menopause. These findings are supported by prior research indicating hormonal and behavioural differences in disease progression(Kirtikar et al., 2020; Nappi et al., 2022). Overall, the results point to a divergence for metabolic risk and genetic risk factors for diabetes with age and a potential convergence in hypertension, emphasizing the importance of adopting a life course perspective in chronic disease prevention.

Conclusion

The findings highlight the critical role of metabolic risk factors in shaping the age-specific gradients of diabetes and hypertension in India. The association between BMI, sleep health, and family history with these conditions becomes stronger with age for diabetes and remain modest. This pattern suggests that preventive health strategies should focus on early intervention to manage modifiable risk factors such as BMI and sleep problems. Individuals with genetic risk such as gender and family history should be given special attention from early age. Public health programs must prioritize routine screening for older adults and provide targeted interventions that address both metabolic and genetic factors. Furthermore, the gender-specific findings indicate the need for health interventions that account for the higher risk of hypertension among older women and of diabetes among older men. Given the aging population in India, addressing these risk factors is critical to controlling the growing burden of non-communicable diseases like diabetes and hypertension. The results also underscore the importance of including sleep health in discussions on metabolic disease prevention, as it plays an independent role in exacerbating these risks. Future research should

consider longitudinal analyses to better understand how these risk factors evolve over time and contribute to chronic disease development in aging populations.

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