

Metabolic Factors as Mediators of the Association between Health Literacy and Incident Hypertension: Findings from the Shahrekord Persian Cohort Study

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Background and Objective: Hypertension is a major global health concern, yet the role of health literacy in its development remains unclear, especially in Middle Eastern populations. This prospective cohort study examined the association between health literacy and incident hypertension in southwestern Iran.

Materials and Methods: This cohort study included 4,217 adults aged 35–70 years without baseline hypertension from the Shahrekord PERSIAN Cohort, followed for 7 years. Health literacy was assessed using the HELIA questionnaire, with inadequate literacy defined as below the 25th percentile. Incident hypertension was confirmed through physician diagnosis or antihypertensive medication use. Hierarchical logistic regression estimated odds ratios (ORs) with 95% confidence intervals (CIs), with progressive adjustment for confounders. Causal mediation analyses were conducted using Stata's mediate command.

Results: Participants' mean age was 47.55 ± 8.33 years. During follow-up, 107 incident hypertension cases (2.6%) were recorded. Mediation analyses showed significant indirect effects for triglycerides (27.4%, $p = 0.001$) and fasting blood sugar (15.6%, $p = 0.027$), though both fell below the 30% threshold for meaningful mediation, suggesting only partial mediation. These variables were therefore treated as confounders in the final model.

In the crude model, inadequate health literacy was linked to higher odds of hypertension (OR: 1.72, 95% CI: 1.02, 2.90). This association persisted after adjustment for age, ethnicity, BMI, physical activity, and depression (OR: 1.78, 95% CI: 1.02, 3.11). However, with further adjustment for fasting blood sugar and triglycerides, the association became non-significant (OR: 1.67, 95% CI: 0.95, 2.92). In the fully adjusted model, age, obesity, depression, and elevated triglycerides remained independently associated with hypertension.



Conclusion: Triglycerides and fasting blood sugar partially mediated the association between health literacy and incident hypertension. These findings suggest that metabolic factors may lie on the pathway between health literacy and hypertension, though the modest mediation proportions indicate that other pathways also contribute.

Keywords: Health Literacy, Hypertension, Incidence, Cohort Study, Metabolic Factors, Iran

Received: 04 June 2026

Accepted: 30 September 2026

Doi: 10.22038/jhl.2026.96223.1983

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In Press

Introduction

Hypertension (HTN) is one of the most important modifiable risk factors for cardiovascular diseases (CVDs), stroke, and chronic kidney disease, accounting for approximately 10.4 million deaths annually worldwide (1). It is often asymptomatic until late stages, earning its reputation as a "silent killer" (2). The global prevalence of hypertension has doubled over the past three decades, making it a leading public health challenge (1, 3). Despite substantial advances in pharmacological treatments, hypertension (BP) control remains suboptimal in many populations, highlighting the urgent need for effective primary prevention strategies, particularly those targeting less traditional risk factors (4).

Globally, hypertension affects approximately 1.3 billion adults aged 30–79 years, with an age-standardized prevalence of 33% according to the WHO 2023 Global Report (5). Notably, 46% of affected individuals are unaware of their condition, only 42% receive treatment, and merely 21% achieve adequate hypertension control. More than three-quarters of these patients reside in low- and middle-income countries (LMICs), including Iran. In Iran, the national STEPs survey (2021) reported an age-standardized hypertension prevalence of 32.0% among adults, with a higher burden in women (32.9%) than men (30.9%) (6). The prevalence is even higher among older adults (60+ years), reaching 60.6% in males and 71.8% in females (7, 8). These statistics highlight the persistently high burden of hypertension in Iran and the urgent need for innovative primary prevention strategies targeting modifiable risk factors beyond traditional biomedical approaches.

Well-established risk factors for incident hypertension include advanced age, male sex, obesity, physical inactivity, high dietary sodium intake, low potassium intake, excessive alcohol consumption, smoking, diabetes mellitus, and family history of hypertension (9). However, these factors collectively explain only part of the interindividual variation in hypertension risk (10). Health literacy, the capacity to obtain, process, and understand basic health information needed to make appropriate health decisions, has emerged as a critical yet underrecognized determinant of hypertension outcomes (11). Unlike traditional risk factors such as age or genetics, health literacy is modifiable, making it a promising target for intervention (11). Individuals with limited health literacy face substantial challenges in managing hypertension, including difficulty understanding hypertension numbers, following sodium-restricted diets, adhering to complex medication regimens, and navigating healthcare systems (12). A systematic reviews demonstrated that low health literacy is linked to worse chronic disease outcomes and increased healthcare utilization, even after adjusting for education and socioeconomic status (13). Given that over one-third of adults in many populations have limited health literacy (14), addressing this factor through routine screening and tailored educational interventions represents a viable strategy for improving hypertension prevention and control (11).

To date, only a few prospective cohort studies have longitudinally examined the association between health literacy and hypertension-related outcomes. In a large prospective cohort study from the Netherlands (Lifelines Cohort Study), Loreto et al. (2025) followed 21,725 adults with hypertension and found that although a change from limited to adequate health literacy had no direct association (15). Notably, self-management skills including motivation, self-efficacy, and problem-solving partially mediated this relationship (15). In the United States, the Heart Healthy Lenoir Trial, a prospective non-randomized cohort study of 525 patients with uncontrolled hypertension, reported that both low and high health literacy groups achieved significant systolic hypertension reductions over 24 months (8.1 mmHg and 4.6 mmHg, respectively), suggesting that health literacy-sensitive interventions may benefit all patients regardless of literacy level (16). A retrospective cohort study from a Chinese community (2017) involving 360 hypertensive patients also demonstrated that low health literacy was associated with poorer hypertension management (17).

Despite the consistency of these findings, several critical gaps remain. First, almost all existing studies both internationally and in Iran have employed cross-sectional designs, which preclude causal inference and are susceptible to reverse causality (i.e., hypertension-related cognitive decline could reduce health literacy rather than health literacy preventing hypertension) (12, 18). Second, prospective cohort studies examining the association between baseline health literacy and the incidence of new-onset hypertension (rather than prevalent hypertension or hypertension control among diagnosed patients) are remarkably scarce (19). Third, to the best of our knowledge, no longitudinal study has investigated this relationship in a Middle Eastern population using a validated, multidimensional health literacy instrument such as the HELIA questionnaire (20).

To address these gaps, we conducted a prospective cohort study using data from the Shahrekord PERSIAN Cohort Study. The aim was to investigate whether low health literacy at baseline independently predicts incident hypertension after adjusting for potential confounders. This study hypothesized that inadequate health literacy increases the odds of incident hypertension and that metabolic factors may partially explain this association. The findings may inform primary prevention by suggesting that routine health literacy screening in primary care could identify at-risk individuals who would benefit from tailored educational interventions and enhanced support for hypertension self-monitoring.

Materials and Methods

Study design and setting

This study was designed as a prospective cohort study conducted within the framework of the Prospective Epidemiological Research Studies in Iran (PERSIAN), a large-scale, multi-center population-based cohort study aimed at investigating non-communicable diseases and their risk factors across different ethnicities and geographical areas of Iran. The present analysis specifically used data from the Shahrekord cohort study (SCS), which is part of the PERSIAN cohort and was established in Chaharmahal and Bakhtiari Province,

southwestern Iran, a region characterized by its high altitude and a mix of Lur, Fars, and Turk ethnic groups. According to the study protocol, all procedures for data collection, follow-up, and quality control were predefined and standardized across all PERSIAN cohort sites (21, 22).

Study Population and Eligibility Criteria

The Shahrekord cohort began recruitment in November 2015 and enrolled individuals aged 35 to 70 years from both urban and rural areas. A total of 10,075 participants were recruited at baseline, consisting of 7,034 urban and 3,041 rural residents. All participants provided written informed consent at the time of enrollment, and the study protocol was approved by the Ethics Committee of Shahrekord University of Medical Sciences. The procedures followed the principles of the Declaration of Helsinki. Participants are being followed annually for at least 15 years (until 2036) to ascertain the incidence of various non-communicable diseases, including hypertension (22).

For the present analysis, eligible participants were those aged 35 to 70 years at enrollment who had complete data on health literacy and key covariates. Individuals with a confirmed physician diagnosis of hypertension at baseline and/or those taking antihypertensive medications were excluded from the analysis. According to the study protocol, health literacy was measured in a predefined subgroup of 5,180 participants (22). After excluding participants with prevalent hypertension at baseline (physician-diagnosed or taking antihypertensive medication) and those with missing data on health literacy or other key covariates (963), the final analytical sample comprised 4,217 participants free of hypertension at baseline.

Measurement of Health literacy (Exposure)

The exposure variable of interest was health literacy, assessed at baseline using the Health Literacy for Iranian Adults (HELIA) questionnaire. This instrument was developed and psychometrically validated by Montazeri and colleagues. The HELIA consists of 33 items across five dimensions: access to health information (6 items), reading ability (4 items), understanding of health information (7 items), appraisal of health information (4 items), and decision-making (12 items). All items are answered on a five-point Likert scale ranging from "Always" (5) to "Never" (1). The instrument has demonstrated acceptable internal consistency, with Cronbach's alpha coefficients ranging from 0.72 to 0.89 across the five dimensions (23). The total HELIA score (range 33–165) was linearly transformed to a 0–100 scale for standardization. Consistent with the original HELIA validation study (Montazeri et al.) (24), the 25th percentile of the standardized scores was used as the cutoff point to define inadequate health literacy. Participants with a standardized score below 53 (25th percentile) were categorized as having inadequate health literacy, while those with a score of 53 or higher were considered to have adequate health literacy (24).

Measurement of Hypertension (Outcome)

The primary outcome was incident hypertension (new-onset hypertension) during the follow-up period from baseline (2015–2017) until 2024. During the annual follow-up process, trained interviewers from the PERSIAN cohort contacted participants by telephone to assess

their health status. Whenever a participant reported having hypertension or a history of taking antihypertensive medication, their medical record was reviewed by the cohort physician and the diagnosis was definitively confirmed. According to PERSIAN Cohort Study protocol, all reported cases of hypertension were verified by the cohort physician and then registered as definite hypertension events.

Assessment of Covariates

A range of potential confounders were measured at baseline using standardized PERSIAN cohort questionnaires and clinical assessments. A confounder is defined as a variable associated with both the exposure and the outcome, without being on the causal pathway. All covariates were selected a priori based on their established association with hypertension in previous studies and according to the study protocol.

Sociodemographic variables included age (continuous, years), sex (male, female), and marital status categorized as married versus other (including single, widowed, and divorced). Educational level was dichotomized into non-academic (≤ 12 years of schooling, equivalent to high school diploma or less) and academic (≥ 13 years of schooling, corresponding to college education and above). Ethnicity was classified into four groups: Lur, Fars, Turk, and others.

Lifestyle and behavioral variables were assessed as follows. Smoking status was categorized as never, former, and current daily smoker (21, 22). Non-cigarette tobacco use was defined as use of products such as hookah, pipe, or other traditional tobacco at least once per week for six months or more (yes/no) (21, 22). Alcohol consumption was defined as consumption of approximately 200 ml of beer or 45 ml of liquor at least once per week for a minimum of six months (yes/no) (21, 22). Physical activity was measured as daily metabolic equivalent of task (MET), calculated based on 24-hour activity patterns using standard MET values for each activity. Physical activity levels were classified into three categories according to sample percentiles: low (≤ 25 th percentile, 24–36.5), moderate (26th–75th percentile, 36.6–44.9), and high (> 75 th percentile, > 45). Dietary habits including salt intake were assessed using food frequency questionnaires, and salt intake was categorized according to WHO recommendations as low (< 5 g/day) and high (≥ 5 g/day) (25).

Anthropometric and clinical variables comprised body mass index (BMI) calculated as weight in kilograms divided by height in meters squared, categorized as underweight (BMI less than 18.5), normal (BMI 18.5–24.9), overweight (BMI 25–29.9), and obese (BMI 30 or greater). Diabetes mellitus was defined as fasting blood glucose ≥ 126 mg/dL or current use of glucose-lowering medication, and was categorized into normal (< 100 mg/dL), prediabetes (100–125 mg/dL), and diabetes (≥ 126 mg/dL) according to American Diabetes Association criteria (26). Lipid profile parameters were defined as follows: triglycerides as normal (< 150 mg/dL) and elevated (≥ 150 mg/dL); HDL cholesterol as low (≤ 40 mg/dL in men and ≤ 50 mg/dL in women) and normal/high otherwise; and LDL cholesterol as optimal (< 130 mg/dL) and elevated (≥ 130 mg/dL) (25). Depression and psychiatric disorders were recorded as yes or no based on physician diagnosis. Employment status was categorized as employed versus unemployed.

Statistical analysis

Statistical analyses were performed using SPSS and Stata. A two-sided p-value less than 0.05 was considered statistically significant. Baseline characteristics of participants were summarized using descriptive statistics: continuous variables were presented as mean $\pm$ standard deviation (SD) or median with interquartile range for non-normally distributed variables, and categorical variables as frequencies and percentages. Baseline characteristics were compared between health literacy groups using Mann-Whitney U tests for continuous variables and chi-square (or Fisher's exact tests) for categorical variables. The cumulative incidence of hypertension was calculated overall and stratified by health literacy status.

To examine the association between baseline health literacy and incident hypertension, binary logistic regression models were used to estimate odds ratios (ORs) with 95% confidence intervals (CIs). Given the low incidence rate of hypertension in our cohort (<5%), which satisfies the rare disease assumption, the odds ratios derived from logistic regression closely approximate the hazard ratios from Cox proportional hazards models (27).

A hierarchical model-building strategy was employed to adjust for potential confounders progressively based on the univariable analysis results and to avoid multicollinearity. The crude model (Model 1) included no adjustments. Model 2 was adjusted for age. Model 3 additionally adjusted for ethnicity. Model 4 further included body mass index (BMI), physical activity, and depression. The fully adjusted model (Model 5) additionally included fasting blood sugar and triglycerides. Variables that were not significantly associated with incident hypertension in univariable analysis (including sex, education, marital status, psychiatric disorder, employment, smoking, alcohol consumption, salt intake, and HDL cholesterol) or showed strong collinearity (residence type) were not entered into the multivariable models. To evaluate the contribution of each covariate and avoid over-adjustment for potential partial mediators, a hierarchical logistic regression model was applied. Covariates were selected using a combined approach based on previous literature, biological plausibility, and univariable analysis results ($p < 0.2$).

The Hosmer-Lemeshow goodness-of-fit test was used to assess the calibration of the logistic regression models. A non-significant chi-square statistic ($p > 0.05$) indicated acceptable model fit. The discriminative ability of the logistic regression models was evaluated using the area under the receiver operating characteristic curve (AUC). An AUC value > 0.70 was considered indicative of acceptable discrimination. Multicollinearity among the independent variables was assessed using variance inflation factors (VIF). A VIF value exceeding 10 was considered indicative of problematic multicollinearity (28).

Causal mediation analyses were conducted using Stata's *mediate* command to evaluate whether triglycerides and fasting blood sugar mediate the association between health literacy and hypertension. The total effect (TE), natural indirect effect (NIE), and proportion mediated were estimated using quasi-Bayesian Monte Carlo simulations with 1,000 draws. A statistically significant NIE with $p < 0.05$ was considered evidence of mediation. However, because a significant NIE can occur even with very small effect sizes, particularly in large

samples, we also evaluated the proportion mediated, with values exceeding 30% considered indicative of clinically meaningful mediation, in line with established methodological recommendations (29, 30). Variables with a proportion mediated below this threshold were interpreted as negligible mediators, and were accordingly treated as potential confounders rather than mediators in the final multivariate model, for which adjustment was performed to obtain an unbiased estimate of the total association.

Results

The mean age of the study participants was 47.55 ± 8.33 years. Based on the independent samples Mann-Whitney U test, the mean age of participants with inadequate health literacy was significantly higher than those with adequate health literacy (50.41 ± 8.09 years vs. 46.63 ± 8.21 years, $p < 0.001$). Significant differences were observed across most baseline characteristics between health literacy groups. Participants with inadequate health literacy were more likely to be older (50.41 vs. 46.63 years, $p < 0.001$), female (62.5% vs. 46.0%), rural residents (72.3% vs. 17.8%), and non-academically educated (80.1% vs. 45.9%) compared to those with adequate health literacy (all $p < 0.001$). Additionally, the inadequate health literacy group had higher proportions of unemployment (62.0% vs. 43.0%) and normal weight (34.8% vs. 29.6%), while the adequate health literacy group showed higher rates of current smoking (14.4% vs. 12.1%), alcohol consumption (20.0% vs. 11.1%), elevated triglycerides (40.6% vs. 26.5%), and diabetes (6.6% vs. 3.8%) (all $p < 0.01$). No significant differences were observed for LDL cholesterol ($p = 0.708$) or salt intake ($p = 0.235$) (**Table 1**). In this subgroup of the Shahrekord Persian Cohort (4,217 participants) over 7 years of follow-up, the cumulative incidence of hypertension was approximately 2.6% (107 cases).

Table 1. Baseline characteristics of study participants by health literacy status

Characteristic	Total N=4,217	Inadequate HL (n=1,024)	Adequate HL (n=3,193)	P- value*
Residence type, n (%)				
Rural	1,308 (31.0)	740 (72.3)	568 (17.8)	<0.001
Urban	2,909 (69.0)	284 (27.7)	2,625 (82.2)	
Ethnicity, n (%)				
Lur	2,115 (50.2)	820 (80.1)	1,295 (40.6)	<0.001
Fars	1,671 (39.6)	163 (15.9)	1,508 (47.2)	
Turk	276 (6.5)	18 (1.8)	258 (8.1)	
Others	155 (3.7)	23 (2.2)	132 (4.1)	
Gender, n (%)				
Male	2,109 (50.0)	384 (37.5)	1,725 (54.0)	<0.001
Female	2,108 (50.0)	640 (62.5)	1,468 (46.0)	
Education level, n (%)				
Academic (College and above)	1,930 (45.8)	204 (19.9)	1,726 (54.1)	<0.001
Non-academic (≤ High school)	2,287 (54.2)	820 (80.1)	1,467 (45.9)	
Marital status, n (%)				
Married	4,017 (95.3)	952 (93.0)	3,065 (96.0)	<0.001
Other (Single/Widow/Divorced)	200 (4.7)	72 (7.0)	128 (4.0)	
BMI category, n (%)				



Normal	1,301 (30.9)	356 (34.8)	945 (29.6)	0.003
Underweight	57 (1.4)	19 (1.9)	38 (1.2)	
Overweight	1,851 (43.9)	411 (40.1)	1,440 (45.1)	
Obese	1,008 (23.9)	238 (23.2)	770 (24.1)	
Depression, n (%)				
No	3,621 (85.9)	902 (88.1)	2,719 (85.2)	0.019
Yes	596 (14.1)	122 (11.9)	474 (14.8)	
Psychiatric disorder, n (%)				
No	3,887 (92.2)	958 (93.6)	2,929 (91.7)	0.059
Yes	330 (7.8)	66 (6.4)	264 (8.3)	
Employment status, n (%)				
Unemployed	2,007 (47.6)	635 (62.0)	1,372 (43.0)	<0.001
Employed	2,210 (52.4)	389 (38.0)	1,821 (57.0)	
Smoking status, n (%)				
Never	3,519 (83.4)	888 (86.7)	2,631 (82.4)	<0.001
Former	115 (2.7)	12 (1.2)	103 (3.2)	
Current (daily)	583 (13.8)	124 (12.1)	459 (14.4)	
Non-cigarette tobacco use, n (%)				
No	3,286 (77.9)	859 (83.9)	2,427 (76.0)	<0.001
Yes	931 (22.1)	165 (16.1)	766 (24.0)	
Alcohol consumption, n (%)				
No	3,463 (82.1)	910 (88.9)	2,553 (80.0)	<0.001
Yes	754 (17.9)	114 (11.1)	640 (20.0)	
Fasting blood sugar, n (%)				
Normal (<100 mg/dL)	3,106 (73.7)	839 (81.9)	2,267 (71.0)	<0.001
Prediabetes (100-125 mg/dL)	860 (20.4)	146 (14.3)	714 (22.4)	
Diabetes (≥126 mg/dL)	251 (5.9)	39 (3.8)	212 (6.6)	
HDL cholesterol, n (%)				
Normal/High	3,440 (81.6)	784 (76.6)	2,656 (83.2)	<0.001
Low	777 (18.4)	240 (23.4)	537 (16.8)	
Triglycerides, n (%)				
Normal (<150 mg/dL)	2,649 (62.8)	753 (73.5)	1,896 (59.4)	<0.001
Elevated (≥150 mg/dL)	1,568 (37.2)	271 (26.5)	1,297 (40.6)	
LDL cholesterol, n (%)				
Optimal (<130 mg/dL)	3,426 (81.2)	836 (81.6)	2,590 (81.1)	0.708
Elevated (≥130 mg/dL)	791 (18.8)	188 (18.4)	603 (18.9)	
Salt intake, n (%)				
Low (<5 g/day)	2,933 (69.6)	697 (68.1)	2,236 (70.0)	0.235
High (≥5 g/day)	1,284 (30.4)	327 (31.9)	957 (30.0)	
Physical activity (MET), n (%)				
Low (24–36.5 MET-h/week)	1,071 (25.4)	146 (14.3)	925 (29.0)	<0.001
Moderate (36.6–44.9 MET-h/week)	2,142 (50.8)	493 (48.1)	1,649 (51.6)	
High (>45 MET-h/week)	1,004 (23.8)	385 (37.6)	619 (19.4)	

HL: Health Literacy; BMI: Body Mass Index; MET: Metabolic Equivalent of Task

P-value from chi-square test comparing adequate vs. inadequate health literacy groups

Mediation analysis showed significant NIE for triglycerides (NIE = -0.0031, $p = 0.001$) and FBS (NIE = -0.0018, $p = 0.027$), with total effects also significant for both. However, the proportions mediated were 27.4% and 15.6%, respectively (**Table 2**).



Table 2. Mediation analysis results for metabolic factors in the association between health literacy and hypertension

Mediator	NIE (p-value)	TE (p-value)	Proportion Mediated
Triglycerides	-0.0031 (p = 0.001)	-0.0114 (p = 0.023)	27.4%
Fasting blood sugar	-0.0018 (p = 0.027)	-0.0116 (p = 0.019)	15.6%

Univariable logistic regression analysis was performed to identify factors associated with incident hypertension and to guide variable selection for multivariable models (**Table 3**). Variables with a p-value < 0.05 were considered for entry into the hierarchical multivariable models. Accordingly, age, ethnicity (Fars), overweight, obesity, depression, low physical activity, elevated triglycerides, prediabetes, and diabetes were selected as potential confounders. Urban residence, despite its significant association, was excluded due to strong collinearity with ethnicity and health literacy. Elevated LDL cholesterol was also excluded as triglycerides showed a stronger association. Health literacy (inadequate/marginal) was retained as the main exposure variable. Non-significant factors including gender, education, marital status, psychiatric disorder, employment, smoking, alcohol consumption, salt intake, and HDL cholesterol were not entered into the multivariable models.

Table 3. Univariable logistic regression analysis of factors associated with incident hypertension

Variable	OR	95% CI	P-value
Age (year)	1.05	1.03, 1.08	<0.001*
Residence type (Ref: Rural)			
Urban	4.477	2.32, 8.61	<0.001*
Ethnicity (Ref: Lur)			
Fars	1.57	1.05, 2.35	0.028*
Turk	1.22	0.54, 2.74	0.623
Others	0.61	0.14, 2.56	0.505
Gender (Ref: Male)			
Female	1.18	0.80 – 1.74	0.337
Education years (Ref: Academic (College and above))			
Non-academic ($\leq$ High school)	1.21	0.82, 1.78	0.324
Marital status (Ref: Single, Widow, Divorced)			
Married	1.28	0.47, 3.53	0.621
BMI category (Ref: Normal)			
Underweight	3.11	0.69, 13.97	0.137
Overweight	2.28	1.27, 4.09	0.006*
Obese	3.72	2.05, 6.76	<0.001*
Depression (Ref: No)			
Yes	2.32	1.50, 3.59	<0.001*
Psychiatric disorder (Ref: No)			
Yes	1.50	0.81, 2.77	0.189
Employment (Ref: employed)			
Unemployed	1.31	0.89 – 1.93	0.167
Smoking status (Ref: Current)			



Never	2.06	0.63, 6.70	0.227
Former	1.54	0.79, 2.98	0.188
Non-cigarette tobacco (Ref: Yes)			
No	1.32	0.80, 2.18	0.277
Alcohol consumption (Ref: Yes)			
No	1.59	0.88, 2.85	0.120
Health literacy (Ref: Adequate)			
Inadequate	1.72	1.02, 2.90	0.043*
Physical activity (Ref: High)			
Low	2.13	1.19, 3.80	0.010
Moderate	1.44	0.83, 2.51	0.192
Salt intake (Ref: Low <5 g/day)			
High (≥5 g/day)	1.01	0.67, 1.54	0.929
LDL cholesterol (Ref: Optimal <130 mg/dL)			
Elevated (≥130 mg/dL)	1.79	1.17, 2.75	0.007*
Triglycerides (Ref: Normal <150 mg/dL)			
Elevated (≥150 mg/dL)	2.29	1.55, 3.37	<0.001*
HDL cholesterol (Ref: Low)			
Normal/High	1.12	0.67, 1.87	0.665
Fasting blood sugar (Ref: Normal <100 mg/dL)			
Prediabetes (100–125 mg/dL)	1.80	1.15, 2.81	0.009*
Diabetes	3.39	1.92, 5.98	<0.001*

OR: Odds Ratio; CI: Confidence Interval; Ref: Reference category; *p-value<0.05, LDL cholesterol was excluded due to collinearity with triglycerides and to avoid overfitting given the limited number of events (n = 107).

Table 4 presents the results of hierarchical logistic regression models examining the association between health literacy and incident hypertension, with progressive adjustment for potential confounders.

In the crude model (Model 1), inadequate health literacy was significantly associated with higher odds of incident hypertension (OR:1.72 , 95% CI:1.02, 2.90, p=0.043). After adjusting for age (Model 2), the association became stronger (OR: 2.15, 95% CI:1.27 , 3.65, p=0.005), indicating that age acted as a negative confounder. Further adjustment for ethnicity (Model 3) slightly attenuated the effect estimate (OR:1.97 , 95% CI:1.12, 3.44, p=0.018). Adding BMI, physical activity, and depression (Model 4) maintained a significant association (OR:1.78 , 95% CI:1.02, 3.11, p=0.044).

However, after additional adjustment for fasting blood sugar and triglycerides in the fully adjusted model (Model 5), the association between inadequate health literacy and incident hypertension became non-significant (OR:1.67, 95% CI:0.95, 2.92, p=0.075). This suggests that the association between health literacy and hypertension is may be largely attenuated by metabolic factors, particularly triglycerides and fasting blood sugar.

Among other covariates in the fully adjusted model, age (OR:1.06 per year, 95% CI:1.03, 1.08, p<0.001), obesity (OR:2.79, 95% CI:1.51, 5.15, p=0.001), depression (OR:2.06, 95% CI:1.32,

3.22, $p=0.002$), and elevated triglycerides (OR: 1.60, 95% CI: 1.05, 2.42, $p = 0.027$) remained independently associated with incident hypertension.

The Hosmer-Lemeshow goodness-of-fit test results for the hierarchical models were as follows: Model 1 was not computable due to the inclusion of only one predictor variable. Model 2 showed borderline fit ($\chi^2=15.689$, $df=8$, $p=0.047$). Model 3 demonstrated acceptable fit ($\chi^2=15.243$, $df=8$, $p=0.055$). Model 4 showed good calibration ($\chi^2=8.916$, $df=8$, $p=0.349$), and Model 5 (the fully adjusted model) demonstrated the best overall fit ($\chi^2=7.845$, $df=8$, $p=0.449$). The progressive improvement in fit from Model 2 to Model 5, with decreasing chi-square values, indicates that the addition of covariates enhanced model calibration.

The area under the curve (AUC) values for the hierarchical models were as follows: Model 1 (health literacy only): 0.543; Model 2 (+age): 0.674; Model 3 (+ethnicity):0.677; Model 4 (+BMI, physical activity, depression):0.724; and Model 5 (fully adjusted model, + FBS and triglycerides):0.739. The final model demonstrated acceptable discriminative ability (AUC=0.739), indicating that the model could adequately distinguish between individuals who developed hypertension and those who did not. The progressive improvement in AUC from Model 1 to Model 5 suggests that the addition of covariates enhanced the model's predictive performance. The AUC values for Models 1–3 were below 0.70, while Models 4 and 5 exceeded this threshold. Variance inflation factor (VIF) values for all variables in the fully adjusted model ranged from 1.01 to 1.21, with a mean VIF of 1.10, well below the conventional threshold of 10. These findings confirm that multicollinearity is not a concern in our final model.

Table 4. Hierarchical logistic regression models for incident hypertension

Variable	*Model 1 OR (95% CI)	*Model 2 OR (95% CI)	*Model 3 OR (95% CI)	*Model 4 OR (95% CI)	*Model 5 OR (95% CI)
Health literacy (Ref: Adequate)					
Inadequate	1.72 (1.02, 2.90)	2.15 (1.27, 3.65)	1.97 (1.12, 3.44)	1.78 (1.02, 3.11)	1.67 (0.95, 2.92)
Age (per 1 year)		1.06 (1.04, 1.09)	1.06 (1.04, 1.09)	1.06 (1.04, 1.09)	1.06 (1.03, 1.08)
Ethnicity (Ref: Lur)					
Fars			1.28 (0.83, 1.95)	1.18 (0.77, 1.81)	1.09 (0.71, 1.67)
Turk			1.10 (0.48, 2.51)	1.05 (0.46, 2.39)	0.95 (0.42, 2.19)
Others			0.59 (0.14, 2.49)	0.49 (0.11, 2.06)	0.47 (0.11, 1.97)
BMI category (Ref: Normal)					
Underweight				3.27 (0.72, 14.95)	3.69 (0.81, 16.89)
Overweight				2.03 (1.12, 3.65)	1.77 (0.97, 3.21)
Obese				3.34 (1.83, 6.10)	2.79 (1.51, 5.15)
Physical activity (Ref: High)					
Low				1.58 (0.87, 2.88)	1.46 (0.80, 2.67)
Moderate				1.14 (0.65, 2.02)	1.13 (0.64, 2.00)
Depression (Ref: No)					
Yes				2.08 (1.33, 3.25)	2.06 (1.32, 3.22)
Fasting blood sugar (Ref: Normal (<100 mg/dL))					
Prediabetes (100–125 mg/dL)					1.24 (0.78, 1.96)
Diabetes					1.75 (0.96, 3.22)
Triglycerides (Ref: Normal <150 mg/dL)					
Elevated (≥ 150 mg/dL)					1.60 (1.05, 2.42)



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***Model 1** (crude model) included no adjustments. **Model 2** added adjustment for age. **Model 3** additionally adjusted for ethnicity. **Model 4** further included body mass index (BMI), physical activity, and depression. **Model 5** (fully adjusted model) additionally included fasting blood sugar and triglycerides; OR: Odds Ratio; CI: Confidence Interval; Ref: Reference category

Discussion

This prospective cohort study investigated the association between health literacy and incident hypertension among adults free of hypertension at baseline, with approximately seven years of follow-up. After adjusting for a wide range of potential confounders, our findings revealed that inadequate or marginal health literacy was not significantly associated with incident hypertension in the fully adjusted model. The association observed in crude and partially adjusted models was largely attenuated after accounting for metabolic factors, particularly triglycerides and fasting blood sugar. These results suggest that the association between health literacy and hypertension may be mediated through metabolic pathways rather than exerting a direct independent association.

The relatively low cumulative incidence of hypertension in this study (2.6% over 7 years) is comparable to findings from other Iranian cohort studies. The Ravansar Non-Communicable Disease (RaNCD) cohort reported 1,171 new hypertension cases over a median follow-up of 9.3 years, with an incidence rate of 16.50 per 1,000 person-years (31). The Isfahan Cohort Study, conducted among adults aged ≥ 35 years in central Iran, reported a 7-year cumulative incidence of approximately 22% (32). The Tehran Lipid and Glucose Study (TLGS), with a 13-year follow-up, reported annual incidence rates of 29.7 and 25.8 per 1,000 person-years for men and women, respectively (33). These variations reflect differences in follow-up duration, baseline age, risk factor profiles, and geographic diversity across study populations.

In the fully adjusted model, age, obesity, depression, and elevated triglycerides remained independently associated with incident hypertension, while health literacy lost its statistical significance. This pattern of attenuation across hierarchical models provides important insights into the potential mechanisms linking health literacy to hypertension.

Age

The strong independent association between age and hypertension observed in our study is consistent with well-established epidemiological evidence. A large prospective cohort study from Southern Iran by Rezaianzadeh et al. followed middle-aged and older adults and found that older age groups had a substantially higher risk of developing hypertension compared to younger age groups, with a stronger association observed among women (34). Similarly, Babol cohort study in Northern Iran reported that age was an independent predictor of mortality in older hypertensive patients, with each year increase in age associated with elevated risk (35). Internationally, the China Health and Retirement Longitudinal Study (CHARLS) by Fang et al. confirmed increasing age as one of the strongest predictors of incident hypertension (36). The biological mechanisms include progressive arterial stiffening, reduced vascular compliance, and decreased renal function, all of which contribute to age-related hypertension elevation (37).

Obesity

Obesity emerged as one of the strongest predictors of incident hypertension in our fully adjusted model. This finding aligns with extensive national and international literature documenting the relationship between adiposity and hypertension. A large cross-sectional study using data from the Azar cohort in Northwest Iran demonstrated that obesity significantly increased the risk of prehypertension and hypertension among men (38). The Shahedieh cohort study in Yazd by Jambarsang et al. showed that body mass index was the best predictor of undiagnosed hypertension risk in young Iranian adults (39). The Southern Iran cohort study by Rezaianzadeh et al. also found that a high waist-to-height ratio was associated with substantially increased hypertension risk in men (34). Internationally, the CHARLS study in China demonstrated that combined triglyceride-glucose index with body mass index had a strong association with incident hypertension (40). The pathophysiological mechanisms include activation of the renin-angiotensin-aldosterone system, sympathetic nervous system overactivity, insulin resistance, and chronic inflammation, all of which promote hypertension elevation (41).

Depression

Depression was independently associated with incident hypertension in our study. This finding is consistent with growing evidence identifying depression as an independent risk factor for hypertension. A comprehensive systematic review and meta-analysis by Fang et al. demonstrated that depression was associated with increased all-cause mortality among older adult patients with hypertension, with a stronger association observed among females (42). Another meta-analysis by Sathapathi et al., which included multiple observational studies, showed a significant positive association between depression and the risk of developing hypertension, with a stronger association observed in cohort studies (43). The Babol cohort study in Iran reported that a substantial proportion of older hypertensive patients had depressive symptoms (44). Depression may be linked to hypertension through several pathways, including activation of the hypothalamic-pituitary-adrenal axis, increased sympathetic nervous system activity, and behavioral factors such as poor medication adherence, unhealthy diet, and reduced physical activity (45).

Triglycerides and Metabolic Factors

Elevated triglycerides remained significantly associated with incident hypertension in the fully adjusted model. This finding is strongly supported by recent longitudinal evidence from both national and international studies. A national cohort study in China by Fang et al. demonstrated that each standard deviation increase in the triglyceride-glucose index with body roundness index was associated with a significantly increased risk of incident hypertension, with participants in the highest quartile showing substantially higher risk compared to those in the lowest quartile (36). Another study in China by Zhang et al. showed that the triglyceride-glucose index was associated with higher risk of cardiovascular diseases, with systolic hypertension playing a mediating role in this association (46). In Iran, the

Shahedieh cohort study demonstrated that individuals with undiagnosed hypertension had higher mean body mass index, and obesity was a strong predictor of hypertension (39). Hypertriglyceridemia is a key component of metabolic syndrome and often coexists with insulin resistance and abdominal obesity. The clustering of metabolic abnormalities, including dyslipidemia, glucose intolerance, and hypertension, suggests a common underlying pathophysiology related to insulin resistance and chronic low-grade inflammation (47).

Health Literacy and Mediation

Regarding the central finding of our study, the lack of a direct association between health literacy and incident hypertension after full adjustment warrants careful interpretation. The crude model showed a significant association, and the association remained significant after adjusting for age, ethnicity, and lifestyle factors. However, after additional adjustment for fasting blood sugar and triglycerides, the association became non-significant. This pattern suggests that metabolic factors may serve as mediators in the pathway from health literacy to hypertension.

Strong evidence from the Lifelines Cohort Study in the Netherlands by Loretto et al., which followed a large cohort of adults with hypertension, demonstrated that a change from limited health literacy to adequate health literacy had no direct effect on the onset of hypertension-related multimorbidity but did decrease the odds of its progression (15). Importantly, self-management skills such as motivation, self-efficacy beliefs, and problem-solving played mediating roles in this association. These findings support the notion that health literacy influences health outcomes indirectly through behavioral and self-management pathways rather than through direct biological mechanisms.

Furthermore, the Southern Iran cohort study showed that factors such as smoking and opium use in men and history of kidney disease in women were important predictors of hypertension, indicating that different behavioral and clinical pathways exist based on demographic factors (34). In hospitalized patients, McNaughton et al. in the United States found that low health literacy was independently associated with elevated hypertension at hospital presentation, particularly among individuals without a prior diagnosis of hypertension (48). While this cross-sectional finding differs from our prospective results, the difference may be attributable to study design, population characteristics, and the extent of adjustment for metabolic confounders.

Mechanisms and Pathophysiological Pathways

The attenuation of the health literacy association after adjusting for metabolic factors in our study can be explained by several mechanisms. Individuals with limited health literacy may have difficulty understanding and following dietary recommendations, adhering to prescribed medications, and engaging in preventive health behaviors. These behavioral patterns can lead to poor metabolic control, including elevated blood glucose and triglyceride levels, which in turn increase hypertension risk. Evidence from the Lifelines Cohort Study suggests that self-management and problem-solving play key roles in this pathway (15).

The relationship between obesity and socioeconomic status observed in various Iranian studies illustrates the complex interplay of economic, behavioral, and metabolic risk factors. The Azar cohort study demonstrated that body mass index was the best predictor of hypertension in men, while the combination of waist-to-hip ratio and body mass index was the best predictor in women (49). This pattern may influence the observed associations between health literacy, metabolic factors, and hypertension.

Study Limitations and Strengths: This study has several strengths, including the prospective cohort design, large sample size, long follow-up period, and comprehensive assessment of potential confounders measured at baseline. However, limitations include single baseline measurement of health literacy, potential residual confounding, and possible underdiagnosis of hypertension due to passive case ascertainment. The small number of events ($n = 107$) limited statistical power and resulted in wide confidence intervals for some subgroups. The final model had an events-per-parameter ratio of ~ 7.6 , below the recommended 10. Dichotomization of health literacy may have obscured dose-response relationships. Other limitations include lack of formal interaction testing, measurement of health literacy only in a cohort subgroup, absence of regular blood pressure measurements during follow-up, and potential differential misclassification. Despite these limitations, the consistency of findings across sensitivity analyses supports the robustness of the conclusions.

Conclusion

In conclusion, our findings suggest that the association between health literacy and incident hypertension may be largely attenuated by metabolic factors, particularly triglycerides and fasting blood sugar, rather than reflecting a direct independent association. Age, obesity, depression, and elevated triglycerides emerged as the strongest independent predictors of hypertension in this population. These results highlight the importance of addressing metabolic risk factors in hypertension prevention efforts, regardless of health literacy level. Future interventions aimed at reducing hypertension burden may benefit from focusing on improving metabolic health through lifestyle modifications, while also considering health literacy as a factor that may influence the effectiveness of such interventions through behavioral pathways.

Acknowledgements: The authors would like to thank the participants of the Shahrekord PERSIAN Cohort Study for their valuable contribution. We also acknowledge the staff of the PERSIAN cohort for their dedicated work in data collection and follow-up. We are grateful to the Shahrekord University of Medical Sciences for providing access to the cohort data.

Availability of data and materials: The data supporting the findings of this study are available from the Shahrekord PERSIAN Cohort Study but restrictions apply to the availability of these data, which were used under license for the current study. Data are available from the corresponding author upon reasonable request and with permission of the Shahrekord University of Medical Sciences.

Conflicts of interest: The authors declare that they have no competing interests.

Consent for publication: Not applicable. This manuscript does not contain any individual person's data in any form (including individual details, images, or videos).

Ethics approval and consent to participate: This study was conducted in accordance with the Declaration of Helsinki. The protocol of this study was approved by the Ethics Committee of Shahrekord University of Medical Sciences (approval number: IR.SKUMS.NUMHE.REC.1405.016). All participants provided written informed consent at the time of enrollment into the PERSIAN cohort study. For the present analysis, all data were anonymized before access.

Funding: This study received no specific funding from any funding agency in the public, commercial, or not-for-profit sectors. The Shahrekord PERSIAN Cohort Study was funded by the Ministry of Health and Medical Education of Iran and Shahrekord University of Medical Sciences.

Author Contributions: Vahid Khosravi: Conceptualization, Methodology, Writing – Original Draft, Supervision. Maede Hosseinnia: Investigation, Resources, Methodology, Writing – Review & Editing. Ali Ahmadi: Data curation, Methodology, Validation, Writing – Review & Editing. Masoumeh Alidosti: Investigation, Resources, Writing – Review & Editing. Elaheh Tavasooli: Methodology, Visualization, Writing – Review & Editing. Samaneh Torkian: Conceptualization, Formal analysis, Methodology, Supervision, Writing – Review & Editing, Project administration. All authors read and approved the final manuscript.

AI Statement: During the preparation of this manuscript, the authors used DeepSeek AI (deepseek.com) for English language editing, literature search, and summarization. After using this tool, the authors reviewed and edited the content as necessary and take full responsibility for the content of the publication. No AI tools were used for data collection, statistical analysis, or drawing scientific conclusions.

References

1. Zhou B, Carrillo-Larco RM, Danaei G, Riley LM, Paciorek CJ, Stevens GA, et al. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *The Lancet*. 2021;398(10304):957-80. [https://doi.org/10.1016/S0140-6736\(21\)01330-1](https://doi.org/10.1016/S0140-6736(21)01330-1) PMID:34450083
2. ZHANG Dongyan LY. Summary and interpretation of the World Health Organization "Global Report on Hypertension". *Journal of Diagnostics Concepts & Practice*. 2024;23(03):297-304.
3. Chowdhury SH, Hossain MA. Hypertension in Bangladesh: Race Against a Silent Killer. *Journal of Medicine*. 2026;27(1):1-2. <https://doi.org/10.3329/jom.v27i1.88268>
4. Geng T, Xu W, Gao H, Zhang J, Zou J, Wang K, et al. Relationship between control of cardiovascular risk factors and chronic kidney disease progression, cardiovascular disease events, and mortality in Chinese adults. *Journal of the American College of Cardiology*. 2024;84(14):1313-24. <https://doi.org/10.1016/j.jacc.2024.06.041> PMID:39322325
5. WHO. First WHO report details devastating impact of hypertension and ways to stop it Sep 19, 2023 [cited 2026. Available from: <https://epinews.emphnet.net/en/news/the-globe/the-world-health-organization-issues-the-first-report-detailing-the-devastating-impact-of-high-blood-pressure-and-ways-to-stop-it>.
6. Heidari-Foroozan M, Rezaei N, Malekpour M-R, Behnoush AH, Ahmadi N, Abbasi-Kangevari M, et al. Hypertension prevalence and cascade of care in Iran: Updates from the STEPs 2021 national and subnational survey. *Research Square*. 2024. <https://doi.org/10.21203/rs.3.rs-3842876/v1>
7. Raeisi zadeh M, Cheraghian B, Hashemi SJ, Hosseini SA, Rahimi Z, Araban M, et al. Prevalence, Awareness, Treatment, Control, and Determinants of Hypertension: A Population-Based Cross-Sectional Study in Southwest Iran. *Medical Journal of the Islamic Republic Of Iran*. 2026;40(1):74-81. <https://doi.org/10.47176/mjiri.40.11> PMID:42516625 PMCID:PMC13403879
8. Hajebi M, Farzi Y, Fe'li SN, Sharifi F, Rezaei N, Mirzad M, et al. Prehypertension and hypertension among older adults: prevalence, awareness, treatment, control and associated factors - findings from

- Iranian STEPS survey (2016 and 2021). *Aging Clin Exp Res.* 2026;38(1). <https://doi.org/10.1007/s40520-026-03339-x> PMID:41848931 PMCID:PMC13005809
9. Yang H, Jiang Y, Guo J, Wang J, Ma X, Chen K, et al. An atlas on multitudinous risk factors associated with incident hypertension: comprehensive exposome-wide association and wide-angled genetic analyses. *European Journal of Preventive Cardiology.* 2025;32(14):1347-60. <https://doi.org/10.1093/eurjpc/zwae236> PMID:39024416
10. Basson J, Simino J, Rao D. Between candidate genes and whole genomes: time for alternative approaches in blood pressure genetics. *Current hypertension reports.* 2012;14(1):46-61. <https://doi.org/10.1007/s11906-011-0241-8> PMID:22161147 PMCID:PMC7774509
11. Simões CF, Lopes LPN, Lara LDS, Cortês AL. Health literacy for elderly patients with high blood pressure: A scoping review. *Res Social Adm Pharm.* 2024;20(9):846-59. <https://doi.org/10.1016/j.sapharm.2024.06.004> PMID:38890034
12. Beiranvandi A, Beiranvand A, Karami K, Mohammadi R. Association of health literacy, medication beliefs, and illness perception among older adults with hypertension: a community-based study. *BMC Public Health.* 2026;26(1). <https://doi.org/10.1186/s12889-025-26123-4> PMID:41654774 PMCID:PMC12977793
13. Handayani N, Haryanto J, Sari D. Factors Influencing Blood Pressure Control in Older Adults Hypertension: A Systematic Review. *Indonesian Journal of Global Health Research.* 2025;7(1):939-46. <https://doi.org/10.37287/ijghr.v7i1.5300>
14. Horde GW, Huang E, Hammock J, Levitan EB, Zhu A, Hansen R, et al. Health Literacy and Hypertension: A Systematic Review. *Circulation.* 2023;148(Suppl_1):A17353-A. https://doi.org/10.1161/circ.148.suppl_1.17353
15. Loreto L, Linares-Jimenez F, de Zeeuw J, de Winter A. Health literacy and hypertension-related multimorbidity: unravelling the mediating role of self-management-insights from the lifelines cohort study. *BMC Public Health.* 2025;25(1):1530 <https://doi.org/10.1186/s12889-025-22798-x> PMID:40275236 PMCID:PMC12020009
16. Halladay JR, Donahue KE, Cené CW, Li Q, Cummings DM, Hinderliter AL, et al. The association of health literacy and blood pressure reduction in a cohort of patients with hypertension: The heart healthy lenoir trial. *Patient education and counseling.* 2017;100(3):542-9. <https://doi.org/10.1016/j.pec.2016.10.015> PMID:27776790 PMCID:PMC5350034
17. Shi D, Li J, Wang Y, Wang S, Liu K, Shi R, et al. Association between health literacy and hypertension management in a Chinese community: a retrospective cohort study. *Internal and Emergency Medicine.* 2017;12(6):765-76. <https://doi.org/10.1007/s11739-017-1651-7> PMID:28303441
18. Mohammadian Khonsari N, Shahrestanaki E, Ejtahed HS, Djalalinia S, Sheidaei A, Hakak-Zargar B, et al. Long-term Trends in Hypertension Prevalence, Awareness, Treatment, and Control Rate in the Middle East and North Africa: a Systematic Review and Meta-analysis of 178 Population-Based Studies. *Curr Hypertens Rep.* 2021;23(9):41 <https://doi.org/10.1007/s11906-021-01159-0> PMID:34625888
19. Al-Hazmi AH, Alanazi ADM, Thirunavukkarasu A, Alriwely NS, Alrais MMF, Alruwaili ABS, et al. Evaluation of hypertension knowledge and its association with medication adherence among hypertensive patients attending primary health centers: a cross-sectional study from eastern Saudi Arabia. *Front Public Health.* 2024;12:1378561. <https://doi.org/10.3389/fpubh.2024.1378561> PMID:39872100 PMCID:PMC11770004
20. Khosravi F, Jamali J. The Health Literacy Instruments for Adults (HELIA): Comparison of the Multiple Indicators Multiple Causes (MIMIC) Model and Multi-Group Confirmatory Factor Analysis (MG-CFA). *Payesh (Health Monitor) Journal.* 2025;24(3):379-87. <https://doi.org/10.61186/payesh.24.3.379>
21. Poustchi H, Eghtesad S, Kamangar F, Etemadi A, Keshtkar A-A, Hekmatdoost A, et al. Prospective epidemiological research studies in Iran (the PERSIAN Cohort Study): rationale, objectives, and design.



- American journal of epidemiology. 2018;187(4):647-55. <https://doi.org/10.1093/aje/kwx314> PMID:29145581 PMCID:PMC6279089
22. Ahmadi A, Shirani M, Khaledifar A, Hashemzadeh M, Solati K, Kheiri S, et al. Non-communicable diseases in the southwest of Iran: profile and baseline data from the Shahrekord PERSIAN Cohort Study. BMC Public health. 2021;21(1):2275. <https://doi.org/10.1186/s12889-021-12326-y> PMID:34903205 PMCID:PMC8670056
23. Montazeri A, Tavousi M, Rakhshani F, Azin SA, Jahangiri K, Ebadi M, et al. Health Literacy for Iranian Adults (HELIA): development and psychometric properties. 2014.
24. Mahmoud Tavousi, AliasgharHaeri Mehrizi, shahram Rafiefar, Atoosa Solimanian, Fateme Sarbandi, Mona Ardestani, et al. Health literacy in Iran: findings from a national study. Payesh (Health Monitor) Journal. 2016;15(1):95-102.
25. Members WC, Blumenthal RS, Morris PB, Gaudino M, Johnson HM, Anderson TS, et al. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of dyslipidemia: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2026;153(17):e1154-e276.
26. Care D. 2. Diagnosis and classification of diabetes: Standards of care in diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S20-s42. <https://doi.org/10.2337/dc24-S002> PMID:38078589
27. Symons M, Moore D. Hazard rate ratio and prospective epidemiological studies. Journal of clinical epidemiology. 2002;55(9):893-9. [https://doi.org/10.1016/S0895-4356\(02\)00443-2](https://doi.org/10.1016/S0895-4356(02)00443-2) PMID:12393077
28. Hair JF, Black WC, Babin BJ, Anderson RE. Canonical correlation: A supplement to multivariate data analysis. Multivariate Data Analysis: A Global Perspective, 7th ed; Pearson Prentice Hall Publishing: Upper Saddle River, NJ, USA. 2010.
29. MacKinnon DP, Lockwood CM, Hoffman JM, West SG, Sheets V. A comparison of methods to test mediation and other intervening variable effects. Psychological methods. 2002;7(1):83. <https://doi.org/10.1037/1082-989X.7.1.83> PMID:11928892 PMCID:PMC2819363
30. Preacher KJ, Kelley K. Effect size measures for mediation models: quantitative strategies for communicating indirect effects. Psychological methods. 2011;16(2):93. <https://doi.org/10.1037/a0022658> PMID:21500915
31. Dezhkameh M, Moradinazar M, Najafi F. Clustering metabolic and behavioral risk factors for hypertension: evidence from a longitudinal cohort in western Iran. Scientific Reports. 2026. <https://doi.org/10.1038/s41598-026-55844-8> PMID:42225909 PMCID:PMC13457851
32. Sadeghi M, Talaei M, Oveisgharan S, Rabiei K, Dianatkah M, Bamonar A, et al. The cumulative incidence of conventional risk factors of cardiovascular disease and their population attributable risk in an Iranian population: The Isfahan Cohort Study. Advanced biomedical research. 2014;3:242. <https://doi.org/10.4103/2277-9175.145749> PMID:25538928 PMCID:PMC4260292
33. Asgari S, Moazzeni SS, Azizi F, Abdi H, Khalili D, Hakemi MS, et al. Sex-specific incidence rates and risk factors for hypertension during 13 years of follow-up: the Tehran lipid and glucose study. Global heart. 2020;15(1):29-. <https://doi.org/10.5334/gh.780> <https://doi.org/10.5334/gh.847>
34. Rezaianzadeh A, Johari MG, Baeradeh N, Seif M, Hosseini SV. Sex differences in hypertension incidence and risk factors: a population-based cohort study in Southern Iran. BMC Public Health. 2024;24(1):3575. <https://doi.org/10.1186/s12889-024-21082-8> PMID:39716231 PMCID:PMC11668117
35. Babaei FN, Bijani A, Hosseini SR, Ghadimi R, Mouodi S. Predictors of 5-year Survival of Elderly with Hypertension. A Prospective Cohort Study. Journal of Research in Medical Sciences. 2024;29(1):36. https://doi.org/10.4103/jrms.jrms_859_22 PMID:39239083 PMCID:PMC11376721
36. Zhang Y, Zhu Y, He Y, Yan Y, Zhao Q, Du Y. Association of cumulative cholesterol-HDL-glucose index with blood pressure changes and risk of new-onset hypertension in middle-aged and older adults: a cohort study. Cardiovascular Diabetology. 2026. <https://doi.org/10.1186/s12933-026-03081-8> PMID:41559691 PMCID:PMC12903659

37. Franklin SS. Hypertension in older people: part 1. *J Clin Hypertens (Greenwich)*. 2006;8(6):444-9. <https://doi.org/10.1111/j.1524-6175.2006.05113.x> PMID:16760685 PMCID:PMC8109573
38. Faramarzi E, Ostadrahimi A, Nikniaz Z, Jafarabadi MA, Fakhari A, Somi M. Determination of the Best Anthropometric Index of Obesity for Prediction of Prehypertension and Hypertension in a Large Population - Based - Study; the Azar- Cohort. *Iranian Red Crescent Medical Journal (IRCMJ)*. 2024;20(3):1-7. <https://doi.org/10.5812/ircmj.59911>
39. Jambarsang S, Soodejani MT, Tate R, Sefidkar R. How well do obesity indices predict undiagnosed hypertension in the Persian cohort (Shahedieh) adults community population of all ages? *Health Science Reports*. 2024;7(2):e1897. <https://doi.org/10.1002/hsr2.1897> PMID:38405171 PMCID:PMC10885643
40. Yan J, Zhang M-z, He Q-q. Association of changes and cumulative measures of triglyceride-glucose index-body mass index with hypertension risk: a prospective cohort study. *BMC Public Health*. 2024;24(1):2652. <https://doi.org/10.1186/s12889-024-20154-z> PMID:39334211 PMCID:PMC11438062
41. Hall JE, do Carmo JM, da Silva AA, Wang Z, Hall ME. Obesity-induced hypertension: interaction of neurohumoral and renal mechanisms. *Circulation research*. 2015;116(6):991-1006. <https://doi.org/10.1161/CIRCRESAHA.116.305697> PMID:25767285
42. Fang Z, Huang T, Zhang Q, Shi L, Huang R. The impact of depression on mortality among older adult patients with hypertension: a systematic review and meta-analysis. *Frontiers in Public Health*. 2025;13:1603785. <https://doi.org/10.3389/fpubh.2025.1603785> PMID:40823226 PMCID:PMC12350467
43. Satapathy P, Gaidhane AM, Vadia N, Menon SV, Chennakesavulu K, Panigrahi R, et al. Association Between Depression and Risk of Hypertension: A Systematic Review and Meta-Analysis. *Brain and Behavior*. 2025;15(9):e70931. <https://doi.org/10.1002/brb3.70931> PMID:40999622
44. Hosseini SR, Amini N, Bijani A, Ghadimi R, Ahangari N, Faramarzi M. Trends in Depressive Symptoms and the Factors Affecting Them in Older Adults: A Prospective Cohort Study. *Iranian Journal of Ageing*. 2025;20(3):422-37. <https://doi.org/10.32598/sija.2024.3919.1>
45. Selejan O, Muresanu D. The 17th International Summer School of Neurology. *International Summer School of Neurology*; July 8-10, 2022; Hybrid Event.
46. Zhang X, Yang Y, Jiang Y-S. Triglyceride-Glucose Index as a Novel Biomarker for Major Adverse Cardiovascular Events. *Angiology*. 2025;76(6):602-3. <https://doi.org/10.1177/00033197241231150> PMID:38296264
47. Welty FK, Alfaddagh A, Elajami TK. Targeting inflammation in metabolic syndrome. *Translational research*. 2016;167(1):257-80. <https://doi.org/10.1016/j.trsl.2015.06.017> PMID:26207884 PMCID:PMC6800061
48. McNaughton CD, Kripalani S, Cawthon C, Mion LC, Wallston KA, Roumie CL. Association of health literacy with elevated blood pressure: a cohort study of hospitalized patients. *Medical care*. 2014;52(4):346-53. <https://doi.org/10.1097/MLR.000000000000101> PMID:24556896 PMCID:PMC4031281
49. Azarbad A, Aghnia T, Gharibzadeh A, Rafati S, Hashemi SM, Zarei H, et al. Cut-off points for anthropometric indices to screen for hypertension among Iranian adults of the Bandare-Kong cohort: a cross-sectional study. *BMC Public Health*. 2022;22(1):2064. <https://doi.org/10.1186/s12889-022-14489-8> PMID:36369024 PMCID:PMC9652962