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Original Article

Bayesian Spatio-Temporal Modeling of Hyperlipidemia Risk in IRAN; A Repeated Cross-Sectional Analysis

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ABSTRACT

Introduction: The incidence of hyperlipidemia in Iran is on a consistent rise, potentially contributing significantly to increased susceptibility to cardiovascular diseases and other health complications linked to elevated blood lipid levels. This study employs hierarchical Bayesian model to assess the heightened lipid risk on a broader scale across Iran's provinces.

Methods: This study included individuals diagnosed with hyperlipidemia from all provinces of Iran in 2019. The primary focus of the investigation included essential variables such as the mean age, gender distribution, and the documented incidence of hyperlipidemia cases in each province. Population data, stratified by province, age group, and gender, were sourced from the Iranian Statistics Center database. The analysis employed the Besag-York-Mollié (BYM) model, with parameter estimation executed through the Hamiltonian Monte Carlo method.

Results: In this investigation, the prevalence and spatial distribution of hyperlipidemia were explored within a diverse population of 1,609,538 patients across various regions in Iran. The relative risk of hyperlipidemia surpassed 1 in 16% of Iranian provinces (Posterior probability [PP] > 0.8), with a calculated 95% Confidence interval (CI) of 0.304 to 0.879. The overall prevalence of hyperlipidemia was determined to be 0.815. Significant heterogeneity in hyperlipidemia was identified among different provinces, with Tehran exhibiting the highest relative risk (RR=1.701; 95% CrI: 1.69, 1.713). Notably, gender (RR=1.008; CI: 1.007, 1.009 for males and RR=1.005;CI: 1.003, 1.007 for females) and age were not found to have a statistically significant effect on the relative risk of the disease.

Conclusion: In conclusion, the study sheds light on the spatial dynamics of hyperlipidemia in Iran. 16% of provinces displayed a heightened relative risk, emphasizing the need for targeted public health strategies.

Introduction

According to statistics from the World Health Organization (WHO), there has been a consistent increase in non-communicable diseases worldwide. In particular, Among these, cardiovascular diseases (CVD) emerged as one of the leading causes of global mortality

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in 2008.[1] Specifically, CVD is responsible for approximately 30% of deaths worldwide,[2] and in Iran, it accounts for up to around 50% of all fatalities.[3] In Iran, the leading causes of death have shifted over time. In 1960, infectious and diarrheal diseases were predominant, but by recent decades, CVD have become the primary cause of mortality.[4] CVD-related deaths rose significantly, from 26.6% in 1981 to 47.3% in 1995.[5] Reports from the Global Burden of Disease (GBD) study for the years 2010 and 2015 indicate that CVD has consistently been the top cause of both mortality and disability-adjusted life years (DALYs) in Iran, accounting for 48% of all deaths and contributing to 20-23% of the overall disease burden.[6] The GBD 2015 data highlights that Iran, with over 9,000 cases of CVD per 100,000 people, ranks among the countries with the highest prevalence of cardiovascular disease globally.[7] This alarming trend highlights the growing impact of non-communicable diseases on public health. The escalating prevalence of non-communicable diseases, including CVD, has become a significant global public health concern, contributing to a substantial number of deaths both globally and in Iran.[8]

In relation to CVD, hyperlipidemia, a widespread condition affecting over 1 billion people globally, is associated with cardiovascular and secondary diseases.[9] The condition significantly raises the risk of cardiovascular diseases, such as coronary artery disease and stroke, as well as secondary diseases like fatty liver disease and type 2 diabetes.[10,11] Clinically, hyperlipidemia contributes to the development and progression of atherosclerosis, which can lead to life-threatening events such as myocardial infarction and stroke. This condition not only shortens life expectancy but also severely impacts the quality of life due to chronic health issues and the need for continuous medical management.[12] Socially, hyperlipidemia places a heavy burden on healthcare systems through increased healthcare costs associated with long-term treatments, hospitalizations, and lost productivity.[13] The prevalence of hyperlipidemia is also linked to lifestyle factors such as poor diet, lack of physical activity, and increasing rates of obesity, making it a critical target for public health interventions aimed at reducing the overall burden of cardiovascular diseases.[14]

Recent studies highlight that hyperlipidemia in Iran significantly exceeds global standards.[15] This surge in prevalence, which is common in both developed and developing nations, exhibits regional variations within Iran,[15,16] particularly higher rates in urban areas compared to rural regions.[17] The overall hyperlipidemia prevalence in Iran was estimated at 49.2% in 2018, affecting 12.4% of women and 23.9% of men with hypercholesterolemia.[18] However, there is a lack of comprehensive information on the spatial distribution of hyperlipidemia within the country despite its high prevalence.

Employing Bayesian methods in epidemiological research, specifically hierarchical Bayesian modeling, enhances comprehension of unobserved variables and disparities in relevant areas.[19] These methods, known for handling complex data and providing strong predictive power, address uncertainty effectively.[20] By accommodating the hierarchical structure of data and incorporating prior knowledge, hierarchical Bayesian modeling proves valuable in epidemiology for examining disease spatial patterns and identifying high-risk areas.[21] This approach allows researchers to gain deeper insights into the mechanisms driving disease patterns, facilitating the development of more precise and effective strategies for disease prevention and control.[19]

In recent years, studies have explored the spatial patterns of relative risk of hyperlipidemia in various regions across the globe.[22–25] In one study, hierarchical Bayesian models were employed to assess the spatial distribution of infectious diseases such as malaria, providing detailed maps of transmission risk areas essential for targeted intervention strategies.[26] In another example, Bayesian methods were utilized in cancer epidemiology to estimate the incidence of rare cancers, where traditional methods might fail due to small sample sizes.[27] Moreover, Bayesian approaches have been applied in longitudinal studies to model the progression of chronic diseases like diabetes, allowing for the incorporation of individual patient histories and varying follow-up times into the analysis.[28]

Understanding the spatial distribution of hyperlipidemia is crucial for health policy and disease prevention, as it allows policymakers to identify high-risk areas and allocate resources more effectively. By pinpointing regions with elevated risks, targeted interventions can be designed to reduce the burden of hyperlipidemia, ultimately contributing to better cardiovascular health outcomes at a population level. Building on these studies, the objective of this study is to employ hierarchical Bayesian models to examine the spatial pattern of relative risk of hyperlipidemia in different provinces of Iran.

Methods

Study design

In 2019, a comprehensive cross-sectional study investigated hyperlipidemia cases in Iran's 31 provinces. Data, following International Classification of Diseases criteria, compiled reports from health centers, establishing a national database. The study, focused on individuals aged 50years or older, aimed to determine disease prevalence using a representative sample. It explored regional variations and disparities among provinces, utilizing comprehensive data from health organizations.

Study measurements

The study utilized the national database to measure confirmed hyperlipidemia cases in individuals aged 50 and above, considering both genders. Population data, disaggregated by province, age group, gender, and year, were obtained from the Iran Statistics Center. Covariates, including age and gender, were incorporated in the models to evaluate their impact on hyperlipidemia's RR. Hyperparameters were estimated using the Hamiltonian Monte Carlo (HMC) method, an efficient Markov Chain Monte Carlo (MCMC) algorithm for high-dimensional probability distributions.

Statistical analysis

To measure the risk of hyperlipidemia prevalence, we employed the method of Relative Risk (RR) estimation. Within the framework of a hierarchical model for RR estimation, we incorporated a random term and the logarithm of the anticipated number of hyperlipidemia cases in each province as an offset. Let yi represent the recorded number of hyperlipidemia cases in province i, and let x denote the hyperlipidemia rate in the year under study. Here, y_i is the observed count of cases, directly obtained from the health records of each province. The rate x is derived by dividing the total number of hyperlipidemia cases by the total population under study in that year. The calculation of the expected age and sex related prevalence rate of hyperlipidemia (E_i) takes into careful consideration the population at risk (R_i) as follows:

$$E_i = XR_i \quad , \quad X = \frac{\sum_i y_i}{\sum_i R_i}$$

The standardized ratio of y_i (hyperlipidemia cases) to E_i serves as the maximum likelihood estimator for the relative risk associated with the specific area.[29] This ratio, also known as the standardized incidence ratio (SIR), provides an estimate of the relative risk by comparing the observed cases to what would be expected under standard conditions. The hyperlipidemia observations were modeled using conditional-independent Poisson random variables in a general linear model with a logarithmic link function. Statistical significance was assessed by examining the 95% CI of the RR, ensuring it excludes 1.[30]

For risk estimation, we employed the conditional autoregressive (CAR) model proposed by BYM and extended forms of the BYM models. This model enable spatial smoothing and account for both spatial dependence and non-spatial heterogeneity.[20]

The Poisson model, commonly applied in count data analysis, encounters spatial autocorrelation issues, resulting in excessive dispersion. To remedy this, the BYM model is utilized. This model posits that disease risk in each province consists of two components: a spatially structured element, capturing smooth risk variation across provinces, and a spatially unstructured element, addressing random risk variation within provinces. BYM effectively addresses spatial dependence in count data, acknowledging the influence of neighboring regions on a region's risk.[31] To assess the relative risk (RR, denoted as ηi) by province (i), the BYM model employed a composite of spatial components ([CAR] θ_i) along with random effects components accounting for non-spatial heterogeneity (φ_i):[32]

$$\eta i = \mu + x\beta + \varphi_i + \theta_i$$

This model represents the number of hyperlipidemia cases in each province using a Poisson distribution, with the expected number of cases calculated based on the population ratio of each province to the total population and the total number of observed cases. Additionally, the model incorporates the average age and gender of hyperlipidemia cases in each province as covariates.

The BYM model's hyperparameters were estimated via the HMC method, an efficient algorithm for high-dimensional probability distribution sampling. The PP gauged space-time interaction and spatial patterns, with values nearing 1 indicating instability. This method facilitated a thorough analysis.[33] Posterior hyperparameter distribution determined hyperlipidemia relative risk in each province, with values above 1 signifying elevated risk compared to the national average. The analyses were performed using the rstan package in R (version 4.1.3) and OpenBUGS (version 3.2.3). Finally, the results were visualized in ArcGIS software (version 10.7.1).

Ethics Statement

This study was reviewed and approved by Zanjan University of Medical Sciences (Ethic No. IR.ZUMS.REC.1401.161). However, we used aggregate data without individual identifiers.

Results

Table 1 presents the distribution of 1,609,538 patients based on study variables, encompassing both genders across diverse Iranian regions. Results indicate 51.16% males and 48.84% females, with a mean hyperlipidemia patient age of 62.6 years. The overall hyperlipidemia prevalence is 0.815. Table 2 details province-wise hyperlipidemia prevalence, revealing Ilam's lowest incidence at 0.01% (218 cases) and Tehran's highest at 4.77% (76,815 cases).

Table1 . Demographic characteristics in patients diagnosed with hyperlipidemia

Variable		Number	Percentage
Age at diagnosis			
	50-54	36586	2.27
	55-59	38254	2.38
	60-64	34924	2.17
	65-69	15742	0.98
	70+	101148	6.29
Gender			
	Female	786080	48.8
	Male	823458	51.2

Overall Relative risk

Figure 1 depicts the provincial-level risk of hyperlipidemia. High-risk regions are highlighted in red, low-risk areas in green, and regions with a relative risk between 0.5 and 1 are shown in yellow based on the BYM model estimation. The risk of hyperlipidemia exceeded the national mean risk in 16% of the provinces with a posterior probability greater than 0.8. Specifically, higher risk estimates were observed for the following provinces: Fars (RR = 1.19; 95% CrI: 1.173, 1.209), Isfahan (RR = 1.215; 95% CrI: 1.198, 1.232), Khuzestan (RR = 1.438; 95% CrI: 1.416, 1.459), Khorasan Razavi (RR = 1.435; 95% CrI: 1.417, 1.452), and Tehran (RR = 1.701; 95% CrI: 1.69, 1.713).

Table 3 presents the results of the BYM model for 60,000 samples after the initial tuning period. This report includes the posterior mean, posterior standard deviation, Monte Carlo error, median, the shorter 2.5th percentile, the higher 97.5th percentile (the last two being reported as a 95% CI), and the relative risk, calculated as an exponential of the posterior mean provided in this table. The sign (positive or negative) and magnitude of the parameters indicate the direction and size of fixed effects for regression coefficients. In this study, according to the RR value, gender and age did not have a significant effect on the prevalence of the disease. Specifically, the RR values for these variables were close to 1, indicating that any variations attributable to age or gender are not statistically significant in this context.

Spatial Risk by Gender

The study examined the cumulative incidence of hyperlipidemia in Iran in 2019, reporting 860 cases per 10,000 for men and 892 cases per 10,000 for women. The BYM model analysis revealed that the cumulative relative risks (RRs) were significantly greater than 1

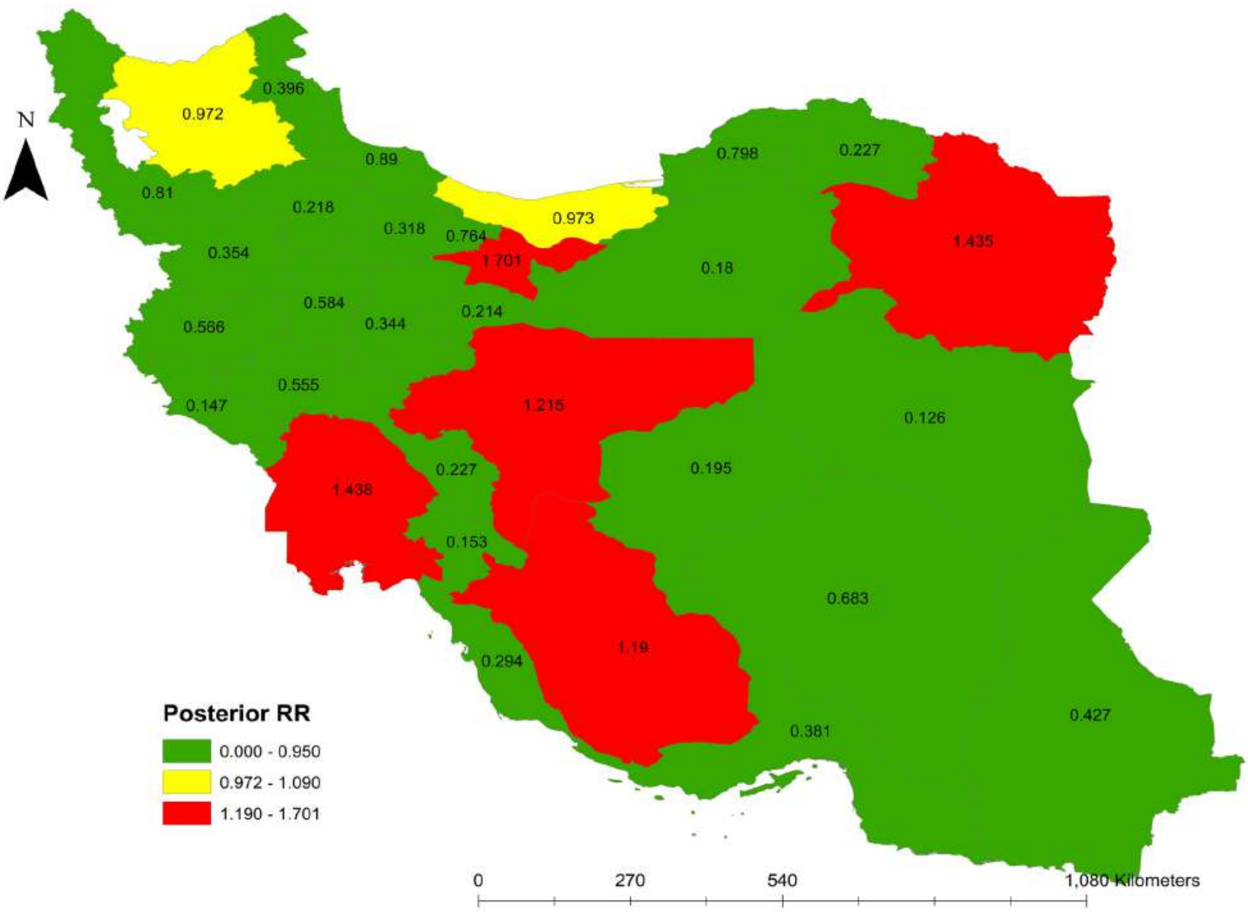

Figure 1. Fitted Incidence Ratio of hyperlipidemia in Iran

in six provinces for women (19.35%), with Tehran having the highest RR (RR=2.006; 95% CrI: 1.999, 2.013). Other provinces with high RRs were Isfahan (RR=1.321), Khuzestan (RR=1.26), Fars (RR=1.063), Gilan (RR=1.061), and Kohgiluyeh and Boyer-Ahmad (RR=1.142). Figure 2 visually represents these findings. Regarding women over 50 years old, the average incidence of hyperlipidemia was approximately 11% lower than the national average (RR=-0.1171, 95% CI: -0.25, -0.011). Similarly, for men over 50, the average incidence was about 15% lower than the national average (RR=-0.152, 95% CI: -0.296, -0.017).

The study also examined the RR of hyperlipidemia in men aged 50 years and above across different provinces in Iran. Seven provinces had significantly greater RRs than 1 for men (22.58%), with Fars (RR=1.256), East Azerbaijan (RR=1.005), Gilan (RR=1.025), Isfahan (RR=1.28), Khorasan Razavi (RR=1.385), Khuzestan (RR=1.283), and Tehran (RR=1.688) showing higher RRs. The highest RR was observed in Tehran (RR=1.688), followed by Khorasan Razavi (RR=1.385). These results are presented in Figure 3.

Table 2. Prevalence of hyperlipidemia by province

Province	Percentage	Number
Alborz	0.40	6404
Ardebil	0.09	1459
East Azarbayejan	0.76	12308
West Azarbayejan	0.46	7364
Bushehr	0.05	766
Chahar Mahaal and Bakhtiari	0.04	573
Isfahan	1.28	20543
Fars	1.07	17186
Qazvin	0.07	1158
Gilan	0.57	9115
Golestan	0.25	4106
Hamadan	0.20	3224
Hormozgan	0.08	1365
Ilam	0.01	218
Kerman	0.33	5376
Kermanshah	0.22	3495
South Khorasan	0.02	257
Khorasan-e-Razavi	1.56	25039
North Khorasan	0.03	543
Khuzestan	1.01	16278
Kohgiluyeh and Boyer-Ahmad	0.02	243
Kurdistan	0.10	1583
Lorestan	0.16	2645
Markazi	0.10	1565
Mazandaran	0.72	11664
Qom	0.04	711
Semnan	0.02	387
Sistan and Baluchistan	0.11	1838
Tehran	4.77	76815
Yazd	0.04	595
Zanjan	0.04	660

Table 3. Posterior summaries for regression coefficients

		Mean	SD	MCE	CI 2.5%	Median	CI 97.5%	Relative Risk
Intercept		0.815	0.106	0.012	0.635	0.824	1.03	-
Gender								
	Female	0.518	0.157	0.01	0.363	0.449	0.964	1.005
	Male	0.86	0.0642	0.007	0.743	0.862	0.982	1.008
Age								
	50-54	0.6	0.12	0.01	0.44	0.58	0.93	1.006
	55-59	0.64	0.13	0.01	0.43	0.65	0.97	1.006
	60-64	0.65	0.21	0.02	0.42	0.53	1.008	1.006
	65-69	0.97	0.02	0.002	0.93	0.97	1.004	1.009
	+70	0.815	0.1	0.012	0.63	0.82	1.03	1.008

SD, Standard deviation; MCE, Monte carlo error ; CI, Confidence Interval

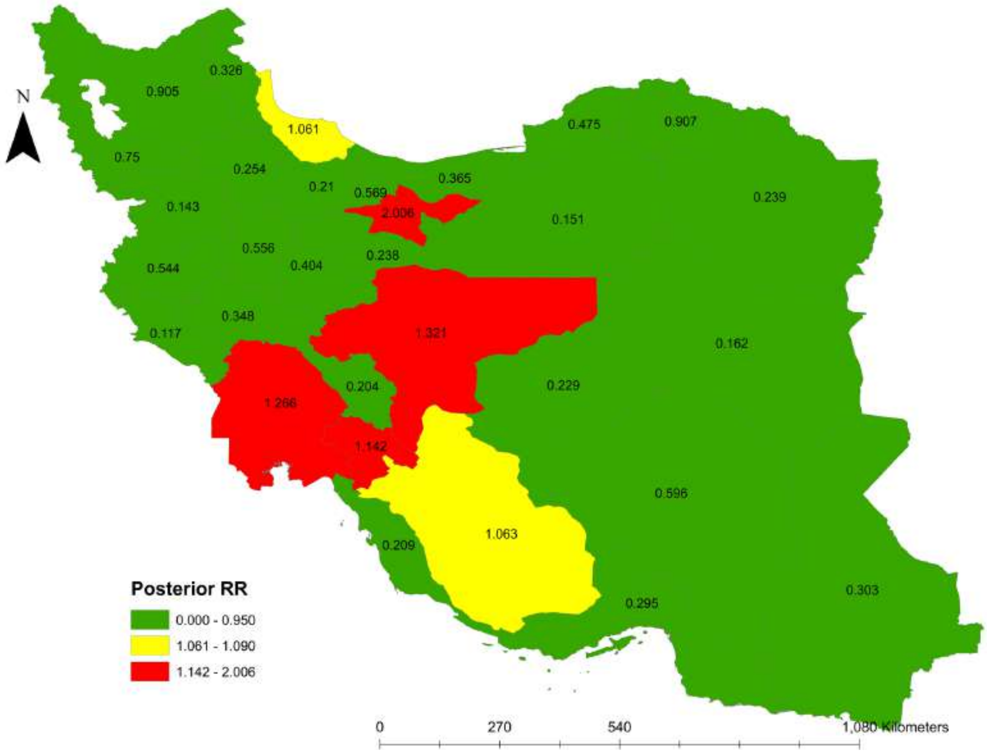

Figure 2. The incidence rate of hyperlipidemia in women

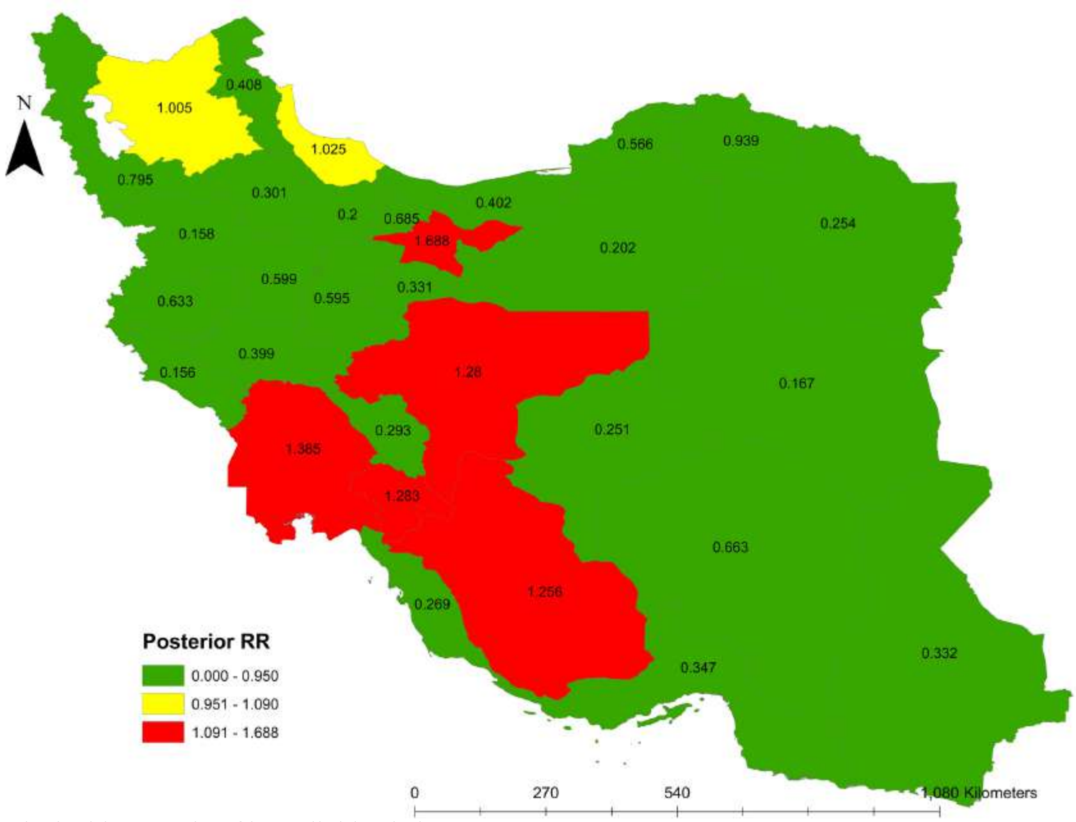

Figure 3. The incidence ratio of hyperlipidemia in men

Spatial risk by age groups

The incidence rate per 10,000 individuals for the age groups 50-54, 55-59, 60-64, 65-69, and above 70 was 606, 647, 650, 975, and 1000, respectively. According to the BYM model, the risk of hyperlipidemia was significantly less than 1 for individuals aged 50 and above. However, in 5 provinces (16.12%), the relative risk (RR) was higher than 1 for individuals aged 50-64. For individuals aged 65-69, RR was higher than 1 in 7 provinces (21.87%), and for those above 70, RR was higher than 1 in 6 provinces (19.35%). Additionally, RR was reported as 1 in 1 province (3.22%) for individuals aged 55-59. The highest risk of hyperlipidemia was observed in Tehran province across all age groups. The results have been presented in Figure 4.

For men in the age range of 65-69 years, the RR of hyperlipidemia was higher than 1 in 9 provinces (29%). Men in this age group residing in East Azarbaijan (RR= 1.287; 95% CrI: (1.18, 1.401)), Fars (RR= 1.847; 95% CrI: (1.722, 1.978)), Gilan (RR= 1.478; 95% CrI: (1.349, 1.608)), Ilam (RR= 2.078; 95% CrI: (1.702, 2.486)), Kermanshah (RR= 1.582; 95% CrI: (1.408, 1.765)), Markazi (RR= 1.314; 95% CrI: (1.127, 1.512)), Razavi Khorasan (RR= 1.877; 95% CrI: (1.752, 2.003)), South Khorasan (RR= 2.295; 95% CrI: (1.933, 2.696)), and Tehran (RR= 1.171; 95% CrI: (1.116, 1.228)) were found to be at a higher risk of hyperlipidemia compared to those in other provinces. Figure 5 provides a graphical representation of these findings.

The observed differences in RR across various provinces in Iran likely stem from

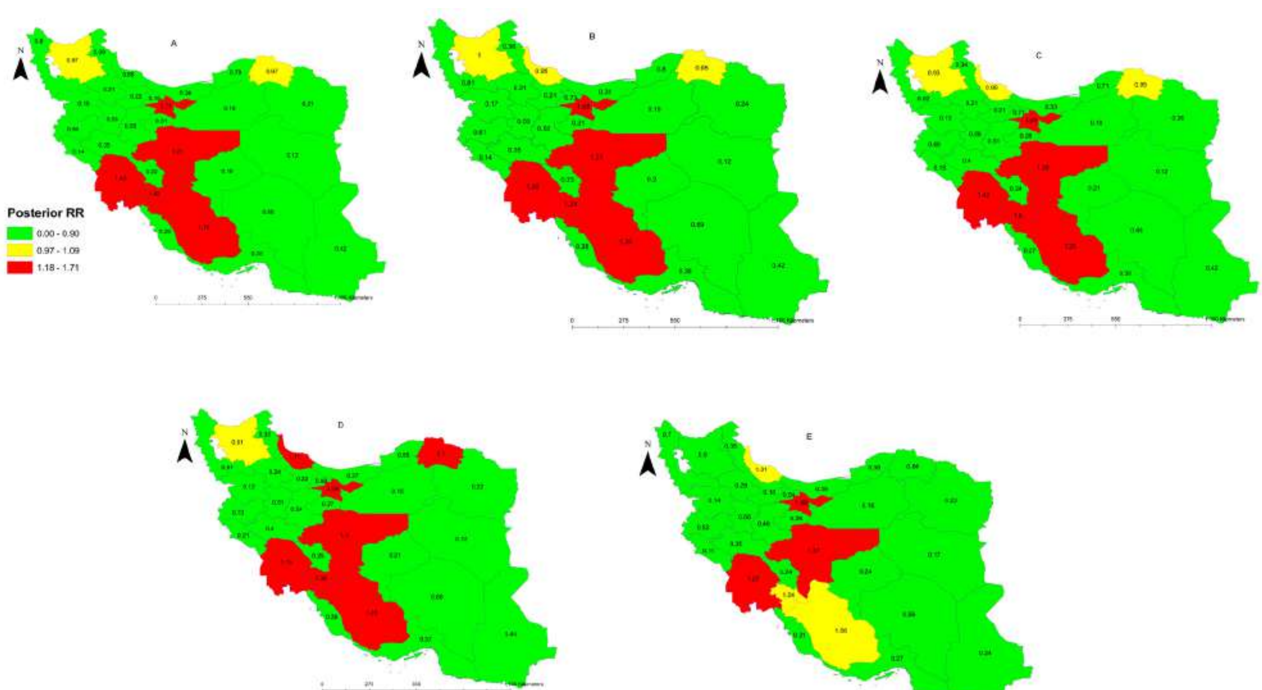

Figure 4. Posterior RR of Incidence of hyperlipidemia in Iran in 2019. The provinces were classified into 3 categories based on posterior probability values (p-values). RR: relative risk; A: People in the age group of 50-54 years ; B: People in the age group of 55-59 years; C: People in the age group of 60-64 years; D: People in the age group of 65-69 years ; E: People in the age group of +70 years

a combination of socioeconomic factors, healthcare access, lifestyle, and dietary habits, which vary significantly across regions.[34] Additionally, gender differences in risk may be due to behavioral and biological factors, such as hormonal changes in women post-menopause or variations in physical activity and diet between genders. Finally, differences in RR among age groups and provinces may reflect disparities in age-related health behaviors, access to preventive healthcare, and regional socioeconomic conditions.[12,13] In urbanized provinces like Tehran, the higher RR in older adults could result from the cumulative impact of a lifelong exposure to urban lifestyles and associated risk factors.

The differences in hyperlipidemia risk between men and women across different provinces suggest the need for gender-specific health policies. For example, the higher risk in women, especially in provinces like Tehran and Isfahan, shows the importance of targeted programs, such as increasing cholesterol screenings and encouraging healthier lifestyle changes for women. On the other hand, the higher risk in men in provinces like Fars and Khorasan Razavi highlights the need for prevention programs that focus on men's health. These findings can help policymakers allocate resources more effectively and create programs that address the specific needs of each gender.

Discussion

This study examined hyperlipidemia

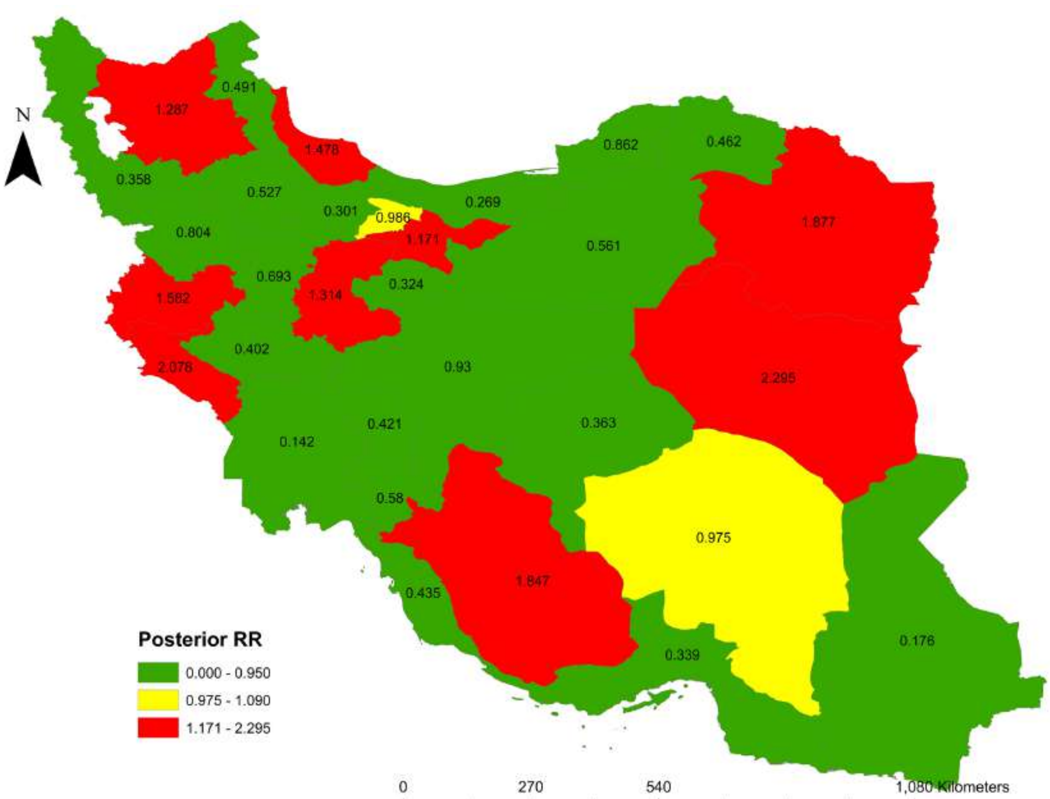

Figure 5. The incidence ratio of hyperlipidemia in men in the age range of 65-69

prevalence in individuals aged 50 and above, with a focus on a dataset of 1,609,538 patients in Iran. Utilizing the BYM model, it identified the highest prevalence in men aged 65-69. The research revealed a 16% elevation in hyperlipidemia risk across certain provinces (RR 1.19-1.70), with Tehran exhibiting the highest RR (1.701). The highest RR was observed in Tehran (RR, 1.701).

Tabatabaei et al. reported that high LDL-C and low HDL-C levels were more prevalent in women, while hypertriglyceridemia was more common in men. Our results align with these findings in terms of gender differences in lipid profiles.[17] Our findings are consistent with those of Khanali et al. (2023), who reported significant geographical variation in dyslipidemia prevalence across Iran. Both studies highlight a higher prevalence of hyperlipidemia in urban areas and certain provinces.[35] Hmwe H Kyu et al. (2020) demonstrated a positive correlation between population growth and the prevalence of non-communicable diseases, including hyperlipidemia, which is consistent with our study.[36] The earlier investigations have also explored the incidence and distribution of hyperlipidemia in Iran. For instance, Sarrafzadegan et al. (2016) found that 54.7% of adults aged 25 and above in Isfahan had hyperlipidemia, with a higher prevalence among women and an increase with age. In contrast, our study, which is based on a national sample, reported a lower overall prevalence rate . This discrepancy could be due to differences in study methodologies, such as variations in sample populations, diagnostic criteria, or geographical focus.[37] Additionally, Esteghamati et al. (2017) reported a higher prevalence of hyperlipidemia among urban residents compared to rural residents in Iran.[38] Our study introduces a novel approach to understanding hyperlipidemia distribution in Iran by utilizing spatial models. The BYM model, commonly used in spatial epidemiology to analyze disease spatial variation and identify high-risk areas,[39,40] was employed in our research. Similar methodologies have been applied in recent studies investigating hyperlipidemia distribution in other countries, such as China[41] and the United States.[42] The BYM model, as seen in Asmarian et al.'s 2019 study on male breast cancer in Iran, proves effective.[43] Finally, the study concludes that population growth in Iran is likely linked to a rise in hyperlipidemia incidence. Prior research supports the positive association between population growth and non-communicable diseases, including hyperlipidemia.[44]

To address the issue of hyperlipidemia, particularly in high-risk provinces identified in our study, we suggest the following health policy measures:

1. Implement targeted screening programs in high-risk provinces to identify individuals with hyperlipidemia early and provide timely interventions.
2. Promote community-based lifestyle modification programs focusing on diet and physical activity, especially in regions with higher prevalence rates.
3. Enhance public awareness campaigns about the risks of hyperlipidemia and the benefits of regular health check-ups, particularly in high-prevalence areas.
4. Strengthen healthcare infrastructure in high-risk provinces to ensure better access to diagnostic and treatment services for hyperlipidemia.
5. Develop region-specific health policies that

consider local dietary habits, socioeconomic factors, and population demographics to effectively manage and reduce hyperlipidemia prevalence.

Given Iran's rapid population increase, these targeted measures are crucial for mitigating the rising incidence of hyperlipidemia and improving overall public health.

Strengths and limitations

The study faced limitations, including reliance on registered disease data, potentially missing undisclosed cases. It focused solely on individuals aged over 50, limiting generalizability to younger age groups. Environmental factors like lifestyle and nutrition, crucial in disease occurrence, were omitted. The study lacked detailed descriptions of additional influencing factors. The strengths of the study are quite noteworthy. The use of the BYM model, which is a sophisticated tool well-regarded for spatial data analysis, provided a significant advantage. This model's capability to identify spatial patterns and variations enabled a more precise evaluation of hyperlipidemia risk across different geographical areas. By employing this model, the study effectively pinpointed high-risk regions, which is essential for targeted public health interventions. Additionally, the study utilized a comprehensive dataset that covered all Iranian provinces for individuals aged over 50. This extensive coverage not only improved the accuracy of the results but also offered valuable insights into the spatial distribution of hyperlipidemia risk across various genders, provinces, and age groups.

In summary, this study offers valuable recommendations for future research. Firstly, exploring the economic and social determinants of hyperlipidemia in Iran is crucial. Investigating factors influencing hyperlipidemia across provinces can enhance disease recognition and management nationally. Comparative studies with other countries are essential. Additionally, understanding the relationship between hyperlipidemia and cardiovascular diseases is vital for prevention and treatment improvement. Lastly, further research on the efficacy of diverse hyperlipidemia treatment methods is needed to develop better approaches and deepen our understanding of treatment strategies.

Conclusion

This study provides crucial insights into hyperlipidemia prevalence and distribution in Iranians aged 50 and above. Significant regional variations were observed, emphasizing the need for targeted prevention and management strategies. The utilization of the BYM model proves valuable in identifying high-risk areas and devising precise interventions. Ultimately, controlling and preventing hyperlipidemia is essential for reducing the burden of cardiovascular diseases and improving overall public health. Effective management of hyperlipidemia not only enhances individual health outcomes but also contributes to the broader goal of minimizing healthcare costs and promoting well-being across communities.

Declarations

Consent for publication

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Not applicable.'

Competing interests

The authors declare that there is no conflict of interest.

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Authors' contributions

All authors read and approved the final manuscript. SHA, SHAJ and KM participated in the data analysis and manuscript preparation.

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