

Epidemiological Profile and Projections of Incidence and Mortality of Ischemic Heart Disease in Nepal: An Analysis of the Global Burden of Disease Study 2021

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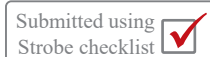
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Abstract

Background and Aim: Ischemic heart disease (IHD) is a leading global cause of disability and mortality, yet systematic epidemiological analyses in Nepal remain scarce. This study aimed to analyze trends in IHD incidence and mortality in Nepal and project future burdens to inform evidence-based interventions.

Methods: Data from the Global Burden of Disease Study 2021 were analyzed. Joinpoint regression identified trends in age-standardized incidence (ASIR) and mortality rates (ASMR), calculating the annual percent change (APC) and the average annual percent change (AAPC). Age-period-cohort (APC) models disentangled age, period, and cohort effects, while Bayesian APC models projected trends from 2022 to 2036. Risk factors were assessed via attributable mortality analysis.

Results: From 1990 to 2021, Nepal experienced an increase in IHD incident cases from 49,265 to 116,482, with males consistently having higher ASIR than females. Recent trends (2015-2021) showed rising ASIR in both males and females, contrasting with global declines. ASMR declined in females (AAPC=-0.74%) but increased in males (AAPC=0.32%). Age effects revealed a steep increase in risk from 40-44 years, peaking at 7420.64/100,000 in the 95+ age group. Notably, post-2007 birth cohorts showed a resurgent IHD incidence risk, representing an emerging threat to younger populations. Projections forecast ASIR rising to 466/100,000 (females) and 726/100,000 (males) by 2036, with male ASMR projected to increase to 260/100,000. For males, high systolic blood pressure; for females, solid fuel pollution were primary sex-specific IHD risk factors.

Conclusion: Nepal's IHD burden exhibits gender and age disparities, including a paradoxical rise in male mortality and resurgent risks in younger populations. Stratified intervention strategies are required, targeting gender-specific risks (hypertension management and tobacco control for males; clean fuel promotion and smoke-control cooking appliances for females) and age-specific needs (geriatric monitoring and intervention in primary healthcare and early health education for youth), alongside modifiable risk factors.

Key words: Ischemic heart disease; Global burden of diseases; Nepal; Incidence; Mortality; Disease Burden Projection; Risk Factors

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Introduction

"Ischemic heart disease (IHD), also known as coronary artery disease (CAD), is one of the major manifestations of atherosclerotic cardiovascular disease (ASCVD).¹ As one of the primary contributors to cardiovascular disease burden, IHD is the leading cause of death in developing countries.² In 2021, IHD was the second leading cause of global disability-adjusted life years (DALYs), accounting for 188 million (95% UI 177-198), a 58.1% (49.5-66.6) increase from 1990.³ Concurrently, IHD caused 8.99 million (95%UI:8.29-9.55) deaths worldwide in 2021, underscoring the urgency of addressing its escalating health impact.

Nepal, a representative low- and middle-income South Asian country, is undergoing rapid epidemiological transition—consistent with regional trends—with a shift from communicable diseases to non-communicable diseases (NCDs) driven by urbanization and lifestyle transformations: increased intake of high-salt, high-fat diets, reduced physical activity among urban residents, and persistent tobacco use (especially among males).⁴ These shifts have directly fueled the proliferation of IHD risk factors (e.g., hypertension, obesity) in Nepal, compounding the dual challenges of growing risk factor prevalence and limited healthcare resources for NCD management.

This study analyzes data from the Global Burden of Disease (GBD) 2021 database to investigate the current epidemiology and project future trends of IHD incidence and mortality in Nepal. It aims to fill regional data gaps and inform evidence-based prevention and control strategies.

Methods

Data collection

The data used in this study were sourced from the Global Burden of Diseases, Injuries, and Risk Factors Study 2021 database. This database systematically quantifies the health losses of 371 diseases and 88 risk factors in 204 countries and regions worldwide from 1990 to 2021.⁵ We extracted the incidence number, crude incidence rate, and age-standardized incidence rate (ASIR) of ischemic heart disease in Nepal from 1990 to 2021, as well as the death number, crude mortality rate, and age-standardized mortality rate (ASMR) of ischemic heart disease in Nepal from 1980 to 2021. The research data are publicly available through the Global Health Data Exchange (GHDx, <http://ghdx.healthdata.org/gbd-2021>). In accordance with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER), this study exclusively employed anonymized aggregate data without individual participant involvement, thereby qualifying for ethical exemption under institutional review board protocols.⁶

Trend analysis (Joinpoint)

The Joinpoint regression model (Joinpoint 5.4.0 software, National Cancer Institute [NCI], part of the National Institutes of Health [NIH]) was applied to conduct segmented trend analysis on ASIR from 1990 to 2021 and ASMR from 1980 to 2021 for IHD in Nepal, aiming to characterize long-term trend patterns and identify key inflection points in the disease burden.⁷ Based on log-linear model principles, this algorithm fits piecewise regression lines to time-series data, detects statistically significant joinpoints (transition points

where trend slopes change), and calculates both annual percent change (APC) for each segment and average annual percent change (AAPC) across the entire study period to quantify trend directionality and magnitude.⁸ Per convention, AAPC/APC values >0 indicate increasing trends in IHD incidence or mortality rates, whereas values <0 denote decreasing trends.

Age-Period-Cohort analysis

The Age-Period-Cohort (APC) model was employed to disentangle the independent effects of age, period, and birth cohort on IHD incidence and mortality risks in Nepal. In data preprocessing, the age effect required dividing age groups into 5-year intervals; since the incidence and mortality rates of IHD among Nepal's residents aged 1-14 were virtually zero, 17 age groups were selected, ranging from 15-19 years to 95+ years. For the period effect, data were grouped into 5-year intervals: incidence analysis used data from 1992 to 2021 (1990-1991 excluded, as they could not form a complete 5-year interval), and mortality analysis used data from 1982 to 2021 (1980-1981 excluded for the same interval integrity reason). Birth cohort years for the cohort effect were calculated as $cohort = period - age$.⁹ The age, period and cohort components were centered at their median values as reference groups in the model. Statistical analyses were performed using R-based tools provided by the NCI website (<https://analysistools.cancer.gov/apc/>).

Forecasting (BAPC)

A Bayesian Age-Period-Cohort Model (BAPC) was fitted using the BAPC package in R to project IHD incidence and mortality trends from 2022 to 2036.¹⁰ The input data were structured using the APCList function, combining case counts and population data stratified by 5-year age groups and calendar years, with a period grouping factor of 5 years. The model was configured to predict 15 years forward ($n_{predict} = 15$) with retrospective fitting enabled ($retro = TRUE$). First-order random walks were specified for the age, period, and cohort effects ($secondDiff = FALSE$). Age-standardization was performed using standard population weights derived from the GBD standard population structure. The model utilized the Integrated Nested Laplace Approximation (INLA) algorithm for Bayesian inference, with verbose output disabled ($verbose = FALSE$).

Results

Description of IHD incidence and mortality in Nepal

From 1990 to 2021, the annual number of incident cases of IHD in Nepal showed an overall upward trend. In 2021, Nepal reported 116,482 (95% UI: 97,300 - 143,067) incident cases of IHD. Among these, 69,555 (95% UI: 58,458 - 84,267) occurred in males and 46,927 (95% UI: 37,930 - 58,013) in females. The ASIR of IHD demonstrated a fluctuating upward trend in the overall population, males, and females. In 2021, the ASIR of IHD for the overall population, males, and females were 511.87, 646.45, and 393.26 per 100,000, respectively. Whether in terms of the number of incident cases or ASIR, the values for males were higher than those for females (Figure 1a).

Between 1980 and 2021, the annual number of deaths from IHD in Nepal showed an overall upward trend. In 2021, the number of IHD deaths in Nepal was 27,632 (95% UI: 22,535 - 34,206), including

17,245 (95% UI: 13,386 - 21,635) cases in males and 10,388 (95% UI: 7,669 - 14,458) cases in females. The ASMR of IHD showed a fluctuating downward trend in the overall population and females, while exhibiting a fluctuating upward trend in males. In 2021, the ASMR of IHD for the overall population, females, and males were 137, 98, and 181 per 100,000, respectively. Whether in terms of the number of deaths or ASMR, males had higher values than females (Figure 1b).

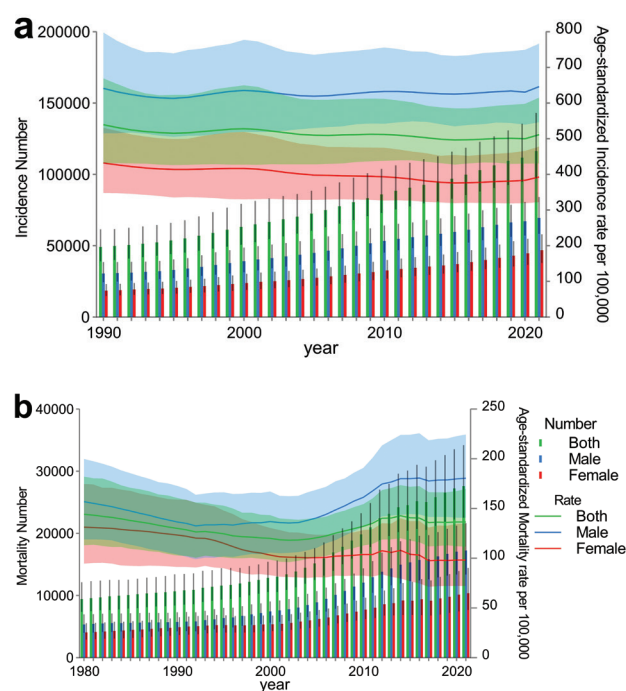


Figure 1a-b: (a) Comparison of incident cases and ASIR in Nepal's overall population, males, and females from 1990 to 2021; (b) Comparison of deaths and ASMR in Nepal's overall population, males, and females from 1980 to 2021.

Joinpoint analysis of IHD incidence and mortality in Nepal

The results of Joinpoint regression analysis showed that from 1990 to 2021, the ASIR of IHD in Nepal decreased at AAPC of -0.2% for the overall population and -0.31% for females, with no significant change in males. However, in recent periods, upward trends were observed in the overall population, females, and males: overall population exhibited an APC of 0.35% (95% CI: 0.17% to 0.52%) from 2015 to 2021; females showed APC of 0.36% (95% CI: 0.25% to 0.47%) from 2015 to 2019 and 1.43% (95% CI: 1.2% to 1.66%) from 2019 to 2021; and males had an APC of 0.41% (95% CI: 0.22% to 0.59%) from 2015 to 2021 (Figure 2a).

For ASMR from 1980 to 2021, declines were observed at AAPC of -0.15% (95% CI: -0.27% to -0.03%) for the overall population and -0.74% (95% CI: -0.92% to -0.55%) for females. In contrast, males experienced a 0.32% increase, the highest APC of mortality occurred during 2004 - 2009 (APC=2.75% , 95% CI: 2.37% to 3.13%) and 2009–2013 (APC=3.32% , 95% CI: 2.73% to 3.92%) (Figure 2b).

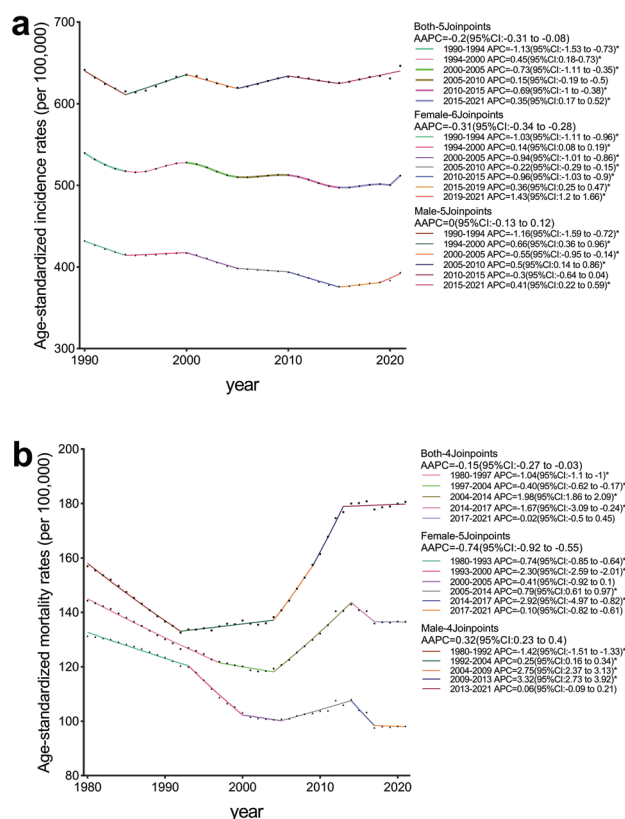


Figure 2a-b: (a) Trends in the ASIR of IHD among the overall population, males, and females in Nepal from 1990 to 2021; (b) Trends in the ASMR of IHD among the overall population, males, and females in Nepal from 1980 to 2021.

Age-period-cohort effects on IHD incidence and mortality

Figure 3a,b,c shows the age-period-cohort effects on the incidence of IHD. The age effect analysis indicated that incidence of IHD began to increase at 15-19 years of age, peaked at 95+ years with a rate of 7420.64 per 100,000.

For the period effect, the relative risk (RR) of IHD incidence remained close to 1.0 across all intervals: decreasing from 1.02 (95% CI: 0.93-1.12) during 1992-1996 to 0.97 (95% CI: 0.88-1.07) during 2012-2016, then slightly increasing to 0.98 (95% CI: 0.845-1.13) during 2017-2021. This stability suggests that macro-level factors—such as national public health policies or economic development—exerted minimal short-term influence on IHD incidence trends in Nepal over the past three decades.

The birth cohort analysis revealed that from 1992 to 2021, the incidence risk of IHD in Nepal followed a trend of first increasing, then decreasing, and increasing again across birth cohorts. Using the 1957-1961 birth cohort as the reference (RR = 1), residents born between 1897 and 1961 had relatively higher incidence risks (all RR > 1), while those born between 1962 and 2021 had lower risks. The incidence risk declined continuously for cohorts born between 1932 and 2006 but showed an upward trend for those born between 2007 and 2021, as it signals emerging IHD threats to Nepal's young population.

Figure 3d,e,f shows the age-period-cohort effects on the mortality of IHD. The age effect analysis indicated that the mortality of IHD began to increase at 15-19 years of age, peaked at 95+ years with a rate of 4450.62 per 100,000.

For the period effect, the RR of IHD mortality decreased from 1.30 (95% CI: 1.26-1.33) during 1982-1986 to 0.98 (95% CI: 0.95-1.00) during 2002-2006, followed by a clear upward trend—all RR > 1 from 2007 to 2021. This upward mortality period effect aligns with the Joinpoint analysis results for males (APC = 2.75% during 2004-2009 and 3.32% during 2009-2013), highlighting a critical worsening of male IHD mortality burden in recent years.

The birth cohort analysis revealed that from 1982 to 2021, the mortality risk of IHD in Nepal followed a trend of first increasing then decreasing across birth cohorts. Using the 1957-1961 birth cohort as the reference (RR = 1), residents born between 1917 and 1941 had relatively higher incidence risks (all RR > 1), while those born between 1942 and 2006 experienced a continuous decline in mortality risk (all RR < 1).

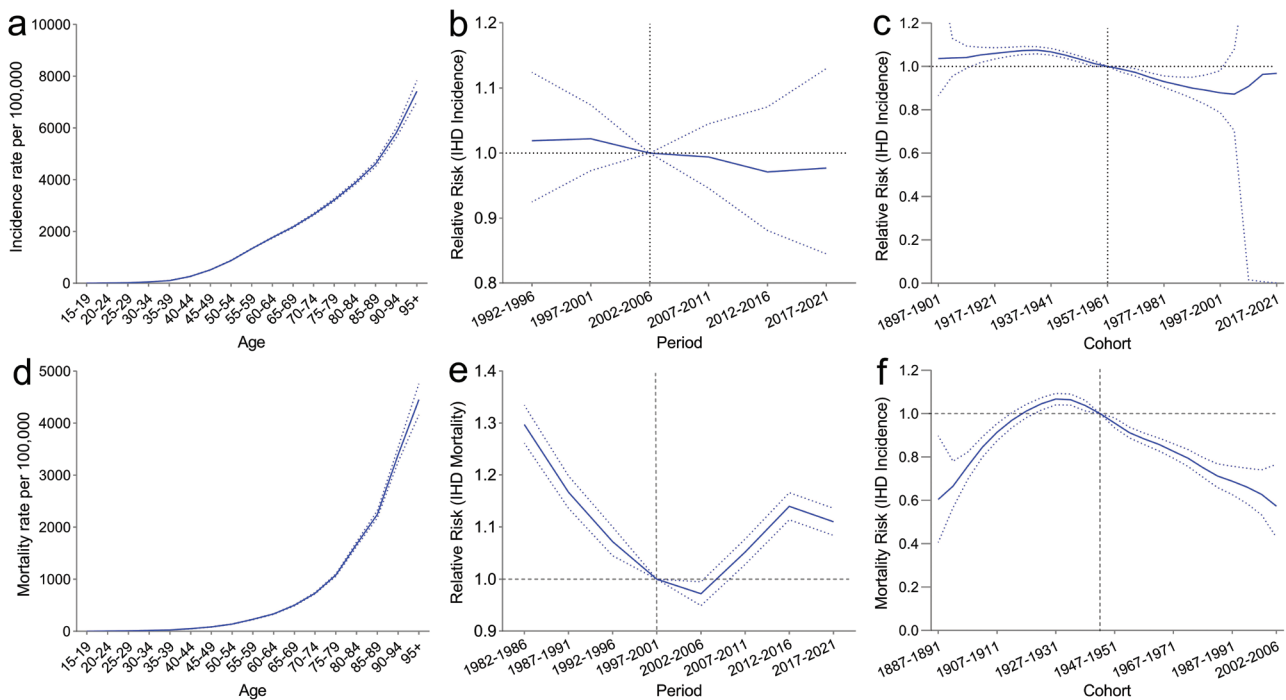


Figure 3a-f: Age, period and cohort effects on IHD incidence and mortality in Nepal. (a-c) Incidence; (d-f) Mortality.

Projections of IHD incidence and mortality, 2022–2036

According to the projections, the ASIR of IHD among the overall population, males, and females in Nepal are projected to show upward trends from 2022 to 2036. The overall population ASIR for IHD is estimated to increase from 514 (95% UI: 505-523) per 100,000 in 2022 to 574 (95% UI: 378-770) per 100,000 in 2036; the male ASIR is projected to rise from 650 (95% UI: 637-663) per 100,000 in 2022 to 726 (95% UI: 462-990) per 100,000 in 2036; and the female ASIR is expected to increase from 396 (95% UI: 387-404) per 100,000 in 2022 to 466 (95% UI: 302-631) per 100,000 in 2036, with male ASIR consistently higher than female ASIR throughout the period.

From 2022 to 2036, ASMR for IHD are projected to decline among the overall population and females but increase among males. The overall population ASMR for IHD is forecast to decrease from 191 (95% UI: 185-196) per 100,000 in 2022 to 187 (95% UI: 92-282) per 100,000 in 2036; the female ASMR is expected to drop from 137 (95% UI: 132-141) per 100,000 in 2022 to 132 (95% UI: 54-209) per 100,000 in 2036; and the male ASMR is projected to rise from 253 (95% UI: 245-261) per 100,000 in 2022 to 260 (95% UI: 116-404) per 100,000 in 2036, with male ASMR consistently exceeding female ASMR.

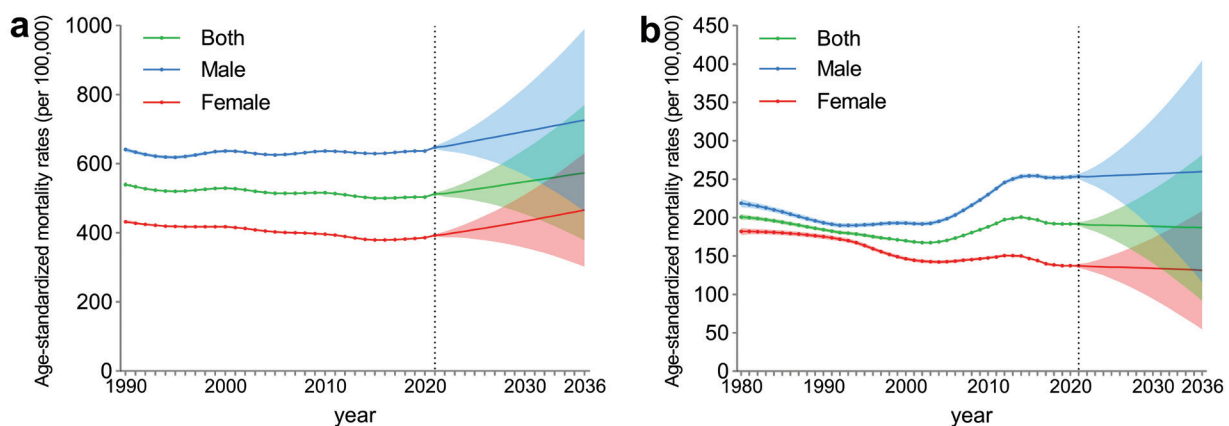


Figure 4a-b: Predicted trends in IHD incidence and mortality in Nepal over the next 15 years (2022-2036). The left side of the dashed line represents the observed trends, and the right side indicates the predicted trends. (a) ASIR; (b) ASMR.

Associated risk factors for IHD in Nepal in 2021

In 2021, the ASMR for IHD attributable to various risk factors are as follows. In males, the ASMR for IHD attributed to high systolic blood pressure was 78.13 per 100,000 (95% UI: 55.9-105.06), to household air pollution from solid fuels was 54.55 per 100,000 (95% UI: 37.04-76.97), to high LDL cholesterol was 45.16 per 100,000 (95% UI: 27.76-65.23), to smoking was 38.46 per 100,000 (95% UI: 28.09-50.99), to kidney dysfunction was 37.37 per 100,000 (95% UI: 25.6-51.87), to high fasting plasma glucose was 30.04 per 100,000 (95% UI: 23.17-38.86), and to ambient particulate matter pollution was 25.17 per 100,000 (95% UI: 14.31-39.27). In females, the ASMR for IHD attributed to household air pollution from solid fuels was 33.4 per 100,000 (95% UI: 21.98-46.97), to high systolic blood pressure was 29.31 per 100,000 (95% UI: 17.77-46.46), to high LDL cholesterol was 25.29 per 100,000 (95% UI: 14.83-38.97), to kidney dysfunction was 21.57 per 100,000 (95% UI: 13.96-32.26), to high fasting plasma glucose was 15.05 per 100,000 (95% UI: 10.48-20.22), and to diet low in seafood omega-3 fatty acids was 14.01 per 100,000 (95% UI: 2.93-24.86).

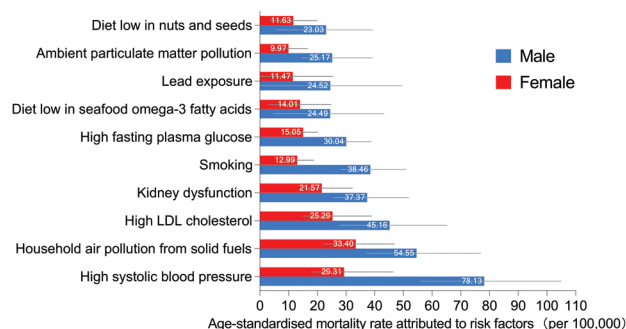


Figure 5: Rankings of risk factors for IHD ASMR by sex in Nepal, 2021.

Discussion

This study comprehensively analyzed the epidemiological trends and future projections of IHD in Nepal using data from the GBD 2021 study. The results demonstrate that as a representative South Asian developing nation, Nepal experienced an increase in IHD incident cases from 49,265 in 1990 to 116,482 in 2021, with a significantly higher ASIR in males (646.45 per 100,000 population) compared to females (393.26 per 100,000 population). These findings align with the 2017 GBD-based study by Sanju Bhattarai et al, consistently indicating elevated disease risks among males.¹¹ However, our study extends prior work in three key ways: first, we used the latest GBD 2021 data (vs. GBD 2017) to capture post-2017 trends, including the potential impact of Nepal's recent urbanization; second, we employed Bayesian APC modeling to project 2022–2036 burdens; third, we quantified gender-specific risk factor attribution. During recent years (2015-2021), the ASIR for all sexes have shown an upward trend, contrasting with the global decline in IHD incidence, which reflects the continuously escalating disease burden in low Socio-Demographic Index (SDI) regions due to inadequate risk factor control and scarce

healthcare resources.¹ The ASMR fluctuated downward in the overall population and females (AAPC of -0.15% and -0.74%, respectively), while the male ASMR increased at an annual rate of 0.32%. In 2021, the male ASMR (181 per 100,000) was 1.85-fold higher than that in females (98 per 100,000).

Age effect analysis indicated that the risk of IHD started to increase rapidly from the age of 40–44, and the incidence rate in the 95+ age group reached 7420.64 per 100,000, which is consistent with the pattern of the increasing risk of cardiovascular diseases with age in the context of global aging, suggesting that the elderly population is the core target for prevention and control.¹² Birth cohort analysis warns that although the risk of disease in the population born between 1932 and 2006 has decreased, the risk in the birth cohort born between 2007 and 2021 has rebounded. This resurgence indicates that Nepal's younger generation is facing new IHD threats due to exposure to modern lifestyles (e.g., high-sugar/high-fat diets, sedentary behavior, and increased stress) amid rapid urbanization, underscoring the urgency of early-life health interventions.^{13,14}

Predictions of the incidence and mortality of IHD in the Nepalese population from 2022 to 2036 were conducted using a Bayesian age-period-cohort model. The results showed that by 2036, the ASIR will continue to rise for both sexes, while the male ASMR is projected to further increase to 260 per 100,000, highlighting the urgency of prevention and control measures.

Risk factor analysis revealed that high systolic blood pressure, household air pollution from solid fuels, high LDL cholesterol were the primary drivers of IHD in Nepal. In 2021, the ASMR attributable to high systolic blood pressure in males reached 78.13 per 100,000,¹⁵ whereas females bore a higher health burden due to solid fuel pollution, reflecting gender-specific exposure patterns—males being more affected by hypertension and females being exposed to air pollution through household environments.^{16,17,18}

From a policy intervention perspective, IHD prevention and control in Nepal must transcend single-factor models and shift toward stratified, precision-based strategies. This shift is critical given Nepal's well-documented health system gaps, including uneven health resource allocation, limited primary cardiovascular disease (CVD) service coverage (only 71% of public facilities offer CVD care), and inadequate integration of CVD management into primary health networks. Notably, such stratified strategies not only address these gaps but also align with optimizing primary health system functions for CVD management—supported by evidence on Nepal's health system constraints (e.g., health workforce shortages, rural care access barriers)—thus boosting the feasibility and contextual relevance of IHD prevention.¹⁹

For males: Strengthen community-based hypertension screening (e.g., "Men's Health Days") and tobacco control measures (e.g., increasing tobacco taxes, implementing public place smoking bans, and enforcing strict regulations on tobacco packaging and retail display of tobacco products).^{20,21}

For females: Promote clean fuel subsidy policies; simultaneously promote the adoption of smokeless cookstoves in rural areas, and the wider adoption of range hoods and exhaust fans in urban settings to reduce indoor pollution exposure.²²

For elderly populations: Incorporate elderly populations into national health plans through establishment of "one-stop" integrated chronic disease management centers at primary healthcare facilities, integrating blood pressure and blood glucose monitoring and intervention.^{23,24}

For younger generations: Address the "initial decline followed by an upward trend" in birth cohort risks through early health education in schools and communities to curb risk factor clustering, such as school-based nutrition curricula and physical activity promotion programs to prevent premature onset of disease.^{25,26}

Limitations

This study has several limitations to note. First, while GBD 2021 data provide standardized estimates, Nepal's limited rural mortality registration may introduce mild under-reporting, especially in earlier years. Second, population-level trends (e.g., urbanization and IHD risk) cannot be inferred to individuals (ecological fallacy). Third, BAPC projections assume stable future trends, which may change with large-scale public health interventions. Fourth, risk factor associations (e.g., hypertension and male IHD) do not equate to individual-level causation, as unmeasured confounders (e.g., genetics) exist.

Despite these limitations, our findings remain robust for addressing Nepal's IHD data gap: we used the latest GBD 2021 data and rigorous methods (Joinpoint/APC/BAPC), and key results (e.g., gender-specific risks, youth cohort resurgence) align with regional NCD trends, supporting their value for policy-making.

Conclusion

Using GBD 2021 data, this study reveals that IHD in Nepal is characterized by "rising incidence (2015-2021), paradoxical increase in male mortality, and concentrated risk in older populations". Ageing remains a core risk factor, with incidence peaking at 7420.64 per 100,000 in the 95+ age group, while younger generations face resurgent risks linked to modern lifestyles. High systolic blood pressure and solid fuel pollution were the primary risk factors for males and females, respectively. Projections indicate sustained increases in incidence for both sexes by 2036, and male mortality may further worsen. Nepal needs tailored strategies for gender and age disparities: hypertension management and smoking intervention for males; clean fuel adoption and innovation in improved smoke-control cooking appliances for females; strengthened primary healthcare screening and chronic disease management for older adults; and early health education targeting youth.

These findings provide evidence for gender-differentiated, life-course prevention strategies in Nepal, emphasizing the importance of prioritizing high-risk populations and modifiable risk factors under resource constraints.

Sources of Funding

None

Conflicts of interest

None

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