Burden of Ischemic Heart Disease in Central Asian Countries, 1990–2017

Michelle Lui a, Saeid Safiri b,c,d, Alibek Mereke e, Kairat Davletov e, Nana Mebonia f, Akbope Myrkassymova g, Timur Aripov h, Erkin Mirrakhimov i,j, Sargis A. Aghayan k, Amiran Gamkrelidze l, Mohsen Naghavi m, Jacek A. Kopec a, Nizal Sarrafzadegan a,n,*

a School of Population & Public Health, University of British Columbia, Vancouver, Canada
b Tuberculosis and Lung Disease Research Center, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
c Aging Research Institute, Tabriz University of Medical Sciences, Tabriz, Iran
d Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
e Health Research Institute, The Faculty of Medicine, Al-Farabi Kazakh National University, Almaty, Kazakhstan
f Department of Epidemiology and Biostatistics, Tbilisi State Medical University, Tbilisi, Georgia
g School of Public Health, Afterdavoyev Kazakhstan National Medical University, Almaty, Kazakhstan
h Department of Public Health and Healthcare Management, Tashkent Institute of Postgraduate Medical Education, Tashkent, Uzbekistan
i Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan
j National Center of Cardiology and Internal Disease, Bishkek, Kyrgyzstan
k Faculty of Biology, Yerevan State University, Yerevan, Armenia
l National Center for Disease Control and Public Health, Tbilisi, Georgia
m Department of Health Metrics Sciences, Institute for Health Metrics and Evaluation, School of Medicine, University of Washington, Washington, USA
n Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

Background: The burden of ischemic heart disease (IHD) is high. There is limited information on the burden of IHD in identified high risk areas like Central Asia (CA) which is comprised of Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Turkmennistan, Mongolia, Uzbekistan and Tajikistan. This study addresses the burden of IHD in CA at the regional and country levels.

Methods: Using data from the latest iteration of the Global Burden of Disease Study (GBD), this study provides age-adjusted mortality, prevalence, and Disability Adjusted Life Years (DALYs) of IHD by sex in the CA region, and national levels for countries in this region from 1990 to 2017.

Results: The CA region has a higher IHD burden than the rest of the world over the studied period. Amongst the countries within this region, age-standardized mortality and DALY rates in Uzbekistan are the highest not only in CA but worldwide, while Armenia consistently has the lowest IHD burden in CA. Unhealthy diet, high systolic blood pressure and LDL-cholesterol are the risk factors with the highest attributable IHD DALYs.

Conclusion: Increasing burden of IHD over time in CA can be partially explained by the economic crisis in the 1990s. There is considerable variation in IHD DALY rates among countries in the CA region. The reasons for such differences are likely multifactorial such as differences in risk factors distribution, health care effectiveness, political, social and economic factors.

© 2021 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Ischemic heart disease (IHD) is a major contributor to the global health burden [1–4]. However, there is limited information on the burden of IHD in identified high-risk areas at the regional or country level. In particular, there is a paucity of knowledge on the burden of IHD in Central Asia (CA) which has been identified by the Global Burden of Disease Study (GBD) to have high IHD burden [5]. According to GBD categorization, CA is comprised of Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Turkmenistan, Mongolia, Uzbekistan and Tajikistan [5]. The limited local data on IHD in CA may be attributable to the aggregation of national data on the diseases of the circulatory system, in addition to the low number and quality of population-based studies in this region [6].
These conditions combined may have led to the underestimation of the true burden of IHD in CA and have impacted the effectiveness of public health policies concerning IHD control. Using data from the 2017 GBD iteration, this study provides estimates of IHD mortality, prevalence, and disability-adjusted life-years (DALYs) by sex and age globally, regionally, and nationally from 1990 to 2017.

2. Methods

The GBD study comprehensively reviews and analyzes the burden of disease in all countries on an annual basis. In the 2017 GBD cycle, estimates were provided for 359 diseases and injuries, 282 causes of death, and 84 risk factors [7–10]. The general methodology of the GBD 2017 study and the main changes compared to previous years were described in previous publications [7–10].

2.1. Case definition

In this descriptive study, IHD included acute myocardial infarction (MI) and chronic IHD [8]. MI was defined according to the third universal definition of MI [11]. Angina was defined based on a clinical diagnosis by a physician, the Rose Angina Questionnaire (RAQ) [12], or the use of nitrate medication [11]. Asymptomatic IHD following MI was assumed for survival beyond 28 days. The following International Classification of Diseases (ICD) codes were used: I20-I21.6, I21.9-I25.9, Z82.4-Z82.49 (ICD-10), 410–414.9 and V17.3 (ICD-9).

2.2. Fatal estimation

Data on IHD deaths in the CA region were obtained from vital registration (VR) [7]. Previous publications [7–10] provided the estimation process flowchart and the Global Health Data Exchange [13] along with a detailed list of data sources used to estimate the fatal burden of IHD in GBD 2017. Cause of Death Ensemble Modeling (CODEm) was the main method used to model IHD deaths. CODEm methodology has been described in several GBD publications [7–10].

2.3. Non-fatal estimation

Compared to VR, there was scarce non-fatal data. The sources of data for non-fatal IHD estimation included inpatient hospital and claims data, survey data (for angina) and the literature. A detailed list of data sources used to estimate the non-fatal burden of IHD in GBD 2017 was available from the Global Health Data Exchange [13].

Non-fatal MI, asymptomatic IHD post MI, and angina were modeled with DisMod MR 2.1 – a Bayesian meta-regression tool designed to provide consistent estimates of disease frequency by location, age group, sex, and year. Input into the model included data on mortality as well as non-fatal IHD. Prevalence of MI was estimated assuming disease duration of up to 28 days post-event. Disability weights were assigned according to time after event for MI (0.432 for days 1–2; 0.074 for days 3–28 days) and severity levels for angina (0 for asymptomatic; 0.033 for mild; 0.08 for moderate; 0.167 for severe).[8] Proportions in each severity level were based on the Medical Expenditure Panel Survey (MEPS) in the United States [14].

2.4. Burden calculation

The prevalence of each severity category was multiplied by severity-specific disability weight (DWs) to calculate years lived with disability (YLDs). Years of life lost (YLLs) were calculated for each age category by multiplying the number of deaths by standard life expectancy. DALYs were calculated as the sum of YLLs and YLDs. Consistent with the methodological literature for descriptive studies to account for uncertainty, the 95% uncertainty intervals were used around the estimates rather than the p-values. Uncertainty intervals were estimated by taking 1000 draws at each computational step and taking the 25th and 975th values of the ordered draws [7–10].

2.5. Risk factors

We provided data for Level 2 risk factors in the GBD hierarchy. We reported on the percentage of DALYs due to IHD which were attributable to the following factors: diet, high systolic blood pressure (SBP), high low-density lipoprotein (LDL) cholesterol, high fasting plasma glucose, high body mass index (BMI), tobacco, air pollution, impaired kidney function, low physical activity, and other environmental risks. Definitions of these risk factors, their relative risk for IHD, and risk factor modelling can be found in the GBD 2017 risk factor publication [10]. Our estimates of burden due to risk factors were derived from analyses in which relative risks were adjusted for confounding factors. Risk factors in GBD were considered independent, so the sum of the attributable burden (%) of IHD due to all risk factors was greater than 100%.

3. Results

Globally, the age-standardized death rate (ASDR) for IHD decreased from 1990 to 2017 by 30% while regionally (in CA), the ASDR increased by 16.7% (Table 1). In 2017, ASDR in CA was 116.9 per 100,000 (95% UI 115.1 to 119.7). Of note, in Uzbekistan, ASDR during the same period increased by 77.2%, and was the highest in the world in 2017. From 1990 to 2005, ASDR for IHD in CA generally increased (Fig. 1). Although a decline or plateau was observed in most CA countries from 2005 to 2017, the rate for Uzbekistan increased mildly during this period and remained visibly higher than other CA countries. Armenia had the lowest ASDR during this time period.

In comparing age-standardized IHD DALY rates in CA to global rates for different age and sex groups in 1990 and 2017, the rate ratio increased with age, starting from the 45–49 age group for both males and females in both years. The effect of age was stronger in 2017 (Fig. 2). Relative to global rates, DALY rates in CA were particularly high in those aged 70–84, and males showed a greater increase in the DALY rate ratio between 1990 and 2017. A general decline in DALY rate ratio was observed from age 84 onwards in both sexes.

During the period 1990 to 2003, Turkmenistan had the highest age-standardized DALY rate but underwent the most significant drop from 2005 to 2009. While the rates in most CA countries were decreasing by 1996 (Fig. 3), Uzbekistan showed the steepest increase in age-standardized DALY rate from 2000 to 2005.

Appendix Fig. 2 illustrated the relationship between age-standardized DALY rates and the sociodemographic index (SDI) for each country-year from 1990 to 2017. All CA countries showed rates higher than the global rates expected based on SDI. Rates were higher than expected for CA in Azerbaijan, Mongolia, Turkmenistan, and Uzbekistan but lower in Armenia, Georgia, Kazakhstan, Kyrgyzstan, and Tajikistan.

Fig. 4 depicted the percentage of IHD-related DALYs attributable to metabolic, behavioral, and environmental risk factors in 2017 for both sexes combined. Sex-specific data were shown in Appendix Figs. 3 and 4, while rankings of the GBD Level 3 (more detailed) risk factors in 1990 and 2017 for DALYs and deaths were presented in Appendix Figs. 5 and 6. The top three risk fac-
Prevalent cases, deaths and DALYs for ischemic heart disease for both sexes in 2017 and percentage change of age-standardized rates during 1990–2017 in Central Asia.

|                      | Prevalence (95% UI) | Deaths (95% UI) | DALYs (95% UI) |
|----------------------|---------------------|-----------------|---------------|
|                      | Counts (2017)       | ASDRs (2017)    | Pcs in ASDRs 90–2017 |
|                      |                     |                 |               |
| Global               | 126,451,501         | 1583.7          | –11.8         |
|                      |                     | 8,930,369       | 1169          | –30          |
|                      |                     | 10,840,455      |               | 170,273,348  |
|                      |                     | 21,358,445      |               | 2132.1       | –27.7       |
| Central Asia         | 1,531,395           | 2150.9          | –7.4          |
|                      |                     | (8,790,696,1191.1) | –13.5          | (115.1, 119.7) |
|                      |                     | 209,672         | 350           | 16.7         |
|                      |                     | 2,045,810       |               | 5762.4       | 9           |
| Armenia              | 90,481              | 2201.2          | –6.6          |
|                      |                     | (204,146,218,558) | –10.1          | (337.1, 264.9) |
|                      |                     | 9443            | 236.6         | –25.3        |
|                      |                     | 153,526         |               | 3723.3       | –27.9       |
| Azerbaijan           | 201,881             | 2270.4          | –10.1         |
|                      |                     | (91,08,9888)    | (228.7, 248.2) | (−8.8, −22.1) |
|                      |                     | 27,269          | 381.8         | 23           |
|                      |                     | 537,717         |               | 6201.9       | 6.6         |
| Georgia              | 1,324               | 2293.8          | –2.9          |
|                      |                     | (25,528, 29,142) | −13.6          | (358.7, 406.2) |
|                      |                     | 15,009          | 249.5         | −30          |
|                      |                     | 239,057         |               | 4098.2       | −33.7       |
| Kazakhstan           | 338,598             | 2070.1          | −20.4         |
|                      |                     | (14,328, 16,071) | −7.9           | (238.4, 267) |
|                      |                     | 38,556          | 275.2         | −1.2         |
|                      |                     | 714,104         |               | 4418.4       | −10.8       |
| Kyrgyzstan           | 72,710              | 1679            | −10           |
|                      |                     | (10,08,11,500)  | −13.7         | (284.9, 302.6) |
|                      |                     | 10,725          | 293.1         | 14.6         |
|                      |                     | 192,730         |               | 4718.9       | 4.3         |
| Mongolia             | 46,906              | 2165.3          | −0.2          |
|                      |                     | (35,42, 4243)   | −5.2           | (228.6, 269.2) |
|                      |                     | 3879            | 248.2         | −33.5        |
|                      |                     | 91,562          |               | 4225.2       | −32.5       |
| Tajikistan           | 92,493              | 1822.7          | –12           |
|                      |                     | (10,49, 12,254) | −15.5         | (249.1, 289.2) |
|                      |                     | 11,322          | 268.1         | 18.5         |
|                      |                     | 244,422         |               | 4849.9       | 19.4        |
| Turkmenistan         | 80,229              | 2186.1          | –5            |
|                      |                     | (10,499, 11,323) | −10.0          | (319.8, 359.7) |
|                      |                     | 10,641          | 339.3         | −10.5        |
|                      |                     | 226,832         |               | 6091.7       | −10         |
| Uzbekistan           | 473,770             | 2332.4          | 10.7          |
|                      |                     | (741,85, 242,501) | −10.0          | (319.8, 359.7) |
|                      |                     | 82,813          | 534.2         | 77.2         |
|                      |                     | 1,659,061       |               | 8346.1       | 59.8        |
|                      |                     | (375,99, 90,281) | 5.7            | (61.1, 95.1) |
|                      |                     | (488.1, 580)    |               | (1,499,577, 1,826,567) |
|                      |                     | (1,911,7)       |               | (7591.9, 9115.7) |
|                      |                     | (44.4, 77.1)    |               |             |

*ASDR: Age Standardized Death Ratio.
**Pc: Percentage Change.

**4. Discussion**

The burden of IHD is an ongoing global health challenge. According to our data, IHD was ranked as the number one cause of age-standardized mortality for both males and females in all CA countries. The ratio of IHD DALY rate in CA to the global rate was much higher in 2017 than in 1990, especially in people aged >45–49 years in both sexes. Consistent with data from many regions in the world, males in CA showed greater age-standardized IHD DALYs than females [7].

IHD was likely a major contributor to the differences in mortality across different regions of the former Soviet Union in the early 1990s [15]. However, relatively few studies of the burden of IHD in countries of this region were conducted during that time and not all of them followed a standardized methodology. In comparison, GBD studies [16–19] produced estimates of the burden of IHD and its risk factors at the global, regional, and country levels. These studies found an increase in IHD burden in CA and Eastern Europe between 1990 and 2015 [16–20].
While ASDR for IHD decreased in Western Europe and globally throughout the study period, ASDR for IHD increased in CA and Eastern Europe from 1990 to 2005 and declined thereafter [5]. This trend might be related to the collapse of the Soviet Union in the early 1990s and the economic challenges that followed, which affected health care systems and consequently the health of the population in CA countries. [20] Considerable attention was likely placed at the time on prevention of infectious diseases and children’s health, while the resources needed for prevention and treatment of non-communicable diseases (NCDs) were limited. According to a WHO study on NCDs that included CVD, diabetes, and cancer, CVD alone accounted for 57% of all deaths in Kazakhstan in 1997 [21].

In our data, even though there was no consistent relationship between SDI and IHD rates in CA countries, comparing observed and expected DALYs was useful in determining how each country was performing relative to what was expected at a given level of development. The socioeconomic status of the CA region, with noted lower gross national product compared to Eastern European countries [22], was likely influenced by the aftermath of the economic crisis in the Soviet Union. It might have been possible that the socioeconomic status of the CA region could have negatively impacted the mental and cardiovascular health of the population [23–27].

IHD burden varied across countries in the CA region. Specifically, there was a high IHD burden in terms of age-standardized death rate of ischemic heart disease per 100,000 population for both sexes in Central Asia and its countries, 1990–2017.
mortality and DALY rates in Uzbekistan while Armenia consistently had one of the lowest IHD burden in CA over the same period. In particular, the incidence of IHD in Uzbekistan was three folds of what was seen in Armenia and Tajikistan, and more than two folds of the incidence in Kazakhstan. Other data supported the finding that Armenia historically had lower IHD mortality rates compared to other CA countries [28]. The results above might be related to differences in the distribution of IHD risk factors in these countries, and probably to having better treatment facilities with higher number of cardiologists and catheterization labs per population in Kazakhstan [20], which would be effective in reducing mortality from acute IHD. Despite Uzbekistan sharing many cultural and historical characteristics with neighboring countries, some authors have speculated that the high death and incidence rates in Uzbekistan might be related to the shortage of resources in healthcare delivery (i.e. clinical expertise, facilities and equipment), income inequality, or limited drug affordability among people with lower socioeconomic status and among the elderly [29].

According to our data, 96% of IHD DALYs in CA for both males and females of all ages was attributable to known modifiable risk factors, with dietary risks, high SBP and high LDL cholesterol as the top three. Historically, some CA countries, such as Kazakhstan, Uzbekistan, and Kyrgyzstan, maintained a diet high in trans-fats and salt [30]. Though GBD data did not show markedly higher diet-
ary sodium levels in Uzbek diet, a study in Uzbekistan using a standard method of 24-hour urine collection estimated salt consumption (14.9 g/day) to be approximately three times higher than the level recommended by the World Health Organization (WHO) [31]. This could contribute to the high prevalence of hypertension and ultimately high IHD in this country. In addition, it might be possible that uncontrolled hypertension could have led to the increased IHD burden due to the insufficient capacity of the national healthcare system in detecting, treating, and controlling hypertension in clinical practice. Furthermore, inadequate public healthcare funding and barriers to patient out-of-pocket payments for medication might have hindered hypertension control and chronic IHD prevention [32,33]. Other modifiable factors worth mentioning in this discussion included alcohol consumption, tobacco use, physical activity level, and ambient air pollution. Despite these factors showing less contribution to IHD burden in our data, Uzbek data 31 pointed to these factors as relevant and necessitating attention.

As noted in some Eastern European countries, [30,34,35] high alcohol intake could have been a dietary risk factor contributing to the high burden of IHD in males aged 14–49 years in some CA countries, such as Kazakhstan, Kyrgyzstan, and Mongolia. Higher consumption of alcohol in men might partly explain the difference in IHD burden between men and women in these countries. [36,37] For example, a study in Uzbekistan, showed that males drink six times as much as females and 1 in 9 male drinkers binged. [38] As for tobacco use and physical activity, findings of the 2014 WHO STEPWise approach to surveillance (STEPS) survey indicated that tobacco was of concern in Uzbekistan as 25% of Uzbek men smoke, and 1 in 6 adults was insufficiently active [38]. With respect to ambient air pollution in CA, it was noted to be comparable to global levels in our analysis of the data. However, the WHO annual satellite data observed a high level of air pollution in Uzbekistan and Tajikistan [39]. Further studies would be needed before correlations could be reasonably made.

Overall, the trends seen in IHD burden within CA as represented in GBD data were likely multifactorial. IHD mortality rates in many regions of the world would have likely been influenced by preventive actions and risk factor control, improvement in socioeconomic status, improvement in healthcare capacity, and access to affordable diagnosis and treatment facilities. Political changes, less-than-optimal quality of healthcare services at primary, secondary and tertiary levels, and the lack of preventive strategies [40] could further compromise the health of the population. Kyrgyzstan, for example, faced two revolutions, in 2005 and 2010, which negatively impacted the economy with subsequent decline in population health. In contrast, in 2007–2009, the government of Kazakhstan launched a program for cardiology and cardiosurgery care to build capacity and improve infrastructure for CVD prevention, diagnosis, and treatment strategies. [41] While this could have contributed to the decrease in IHD death rate in older age groups observed in 2015 onwards, ongoing challenges remain with medication uptake and reaching target cholesterol levels [36].

4.1. Limitations

Our study was subject to all the limitations discussed in previous GBD publications [7–10]. These included gaps, biases, and inconsistencies in data sources as well as limitations in the methods of data processing and estimation. We tried, wherever possible, to consider alternative data sources, mostly publications in Russian. However, comparisons with other studies were limited due to differences in data and estimation methodology. As such, the results should be interpreted with caution. Further research would be required in order to investigate the possible causes of underreporting or miscoding of IHD. Additional data on the IHD risk factors and its social determinants in younger age groups would be needed to better understand the burden of IHD in CA.

5. Conclusion

Compared to global levels, CA showed a substantially higher age-standardized IHD burden. There was considerable variation in IHD DALY rates among countries in this region despite some similarities in socioeconomic and cultural aspects. The reasons for such differences were likely multifactorial and included differences in risk factor distribution, healthcare effectiveness, as well as political, social, and economic factors. Previous increasing trends in IHD burden over time could be partially explained by the economic crisis in the 1990s, which coincided with an increase in CVD mortality in the region. While some work had been underway in addressing IHD and its risk factors in CA, a concerted effort by multiple stakeholders and across multiple sectors (food industry, pharmaceutical companies, mass media, healthcare providers, and public education) would be needed to tackle the complexities of this disease comprehensively. Ongoing monitoring and analysis of IHD burden trends using reliable data would be crucial in public health strategy planning.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

We would like to extend our thanks to the GBD team for allowing us to access their free, comprehensive data base.

Appendix A. Supplementary material

 Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2021.100726.

References

[1] A. Nowbar, J. Howard, J. Finegold, P. Asaria, D. Francis, 2014 Global geographic analysis of mortality from ischaemic heart disease by country, age and income: Statistics from World Health Organisation and United Nations, Int. J. Cardiol. 174 (2) (2014) 293–298.
[2] A. Moran, M. Forouzanfar, G. Roth, et al., Temporal Trends in Ischemic Heart Disease Mortality in 21 World Regions, 1980 to 2010, Circulation 129 (14) (2014) 1483–1492.
[3] J. Finegold, P. Asaria, D. Francis, Mortality from ischaemic heart disease by country, region, and age: Statistics from World Health Organisation and United Nations, Int. J. Cardiol. 168 (2) (2013) 934–945.
[4] M. Forouzanfar, A. Moran, A. Flaxman, et al., Assessing the Global Burden of Ischemic Heart Disease Part 2: Analytic Methods and Estimates of the Global Epidemiology of Ischemic Heart Disease in 2010, Global Heart. 7 (4) (2012) 331–342.
[5] GBD Data Visualizations [Internet]. Institute for Health Metrics and Evaluation. 2019 [cited 15 January 2020]. Available from: http://www.healthdata.org/ gbd/data-visualizations.
[6] M. Rahu, V. Vlassov, F. Pega, et al., Population health and status of epidemiology: WHO European Region 1, Int. J. Epidemiol. 42 (3) (2013) 870–885.
[7] G. Roth, D. Abate, K. Abate, et al., Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017, The Lancet. 392 (10159) (2018) 1736–1788.
[8] S. James, D. Abate, K. Abate, et al., Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017, The Lancet. 392 (10159) (2018) 1789–1825.
[9] H. Kyu, D. Abate, K. Abate, et al., Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic
