Estimating the Proportion of Diabetes to the Attributable Burden of Cardiovascular Diseases in Iran

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Abstract

Background: This study aimed at estimating the proportion of diabetes as a risk factor to the attributable burden of cardiovascular diseases in Iran.

Methods: Comparative Risk Assessment methodology was used to calculating Potential Impact Fraction (PIF). To calculate PIF, data on the prevalence of newly diagnosed diabetes mellitus (NDM) and known diabetes mellitus (KDM) were obtained from 3rd Iranian surveillance of risk factors of non- communicable diseases and data on corresponding measures of effect were derived from a cohort study. PIF were estimated on both theoretical minimum and feasible minimum risk. Uncertainty for the attributable burden was estimated by Monte Carlo simulation-modeling techniques incorporating sources of uncertainty.

Results: According to multivariate- adjusted hazard ratios, by reducing the prevalence of Iranian women with diabetes from 10.05 percent to the feasible minimum risk level i.e. 5 percent, 6.8% (95% uncertainty intervals: 3.5- 9.8) of attributable Disability Adjusted Life Years (DALYs) to CVD are avoidable and the corresponding value for men were 3.1% (95% uncertainty intervals: 1.4- 4.8).

Conclusion: Although data on the prevalence of diabetes and corresponding measures of associations were obtained from an updated and country- specific source, but to better priority setting, PIF should be applied to updated and revised burden of CVDs.

Keywords: Cardiovascular diseases, Diabetes, Potential impact fraction, Burden, Iran

Introduction

Cardiovascular diseases (CVDs) are the number one cause of death including 17.3 million in the world and 82% CDVs related deaths take place in low and middle income countries (1,2). The most important modified risk factors of CVDs are physical inactivity, tobacco use and unhealthy diet and the effects of unhealthy diet in individuals are shown as raised blood glucose (2). Ischaemic heart disease is the first leading causes of death among the world and caused 62.6 million DALYs in 2004 (1). CVDs are the main cause of death in Iran like the world and the prevalence of impaired fasting glucose (IFG) and diabetes among Iranian adults (25- 64 years) are 3.36% (95% CI: 2.99- 3.77) and 9.73% (95% CI: 8.95- 10.58), respectively (3).

The role of diabetes mellitus in increasing the risk of CVDs has been well established (4). Fasting blood glucose is an important contributor of attributable burden to CVDs. Moreover there is a dose response association between fasting blood glucose and CVDs (5).

Knowledge of the magnitude of attributable burden to CVDs by diabetes, especially based on updated data on prevalence and national- specific

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measures of association is needed for health policy, priority setting and preventing CVDs deaths. The contribution of a risk factor to disease or death can be estimated by comparing the burden due to the observed exposure distribution in a population with that from another distribution (rather than a single reference level such as non-exposed) as described by the generalized "potential impact fraction"(PIF) (6). PIF or the generalized impact fraction introduced by Walter in 1980 and defined as the fractional reduction of a disease resulting from changing the current level of a risk factor to other modified levels (7). Such modified levels which considered to some alternative distribution of exposure in the counterfactual analysis have previously been reported elsewhere (8, 9).

With consideration to lack of the knowledge of the magnitude of attributable burden to CVDs by diabetes, especially based on updated data, this work aimed at estimating the contribution of diabetes to the attributable burden of cardiovascular disease by sex in Iran.

Materials and Methods

Estimates of avoidable burden

Estimates of attributable burden were made Using World Health Organization comparative risk assessment (CRA) methodology. CRA is a methodology that evaluates both the disease burdens attributable to the existing risk factors, but also the effects of interventions on these risk factors, and the potential avoidable future burden (6). According to this methodology, PIF is calculated to estimate avoidable burden using prevalence of a specific risk factor and its related association with a disease. PIF were defined as follows:

$$PIF = \frac{\sum_{i=1}^{n} P_i RR_i - \sum_{i=1}^{n} P_i' RR_i}{\sum_{i=1}^{n} P_i RR_i}$$

Where RR(i) is the relative risk or measure of association between an outcome and the exposure at level i, P(i) is the population distribution of exposure, P' (i) is the counterfactual distribution of exposure, and n the level of exposure (7). The detailed description of the concept of PIF is explained above in the introduction section.

Prevalence of diabetes

Prevalence of our interested risk factor among Iranian adults was obtained from the third STEPS survey of chronic disease risk factors (3). This STEPS survey of chronic disease risk factors in Iran was carried out in 2007(10). PIF was estimated on both theoretical minimum and feasible minimum risk. In present study, lowest minimum risk for diabetes was considered as zero in the 1st scenario. Feasible minimum risk, the second scenario, for diabetes was determined at 5% levels. Diabetes is defined as either newly diagnosed diabetes mellitus (NDM) and known diabetes mellitus (KDM). NDM is defined as individuals who had fasting plasma glucose (FPG) equal or greater than 7.0 mmol/l. Those individuals who currently are on medication for diabetes were considered as KDM. Prevalence of diabetes in both sexes is shown in Table 1.

Measure of association between diabetes and CVDs

Data on corresponding measures of association were derived from a national- specific study with age and multivariate adjusted hazard ratios (4). Corresponding measures which measured association between CVDs and diabetes are shown in Table 1. In our work, we used multivariate adjusted hazard ratios as the best accurate of the measure of association for estimating PIFs. Since, IFG did not have a significant hazard ratio for CVD, so its contribution was not estimated in present study.

Sensitivity analyses

Uncertainty for the PIFs is estimated by Monte Carlo simulation procedure which incorporating sources of uncertainty around point estimate of the prevalence of diabetes. We used the @RISK software version 5.5 for Excel (11) which allows multiple recalculations of a spreadsheet, each time choosing a value from the normal probability distributions which defined for the interested risk

factors. For each of the input variables (Prevalence of diabetes), 95% uncertainty ranges were calculated bounded by the 2.5th and 97.5th percentiles of the 1000 iteration values generated. At the next step, 95% uncertainty intervals for PIFs were calculated using estimated uncertainty ranges for the each risk factor by the above mentioned simulation procedure.

Results

The PIFs for diabetes based on multivariate- adjusted hazard ratios are shown for males and females in Table 1 for CVD. In addition, Table 2 shows the 95% uncertainty intervals for diabetes related PIFs at both lowest and feasible minimum

risk level. With consideration to multivariate- adjusted hazard ratios, we found that by reducing the percent of Iranian women who have a diabetes from 10.05 percent to feasible minimum risk level i.e. 5 percent, 6.8% (95% uncertainty intervals: 3.5- 9.8) of attributable Disability Adjusted Life Years (DALYs) to CVD are avoidable and the corresponding value for men were 3.1% (95% uncertainty intervals: 1.4- 4.8) (Table 1 and 2).

In general, modifying the current prevalence of the diabetes to the lowest minimum risk level i.e. zero lead to avoided 6.6%(95% uncertainty intervals: 5- 8.3) of DALYs which attributed to CVD in males and 13.6% (95% uncertainty intervals: 10.5- 16.3) in females, respectively (Table 1 and 2).

Table 1: Diabetes related PIFs for men and women based on multivariate- adjusted Hazard Ratios[a]

Exposure Variable	Measure of Association (Multivariate-adjusted Hazard Ratio)		Prevalence of diabetes % (95% CI)	Theoretical Minimum Risk (Scenario 1)	Feasible Minimum Risk (Scenario 2)	PIF (Scenario 1) %	PIF (Scenario 2) %
Either NDM[b] (Fasting plasma glucose equal or greater than 7.0 mmol/l)	Men	1.75 (1.21-2.52)	9.43 (8.31- 10.69)	0	5	6.6	3.1
or KDM[c] (Currently on medication for diabetes)	women	2.56 (1.71-3.85)	10.05 (9.01- 11.19)	0	5	13.6	6.8

[a]HRs as an accurate measure of association between diabetes and cardiovascular diseases in men adjusted for age, systolic blood pressure, diastolic blood pressure, total cholesterol, HDL-cholesterol, smoking and hypertension medication. [a]HR in women adjusted for age, systolic blood pressure, total cholesterol, hypertension medication and family history of CVD./ [b]NDM stand for newly diagnosed diabetes mellitus. / [c]KDM stand for known diabetes mellitus.

Table 2: Uncertainty intervals for PIFs based on estimated uncertainty ranges around point estimate of diabetes using Monte Carlo simulation procedure

Risk Factor	Hazard Ratio		Prevalence % (95% Uncertainty ranges)	PIFs % (95% Uncertainty Interval)[a]	
				At the theoretical Minimum Risk level	At the feasible Minimum Risk level
Diabetes (Either NDM[b]	Men	1.75	9.43 (7- 12)	6.6 (5- 8.3)	3.1 (1.4- 4.8)

			10.05	13.6	6.8
or KDMc)	Women	2.56	(7.5- 12.5)	(10.5- 16.3)	(3.5- 9.8)

a Incorporating sources of uncertainty for the prevalence of diabetes./ b NDM stand for newly diagnosed diabetes mellitus. /c KDM stand for known diabetes mellitus.

Our findings showed the PIFs for diabetes at lowest minimum risk were 6.6% (95% uncertainty intervals: 5- 8.3) and 13.6% (95% uncertainty intervals: 10.5- 16.3) for men and women, respectively. In addition, diabetes related PIFs were higher in women. On the other hand, IFG did not have a significant hazard ratio for CVD, so its contribution was not estimated in present study. This finding indicates the important role and greater contribution of diabetes in comparison to IFG among Iranian adults.

As we declared in the methods, we used multiple adjusted hazard ratio of diabetes on CVDs which considered the role of age, systolic blood pressure, diastolic blood pressure, total cholesterol, HDL-cholesterol, smoking and hypertension medication in men and age, systolic blood pressure, total cholesterol, hypertension medication and family history of CVDs in women. Since decreasing attributable risk of CVDs from diabetes requires a more robust analysis of confounders, we tried to incorporate above factors.

The results of other studies support the present study as we indicated below. Bradshaw D. and his colleagues(12) found that about 14% of IHD, 10% of stroke, 12% of hypertensive disease and 12% of renal disease burden among south African adults were attributable to diabetes. In another study, population attributable fractions ranged from 2% to 12% for coronary heart disease, 1% to 6% for haemorrhagic stroke, and 2% to 11% for ischaemic stroke (13). Medrano MJ reported that among women, 24.8% (95% CI 12.0%-31.9%) of IHD cases were attributable to diabetes (14). In addition, Woodward M found that the hazard ratio (95% CI) associated with diabetes was 1.97 (1.72-2.25) for fatal cardiovascular disease (15).

The results of a study(16) which was conducted to quantify population-level effects of all higher-than-optimum concentrations of blood glucose on mortality from ischaemic heart disease and stroke worldwide found that higher-than-optimum blood glucose is a leading cause of cardiovascular mortality in most world regions and reported that "in addition to 959,000 deaths directly assigned to diabetes, 1 490,000 deaths from ischaemic heart disease and 709,000 from stroke were attributable to high blood glucose, accounting for 21% and 13% of all deaths from these conditions. 792,000 (53%) of deaths from ischaemic heart disease and 345,000 (49%) from stroke that were attributable to high blood glucose were in men. Largest numbers of deaths attributable to this risk factor from ischaemic heart disease were in low-and-middle-income countries of South Asia (548,000) and Europe and Central Asia (313,000), and from stroke in South Asia (215,000) and East Asia and Pacific (190,000)."

With consideration to the Table 2, estimated uncertainty interval for PIFs which incorporated uncertainty ranges around the prevalence of diabetes indicates that sources of uncertainty does not averted the estimated attributable burden dramatically. However, implementing another source of uncertainty i.e. RR uncertainty is a necessary for real estimation of attributable burden. As it is mentioned above, we used a more robust analysis of age, systolic blood pressure, diastolic blood pressure, total cholesterol, HDL-cholesterol, smoking, hypertension medication and family history of CVDs rather than simply examining blood sugar or diabetes which may misleads the public health community and leads to expensive and ineffective pharmacological approaches to glucose control.

With consideration to CRA's methodological issues and besides the main advantages of our study such as considering the joint effect of multiple risk factor using adjusted relative risk and sources of uncertainty, there are two main limitations(6). Comparing the burden of CVDs due to the exists

prevalence of diabetes in the study population with the burden from a series of hypothetical distribution such as theoretical and feasible minimum risk level rather than non exposed level is one of the main challenge in this study. The second methodological issue regarding CRA's methodology and our study is calculating attributable burden without consideration of discounting.

Deriving the current distribution of risk factors from an almost updated source i.e. STEPS 2007, is the strength of present study. On the other hand, corresponding measures of effect in present study were obtained from a country specific source (4). So we proposed future studies estimates PIFs and attributable burden using an updated source. Finally, we concluded that for better planning, decision making and convincing health authorities as well as reporting avoidable DALYs rather than the percentage of avoidable burden, PIF should be applied to update and revise burden of CVD.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

Acknowledgments

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