Original article:

Cost-Of-Illness and its Determinants for Type 2 Diabetes Mellitus in Bangladesh: Protocol for a Cross-Sectional Study

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Abstract:

Background: Diabetes is one of the most prevalent non-communicable diseases (NCDs) all over the world and leading cause of death, disability, and economic loss. Diabetes imposes a heavy economic burden on individuals, their families and society as a whole. The aim of this study is to estimate the economic burden of type 2 diabetes mellitus (T2DM) in Bangladesh and to find association between glycemic control and Health Related Quality of Life with cost-of-illness (COI). **Methodology:** This will be an analytical cross-sectional cost-of-illness study. Within a specific time period participants aged ≥18 years, registered with Bangladesh Diabetic Somiti and having type 2 diabetes for more than one year will be recruited from selected hospitals inside and outside Dhaka to cover all level of health care services. A pre-tested electronic questionnaire will be used for data collection. The questionnaire will include demographic, clinical, behavioral information of the participants and all cost related information related to diabetes management during last one years. Descriptive statistics will include mean (±SD) or median (percentile) or relative frequencies (percentage) depending on the data. Two samples independent t-test or Mann-Whitney U-test, ANOVA or Kruskal-Wallis test and chi-squared tests will be used for univariate analysis. The multivariable regression analysis and bootstrap method will also be employed to analyze the relationship between the total cost of care (dependent variable) and several potential explanatory variables (independent variables). Logistic regression analysis will be performed to assess the factors affecting glycemic control and health related quality of life (HRQoL). The calculated total cost-of-illness will be projected for T2DM in Bangladesh by a mathematical modelling. **Discussion:** The results of the study will be useful as background information to forecast the economic burden of type 2 diabetes mellitus in Bangladesh and will be beneficial to conceptualize health strategies at national level. Furthermore, recognizing the factors of cost-of-illness will help both patients and health care providers to improve the management plan and cost control and hence, to have better quality of life. Evidence about the magnitude of the burden of T2DM is important for public health policymakers who are involved in making health care priorities and allocating scarce resources to facilitate the greatest benefits for type 2 diabetic people in Bangladesh.

Keywords: Bangladesh, Cost-of-illness, Direct and indirect cost, Economic burden, Type 2 diabetes mellitus

Background

Diabetes is one of the most prevalent non-communicable diseases (NCDs) globally. It is identified as a major threat to global development as it is the leading cause of death, disability and economic loss [1-4]. The burden of diabetes and its related mortality and disability has been rising around the globe, especially in South-East Asia. According to recent estimates by the International Diabetes Federation (IDF), the South East-Asia (SEA) region is home to more than 79 million adults (age group 20-79 years) with diabetes in 2017, and

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this number is projected to be 629 million in 2045 [5]. Results of several small-scale population-based studies in Bangladesh showed an increasing trend of diabetes prevalence in rural [6-12], semi-urban [12], and urban [8, 13] communities.

Diabetes is an expensive disease due to its chronic nature and its related complications. An estimated amount of US$727 billion of global healthcare expenditure was spent in 2017 to treat and prevent diabetes and its related complications, which represents an 8% increase compared to the 2015 estimate and the amount is projected to be USD 776 billion by 2045 means 7% growth [5]. People living in low- and middle-income countries pay a larger share of out-of-pocket health expenditures due to lack access to health insurance or publicly available medical services, compared with people living in high-income countries. Low- and middle-income countries which are home to 75.4 % of total population with diabetes, only 19% of global health expenditure on diabetes was spent on them [14]. An increasing trend of expenditure associated with diabetes was observed in developed [15-19] and developing [20-26] countries.

Maintaining the blood glucose level within the recommended range reduces the risk of diabetes complications and thereby reduce related cost. Thus, it has positive impact on economy. The role of improved glycemic control in the reduction of micro- and macrovascular complications of diabetes has been supported by many observational studies and randomized controlled clinical trials [10, 27-29]. Privation of optimal awareness of diabetes control may result in less-strict disease management, which in turn may lead to increase risk of diabetes-related complications [30] and associated higher healthcare costs [31]. Studies have shown that more intensive management of the disease, while initially costly, can be very cost-effective or can lead to long-standing cost savings by reducing the incidence or delay the progression of the costly complications [32-34]. To be able to assess the financial burden of diabetes and plan the future health care needs, estimation of the cost-of-illness of diabetes is an empirical need.

Among the south-east Asian countries, Bangladesh has the second-highest prevalence of diabetes. Therefore, diabetes and its related complications are placing a significant financial burden on individuals, the health care system and on the economy of the country as a whole. In order to allocate limited resources and to set healthcare priorities, it is important for public health policymakers to understand the magnitude of the burden of diabetes.

However, in the context of Bangladesh, background data associated to the economic burden of diabetes is limited in the literature. The aim of the current study is to estimate the direct and indirect costs of type 2 diabetes and its association with glycaemic control and quality of life. Furthermore, to formulate a cost model to evaluate the economic burden of diabetes on individuals and at a country level.

Specific objectives

This study has three main objectives. Firstly, to estimate the cost-of-illness and to evaluate the determinants of cost-of-illness of type 2 diabetes mellitus in Bangladesh. Secondly, to find the determinants of glycaemic control and health-related quality of life. Thirdly, to assess the potential relationship of poor glycaemic level and health related quality of life with diabetes-related hospitalization costs. The secondary objective is to estimate the national economic burden of type 2 diabetes mellitus in Bangladesh by a mathematical modelling.

Outcome measures

The primary outcome measures will be cost-of-illness of T2DM in a descriptive manner. The determinants of cost will be assessed by an analytical operation. To evaluate the determinants of glycemic control and quality of life all potential variables including COI will be considered as independent variable.

The secondary outcome measure of the study is to estimate the economic burden of T2DM in Bangladesh.

Methodology

Ethical Approval

The project has been approved by the Monash University Human Research Committee and the Ethical Review Committee of the Bangladesh University of Health Sciences. The approval from the Diabetic Association of Bangladesh (BADAS) was also obtained.

Study Design

For primary outcome measure the study design will be observational analytic with a cross-sectional bottom–up prevalence-based approach. For secondary outcome the study will be based on mathematical modeling.

Study Population

The study population will consist of people with type 2 diabetic attending two tertiary level hospitals (BIRDEM and BIHS Hospitals) in Dhaka (the capital), two tertiary level hospitals in Dinajpur and Thakurgaon (two north-western districts in Bangladesh) and two secondary level health care centers in the same northern districts. All these

facilities are directly or indirectly (through affiliated local Associations) are owned by the Diabetic Association of Bangladesh (a not-for- profit but mostly self-sustained social welfare organization). All of these, in addition to tertiary or secondary health care, provide primary health services to the diabetic subjects. The comprehensive care, provided by these facilities, are fairly structured following policies and guidelines by the central Association.

The primary reason for choosing these facilities in the present study is their cost recovery approach which gives a fairly good idea about the cost of illness, to be explored in the present study, under an acceptable clinical management level. The selection of the specific facilities was done to create a rural-urban as well as professional mix and to get a population attending various levels of services. Data from the present facilities will also have the advantage of representing the mid-level costs which can be downscaled to the cost of public sector of facilities (with deduction of certain costs) and those can also be up scaled to the cost of the for-profit private sector facilities (by adding certain costs and profit). Thus the data will be useful for attaining the national economic burden of type 2 diabetes in Bangladesh by the mathematical modeling.

Sample Size

The present study is the first study which will estimate cost-of-illness of type 2 diabetes in Bangladesh, there is no sufficient background information to calculate a formal sample size for this study. Based on available budget and time, data will be collected from patients attending the selected hospitals. In order to attain a good power, we are aiming to recruit at least 1200 participants during a time period of six months.

Recruitment

A systematic random sampling method will be used to recruit participants. The expected number of participants that will be recruited every day is 10. Each day, the data collectors will start by randomly selecting a participant with type 2 diabetes from the first K participants attending the hospital and invite him/her to participate. The value of K will depends on the number of people attending the hospital every day. After that, every K-th patient will be approached. If the K-th person declines or he/she is not a type 2 diabetic, the next person will be invited. The recruitment will continue for a period of six months.

Patients' consent

At the beginning of the interview, the data collector will briefly inform each participant about the purpose of the study, the data collection procedure (interview, anthropometric measures and review of medical record), freedom of participation and the use of collected information. The eligible participants will be invited and an explanatory statement will be given with instructions to read and ask for clarification (if any). Upon their agreement to participate by signing the consent form, they will be interviewed.

Data collection instrument

A structured questionnaire has been developed based on published literature and using different standardized questionnaires. It has been developed in simple and plain English language and again have been translated into Bangla. Then, the Bangla version has been translated back into English to check the consistency of meaning between versions. A minor modification (vocabulary to ensure a better understanding) has done after the pilot survey. The approximate time for data collection using the questionnaire was about 35 minutes per participant. Research Electronic Data Capture (REDCap) will be used to collect and manage the data [35]. REDCap is a secure web-based application for constructing electronic surveys and collecting data for research studies. It provides a user-friendly interface with validated data entry, audit trails for tracking data manipulation, and an automated export procedure for seamless data downloads into common statistical software packages.

Using the same questionnaire for all participants, the following information will be collected:

- Diabetes centre detail and participant's identification: hospital name, participant's name, contact details.
- Participant's socio-demographics and economic factors: age, gender, marital status, religion, education, professional status, personal income, household income and number of children.
- Anthropometric information: weight, height, waist circumference, hip circumference and neck circumference.
- Medical history: duration of diabetes, family history of diabetes, frequency of follow up, mode of treatment, self-monitoring blood glucose, hypoglycaemic events, and medical history of diabetes-related comorbidities and complications.
- Diabetes cost information: cost regarding treatment, duration of leave for each visit, information about the accompanying person, information about the treatment bearer due to cost, information about in-patient events.
- Adherence to management: medication, blood

glucose monitoring, diet, exercise.

- Family support for diabetes
- Lifestyle data including smoking status, dietary habits [36] and physical activity [37].
- Psychological aspects including depression (The Patient Health Questionnaire-2 (PHQ-2) [38] and anxiety (Generalized Anxiety Disorder Scale (GAD-2) [39]
- Patient's health-related quality of life (EQ-5D-5L) [40] and six-item Cognitive impairment test (6CIT) [41].
- Information from the patient's guide book: most recent blood pressure measures, fasting blood sugar measures, after-breakfast blood sugar measures, HbA1c, lipid profile, SGPT, serum creatinine, urine albumin, albumin/ creatinine ratio, eGFR and currently prescribed medications.
- Anthropometrics: height, weight, blood pressure and waist and hip circumference. Information about height and weight will be recorded from patient's registered guide book. Waist and hip circumference of the patient will be measured using measuring tape following the procedures below:

Waist circumference: Participants will be measured against thin clothing (for cultural reasons), on exhalation, midway between the lower rib margin and the anterior superior iliac spine (hip bone), or the narrowest abdominal point. The subject should be relaxed with arms held loosely at their sides. The tape measure must be kept horizontal for a standing measurement. This will be done twice and if the measurements differ by more than 2 cm, a third measurement will be taken. The waist circumference will be recorded to the nearest 0.5 cm.

Hip circumference: Will be measured at the widest circumference around the hip bones, so that the tape passes over the greatest protrusion of the gluteal muscles. The tape measure must be kept horizontal for a standing measurement. This will be done twice, and if the measurements differ by more than 2 cm, a third measurement will be taken. The hip circumference will be recorded to the nearest 0.5 cm.

Data management and analysis

During the data-collection period, the data will be saved in the secure web-based application REDCap hosted by Monash University. The application will be accessible by the research team only. After completion of data collection, data will be exported to the IBM SPSS statistical package and will be saved on the secure network storage (Monash (S:) drive) allocated by School of Public Health and Preventive Medicine at Monash University. Participants' names will be removed from the database and each participant will be identified by a numeric code generated by REDCap. The database containing all information will be saved in a separate secure electronic folder, which will not be used for data analysis. Only the research team will have access to the identified and de-identified electronic databases.

Descriptive statistics will include either mean (±SD) or median (lower and upper quartiles) for continuous data, and relative frequencies (percentages) for categorical data. The t-test or Mann-Whitney U-test, and the ANOVA or Kruskal-Wallis test will be used for comparing two and multiple groups, respectively. Categorical variables will be compared using chi-squared tests. The liner regression analysis will be employed to analyze the relationship between the total cost of care (dependent variable) and several potential explanatory variables (independent variables). Multilevel logistic regression will be used to assess the factors affecting glycaemic control and health-related quality of life (HRQoL) as outcome variable, and to find its association with cost of care as independent variable. One-way sensitivity analysis will be used for analyzing the uncertainty of the results. The national economic burden of type 2 diabetes mellitus in Bangladesh will be estimated using a mathematical modelling.

Outcomes measures

Cost calculation method: The COI studies traditionally represents the earliest form of economic evaluation that stratify costs into three categories: direct, indirect, and intangible costs. Since the intangible costs have seldom been quantified in monetary terms due to the measurement difficulties, we mainly focus on the first two cost categories: direct and indirect costs.

The direct economic costs will reflect the resources used in treating or coping with the disease including expenditures for medical care and the treatment of diabetes. Direct cost will be calculated under two sub categories – (a) direct medical costs which will include costs of hospitalization, outpatient visits, drug, laboratory tests, materials, emergency services, and (b) direct non-medical costs will include cost of transportation to the health care providers, household expenditures, costs of meal and informal cares of any kinds.

To calculate direct cost the micro-costing approach will be used by identifying cost items as much detail as possible. Patients' demographic characteristics,

Afsana Afroz, Khurshid Alam, Mohammed J Alramadan, Md Nassif Hossain, Hasina Akhter Chowdhury, Liaquat Ali, Dianna J Magliano, Baki Billah

clinical status, quantities of medical services received, types and quantities of drugs and medical supplies used during last one year will be retrieved by reviewing patient's guide book. The drug cost will be calculated based on cost per defined daily dose (DDD) [42] of each drug and therapy duration. Costs of outpatient visits and laboratory testing will be calculated using the regular rate of BIRDEM or BIHS hospital. Drug cost will be calculated considering the regular rate of BIRDEM or BIHS pharmacy. Calculation of unit cost of medical services will employed the standard costing approach[43]. The calculation will be composed of four steps, i.e., calculation of the unit cost of medical services, direct cost determination, indirect cost determination, and total cost determination. The annual average costs on medical care will be estimated by multiplying the average per visit costs by the number of visit (records from patients guide book) per year.

The indirect costs will consist of opportunity cost of time lost due to morbidity (temporary disability). The morbidity related component includes the productivity losses of time invested by patients and their accompanying person. Indirect cost will be calculated using the human capital approach[44] for those who are currently working or keeping house but not for persons who are unable to work or who choose not to work.

All costs will be measured in Bangladeshi Taka (BDT); later will be converted to USD applying the current currency conversion rate.

Glycemic control: The proportion of glycosylated haemoglobin (HbA1c) measured as a percentage will be categorized as: good control (HbA1c $\leq$ 7.0%), fair control (HbA1c 7%-8%) or poor control (HbA1c >8.0%).

Quality of life: EQ-5D-5L health states scores will be converted into a single index value between 0 and 1, and the quality of life will be categorised as Good quality of life (0.67-1.00), fair quality of life (0.34-0.66) and poor quality of life ($\leq$ 0.33).

Personnel and training

Two interviewers who has completed university graduation and have prior experience with surveys will be recruited for data collection. The objectives of the study and contents of the questionnaire will be explained to the interviewers. They will be trained on approaching the potential participants, measuring anthropometrics, filling in the electronic questionnaire and obtaining information from the medical records. Training session will also include mock interviews between participants and field practice as a pre-test.

Quality assurance measures for data collection

To ensure the quality of data collection, the procedure will be monitored by the student investigator. In addition, the student investigator will carry out a random consistency check for at least 5% of the interviewed questionnaires.

Pilot study

The questionnaire was piloted on 31 participants attending Bangladesh Institute of Health Sciences Hospital over a period of one weeks. The questionnaire was found to be acceptable by most of the participants and practical by data collectors. The average time required to complete data collection from one participant was almost similar (around 40 minutes) as planned. The pilot study does not recommend any major change to the questionnaire.

Discussion

This study is a comprehensive multi-center study which will provide the most up-to-date in-depth information and a clear picture of economic burden of diabetes in Bangladesh. The study findings will serve as a research-based evidence to priorities and allocate scarce resources and will be beneficial to conceptualize national level health strategies. Furthermore, recognizing the factors of cost-of-illness and the relationship between glycemic control and quality of life with cost-of-illness will aid both patients and health care providers to improve the management, to control the cost and hence, to have improved quality of life. Evidence about the magnitude of the burden of T2DM will assist public health policymakers to develop programs and policies and cost-effective strategies for the better management of diabetes in the context of Bangladesh.

Author disclosure

All authors report no relation or financial interest with any entity that would pose a conflict of interest.

Authors' contribution

All authors were involved to the conception and design of the study. All authors critically review to improve the content and final approval of version to be submitted

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