

Cost-Effectiveness Analysis of Medical Intervention in Patients with Early Detection of Diabetic Retinopathy in a Tertiary Care Hospital in Bangladesh

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Abstract

Background and aims: The economic burden resulting from diabetic retinopathy (DR) consumes a major portion of resources allocated for health-care services. The present study was undertaken to assess the cost-effectiveness of medical intervention in patients with DR.

Materials and methods: Two hundred patients with DR, at least 1 year of follow-up, were purposively selected from Out-Patient Department of BIRDEM (tertiary diabetes care hospital), Bangladesh. Of them 100 were late in detection of DR (LDR) and 100 were detected early (EDR). Comparison was made between the groups.

Results: In LDR group, 42.4% had mild nonproliferative DR (NPDR), 31.4% had moderate, 15.1% had severe NPDR and 11.1% had proliferative DR (PDR). In EDR group, 58.4% had mild and 41.6% had moderate NPDR. About 17% patients in LDR and 34% in EDR were free of diabetic complications other than DR. In LDR and EDR, 18% and 46% had one complication, 27% and 8% had two and 30% and 4% had more than two complications respectively. The most frequent complication was cardiopathy, which affected 31% patients in LDR and 25% in EDR, followed by peripheral neuropathy 19% and 16%, nephropathy 15% and 11%, and peripheral vascular disease 8% and 4% respectively. The average annual cost of care was US\$ 27954 (direct US\$ 16983 and indirect US\$ 10971), with an average US\$ 140 per patient. Among the average annual cost LDR consumed US\$ 19737 (US\$ 197 per patient) and EDR US\$ 8217 (US\$ 82 per patient). The regression equation showed that medical cost is significantly related to complications tested in both univariate ($p < 0.0001$) and multiple linear regression analyses ($R^2 = 0.53$; $F = 82.3$; $p < 0.0001$).

Conclusion: Proper management with regular screening substantially reduces the expenditure related to care of patients with diabetic retinopathy and related complications even in a developing country.

Keywords: Cost-effectiveness; Early detection; Diabetic retinopathy; Bangladesh

Introduction

The incidence of diabetes is increasing. With roughly 800,000 new cases diagnosed each year, the prevalence of diagnosed diabetes has increased by 33% between 1990 and 1998 [1]. Currently, an estimated 15.7 million people, of whom only 65% have been diagnosed, have diabetes. It is also estimated that by 2025 over 20 million people will have diabetes [2].

Accompanying this increased prevalence of diabetes is an increase in the number of associated complications. Diabetes can affect every organ of the body. Poor glycemic control can lead to blindness, lower extremity amputations, and dental disease [3]. Diabetes is the leading cause of blindness, and complications related to diabetes account for over half of the lower extremity amputations in the United States.

Diabetic retinopathy, the main contributor to blindness, is a term for certain abnormalities in the small blood vessels of the retina that are caused by diabetes. Early detection of diabetic retinopathy is essential since retinopathy is often asymptomatic [4]. When first diagnosed, approximately 21% of people with type 2 diabetes show some retinopathy. People with type 1 diabetes tend to develop retinopathy after three to five years from the onset of diabetes [4]. One of the strongest predictors of developing retinopathy is the length of time an individual has had diabetes; the longer the duration, the greater the probability of developing retinopathy [5]. A dilated eye exam is the most effective means for detecting diabetic retinopathy; to ensure an

accurate diagnosis to occur, however, the exam must be administered by a person skilled in conducting the procedure and in interpreting its results [5]. Besides routine eye exams, glucose control is recommended to prevent the onset of retinopathy. Although early detection and treatment of eye complications could prevent approximately 90% of new cases of diabetes-related blindness [4], many diabetics in the United States are not receiving the recommended preventive eye screenings [5].

Epidemiological data have identified duration of diabetes, systolic blood pressure (SBP), glycemic control, and urinary albumin as risk factors in the development of diabetic retinopathy [6,7]. Other factors, including Body Mass Index (BMI), smoking, serum lipids, and C-peptide, have shown varying results [6].

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Aims and Objectives

The aim of the study was to investigate whether early detection and management can substantially reduce complications of retinopathy with type 2 diabetes, can substantially reduce the cost of complications, and can increase survival and the interval without complications, and whether cost effectiveness ratio will be able to compare favorably with many accepted healthcare programmes.

Materials and Methods

It was a cross-sectional study and retrospective in nature. BIRDEM, tertiary diabetes care hospital and the centre of excellence, have the largest OPD of the South East Asia. Primary data was taken through a self-administrated pre-set questionnaire. Two hundred patients with Diabetic Retinopathy, with at least 1 year of follow-up were purposively selected from BIRDEM (tertiary diabetes care hospital) of Bangladesh. Of them 100 were late in detection (If few specks of blood, or spots, "floating" in vision. If spots occur, there may need treatment before more serious bleeding occurs. Hemorrhages tend to happen more than once, often during sleep. However, bleeding can reoccur and cause severely blurred vision. If left untreated, proliferative retinopathy can cause severe vision loss and even blindness. Diabetic retinopathy and macular edema are detected during a comprehensive eye exam that includes: Visual acuity test, Dilated eye exam and Tonometry, Late detected DR (or Late detected diabetic retinopathy) and 100 were detected early. Often there are no symptoms in the early stages of the disease, nor is there any pain. Be sure to have a comprehensive dilated eye exam at least once a year. Blurred vision may occur when the macula—the part of the retina that provides sharp central vision—swells from leaking fluid. This condition is called macular edema. If new blood vessels grow on the surface of the retina, they can bleed into the eye and block vision (Leaking blood vessels). Retinal swelling (macular edema), Pale, fatty deposits on the retina--signs of leaking blood vessels, Damaged nerve tissue, (any changes to the blood vessels), Early detected DR (or Early detected diabetic retinopathy). The Retinopathy department identified those patients who have been come here for follow up. The inclusion criteria were patients with Diabetic Retinopathy, with at least one year of follow up. The exclusion criteria were patients with serious illness, pregnant women and person with mental disorders. The variables are the degree and extent of complications like cardiopathy, peripheral neuropathy, retinopathy and peripheral vascular diseases, treatment outcome, clinical effectiveness of interventions and direct, indirect and incremental cost of complications were calculated. Comparison was made between the groups. Cost included drugs, hospitalizations, diagnostics and visits. A detailed history of the clinical and cost data was taken from the patient's diabetic guide book, thorough questionnaire, general examinations were carried out by the doctors of the ophthalmology department, findings of the performed investigations was recorded, in light of the study protocol. Relevant associated medical conditions were recorded carefully.

Eye examination

The ophthalmologic examination included best corrected visual acuity with an illuminated Snellen chart [7], slit-lamp biomicroscopy and also detailed fundus examination [8] by both indirect ophthalmoscopy and contact lens biomicroscopy (with pupils dilated) conducted by retinal specialist. All patients were examined at the BIRDEM outpatient door and were reconfirmed by a senior ophthalmologist. Eye examination was recorded from the patient registry book. After completion of eye examination, the necessary treatment was provided.

The grading of retinopathy was defined and classified [9] into the most commonly used clinical classification which is the modified

Airlie House classification as introduced by ETDRS: Non-Proliferative Diabetic Retinopathy (NPDR) or background retinopathy:- NPDR was classified into: 'mild', 'moderate', and 'severe'. Proliferative Diabetic Retinopathy (PDR):- PDR was classified into: 'early PDR', 'PDR with high risk criteria', 'PDR including advanced diabetic eye disease'. The ETDRS classified diabetic macular edema as non-clinically significant and clinically significant (CSME) [10].

Anthropometric measurements

Anthropometric measurements such as weight, height, waist and hip circumferences were taken from the patients wearing light clothes and without shoes. The weight was measured to the nearest 0.1 kg using a Sohenle mechanical weighing scale and the machine were calibrated daily by known standard weight. Height was taken to the nearest 0.5 cm using a portable, locally manufactured stadiometer with subjects standing upright on a flat surface without shoes having the back of the heels and the occiput on the stadiometer. A waist circumference was measured by placing a plastic dressmaker's tape horizontally midway between the lower border of the ribs and the iliac crest on the mid-axillary line. The measurement was recorded to the nearest centimetre. Hip circumference was measured to the nearest centimetre at the greatest protrusion of the buttocks just below the iliac crest. Waist hip ratio was taken as waist/hip circumference. Body Mass Index (BMI) was calculated as the ratio of weight in kilograms over height in meters squared [weight (kg)/height (m²)]. The definition of overweight and obesity was based on BMI 25 kg/m² and 30 kg/m² respectively [11].

Measurement of blood pressure

Three readings of blood pressure were taken from each participant. Measurements was taken on participants on a sitting position after 10 minutes rest, by trained and certified health workers following AHA procedures, using electronic AND 0 78 Model UA-767 fully automatic, clinically validated digital BP monitor, with a suitable sized cuff at the forearm. Hypertension was deemed to be present when the systolic pressure was greater than 140 mmHg or when the diastolic pressure was greater than 90 mmHg [12].

Biochemical measurements

Fasting plasma glucose ≥ 7 mmol/l, 2-hr ABF ≥ 11.1 mmol/l [6] and Hemoglobin A_{1c} $>7\%$ were considered as diabetic patients in this study. Lipid abnormalities were deemed to be present when the TC was >200 mg/dl, TG was >150 mg/dl, LDL was >100 mg/dl, HDL was <40 mg/dl for men and <50 mg/dl for women [13].

Free flowing 10 ml. venous blood was collected in ethylenediamine tetraacetic acid (EDTA) tubes after overnight fasting of at least 8 h and centrifuged. Plasma glucose was estimated by a glucose oxidase method and glycosylated hemoglobin (HbA_{1c}) was measured by high-performance liquid chromatography (HPLC). Lipid profile includes total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides (TG), which were measured by enzymatic technique. The Friedewald formula was used to calculate the LDL cholesterol (except for subjects with triglycerides >400 mg/dl).

Socio-demographic and economic data collection

Socio-demographic and economic data were collected by interview. A structured questionnaire was developed in Bengali language (local language) and revised after pre-testing.

Ethics

Informed written consent was taken from each of the individuals prior to inclusion. Self decision of patients to participate or not in the research was properly honored by the Team. The relevant Bangladeshi

Ethical Committees approved the protocol. Data were analyzed in SPSS methods and appropriate statistical methods were used where necessary.

Results

A total of 200 patients were considered for an average of 365 days, amounting to 656 person-years of observation in total.

In LDR group, 42.4% had mild nonproliferative DR (NPDR), 31.4% had moderate, 15.1% had severe NPDR and 11.1% had proliferative DR (PDR). In EDR group, 58.4% had mild and 41.6% had moderate NPDR (Table 1).

The mean ± SD fasting serum glucose of the groups (LDR and EDR respectively) was 9.36 ± 0.40 and 4.78 ± 0.38 mmol/l, total cholesterol was 206.50 ± 42.60 and 104.20 ± 35.50 mg/dl, HbA_{1c} was $9.80 \pm 0.50\%$ and $5.70 \pm 0.38\%$, TG was 163.76 ± 99.46 and 155.67 ± 94.84 mg/dl, SBP was 172.5 ± 20.9 and 109.5 ± 11.9 mmHg and DBP was 97.7 ± 10.0 and 70.7 ± 9.3 mmHg (Table 2).

The result showed that fasting serum glucose, total cholesterol, HbA_{1c} , TG, Serum creatinine, HDL, LDL, SBP and DBP were significantly higher among the Late Detected Retinopathy groups. It has been found that there was a significant correlation between the serum creatinine level and blood pressure level (Systolic and Diastolic) tested at 5% level of significance ($r=0.90$, $r=0.77$) (Table 2A).

The body mass index among the Late Detected Retinopathy groups was significantly higher but there was no significant difference among the groups in terms of Waist Hip Ratio.

About 17% patients in LDR and 34% in EDR were free of diabetic complications other than DR. In LDR and EDR, 18% and 46% had one complication, 27% and 8% had two and 30% and 4% had more than two complications respectively. The most frequent complication was

Variables	Description	Percentage Distribution
Age	40-50	57.2
	51-60	40.1
	> 61	2.7
Education	Literate-below SSC	95.7
	SSC – HSC	3.7
	Graduate and above	0.5
Family Members	1-4	43.9
	5-8	52.9
	> 8	3.2
Socioeconomic status	Status 1 (<70)	10.2
	Status 2 (70-140)	0.5
	Status 3 (140-285)	19.3
	Status 4 (285-570)	36.4
	Status 5 (570-1140)	20.9
	Status 6 (>1140)	12.8
Occupation	House wife	61.0
	Services	10.7
	Others	28.3

Table 1: Percentage Distribution of the study subjects according to the Demographic Variables.

Group/ Types of Diabetic Retinopathy	Early detected Diabetic Retinopathy	Late detected Diabetic Retinopathy
Mild Nonproliferative Diabetic Retinopathy	58.4%	42.4%
Moderate Nonproliferative Diabetic Retinopathy	41.6%	31.4%
Severe Nonproliferative Diabetic Retinopathy	0	15.1%
Proliferative Diabetic Retinopathy	0	11.1%

Table 2: Distribution of types of diabetic retinopathy according to their severity.

Clinical Parameters/ Group	Early detected Diabetic Retinopathy	Late detected Diabetic Retinopathy	p Value
FBS (mmol/l)	4.78 ± 0.38	9.36 ± 0.40	0.004
T Chol (mmol/dl)	104.20 ± 35.50	206.50 ± 42.60	0.006
HbA_{1c} (%)	$5.70 \pm 0.38\%$	$9.80 \pm 0.50\%$	0.004
TG (mmol/dl)	155.67 ± 94.84	163.76 ± 99.46	0.0001
Serum Creatinine (mmol/l)	0.89 ± 0.03	4.90 ± 1.17	0.004
HDL (mmol/dl)	11.57 ± 1.25	16.16 ± 1.61	0.091
LDL (mmol/dl)	123.05 ± 32.05	131.98 ± 39.88	0.0001
SBP (mm/ Hg)	72.5 ± 20.9	109.5 ± 11.9	0.0001
DBP (mm/ Hg)	70.7 ± 9.3	97.7 ± 10.0	0.0001

Table 2A: Mean ± SD of the clinical findings between the groups.

cardiopathy, which affected 31% patients in LDR and 25% in EDR, followed by peripheral neuropathy 19% and 16%, nephropathy 15% and 11%, and peripheral vascular diseases 8% and 4% respectively.

The average annual cost of care was US\$ 27954 (direct US\$ 16983 and indirect US\$ 10971), with an average US\$ 140 per patient. Among the average annual cost LDR consumed US\$ 19737 (US\$ 197 per patient) and EDR US\$ 8217 (US\$ 82 per patient) (Table 3).

US\$ 13473 (48%) of costs was attributable to drugs for both groups of which US\$ 10817 (80%) was for LDR and US\$ 2656 (20%) for EDR, US\$ 8739 (31%) to hospitalizations of which US\$ 5211 (60%) for LDR and 3528 (40%) for EDR. In case of diagnostics and visits the corresponding values were US\$ 2136 (60%) and 1419 (40%) and US\$ 1673 (76%) and 514 (24%) for LDR and EDR respectively. The annual medical costs increased with the increased number of complications from US\$ 1322 to 2298 and to 3991 in LDR with one, two and more than two complications (other than DR) which is increasing at a rapid rate and US\$ 917 to 1556 and to 2372 in EDR respectively, increasing at a diminishing marginal rate. The regression equation showed that medical cost is significantly related to complications tested in both univariate ($p<0.0001$) and multiple linear regression analyses ($R^2=0.53$; $F=82.3$; $p<0.0001$) (Tables 4 and 5).

Table 6 showed that there is a significant association between the complications and the cost. ($p<0.000$, $p<0.004$, $p<0.001$, $p<0.001$, respectively).

Table 7 showed that there was a significant relation among the biochemical parameters {Serum glucose (mmol/l), S_Creatinine (mmol/l), HbA_{1c} (%), Triglyceride (mg/dl), Total cholesterol (mg/dl), LDL-Chol (mg/dl) and HDL- Chol (mg/dl)} and the cost involved (But HDL found not to be significant association with cost).

The annual medical costs increased with the increased number of complications from US\$ 1322 to 2298 and to 3991 in LDR with one, two and more than two complications (other than DR) which is increasing at a rapid rate and US\$ 917 to 1556 and to 2372 in EDR respectively, increasing at a diminishing marginal rate. The regression equation showed that medical cost is significantly related to complications tested in both univariate ($P<0.0001$) and multiple linear regression analyses ($R^2=0.53$; $F=82.3$; $p<0.0001$).

Discussion

Diabetes is one of the most costly diseases ever in both human and economic terms. To reduce today's burden and that on future generations, it is in everyone's interest that cost-effective measures to prevent diabetic retinopathy and related complications are identified and implemented even in developing countries. In this study showed that timely management of patient with diabetic retinopathy and early detection of retinopathy complication will reduce the cost. It

Anthropometrics parameters	Early detected Diabetic Retinopathy	Late detected Diabetic Retinopathy	P Value
BMI	21.24 ± 4.38	29.71 ± 3.47	0.0001
WHR	0.8954 ± 0.006	0.8886 ± 0.006	0.453

Table 3: Mean ± SD of the anthropometrics parameters of the study subjects.

	LDR	EDR	Total (US\$)
Cost of the Patients	19737	8217	27954
Average/patients	197	82	140

Table 4: Cost Components among the study groups.

	Total	%	LDR	%	EDR	%
Drug	13473	48	10817	80	2656	20
Hospital	8739	31	5211	60	3528	40
Diagnostic	3555	13	2136	60	1419	40
Visits	2187	8	1673	76	514	24
Grand Total	27954	100	19737	71	8217	29

Table 5: Cost Distribution.

Complications	Std. Error	Standardized Coefficients Beta	t	Sig.
(Constant)	15285.404		4.681	0.000
Cardiopathy	12645.198	-.069	3.930	0.004
Retinopathy	14226.417	.009	3.107	0.001
Neuropathy	6443.232	-.072	8.886	0.004
Peripheral vascular diseases	15273.074	.029	.952	0.001

Table 6: Cost and Complications.

	Std. Error	Standardized Coefficients Beta	t	Sig.
(Constant)	268538.58		1.051	.003
Serum glucose (mmol/l)	53039.465	.098	1.199	.002
S_Creatinine (mmol/l)	22682.870	.056	.223	.003
HbA1C (%)	39242.222	.100	.501	.003
Triglyceride (mg/dl)	283.623	.026	.268	.002
Total cholesterol (mg/dl)	482.815	.014	.149	.001
LDL-Chol (mg/dl)	586.022	.025	.307	.003
HDL- Chol (mg/dl)	1379.778	.062	.767	.744

*Dependent Variable: Cost

Table 7: Multiple Linear Regression taking cost as a dependent variable.

can increase survival and the intrival without complications and the cost effectiveness ratio will be able to compare favorably with many healthcare programs' which reduce the burden of diabetic retinopathy even in developing countries. In the study of American Diabetes Association 2001 has shown that the increasing prevalence of type 2 diabetes also brings with it a commensurate increase in the burdens of a chronic disease. Diabetes and its related complications incur both societal (indirect) and economic (direct) costs. In 1997, an estimated \$98 billion was spent on diabetes. Approximately \$44 billion was spent on direct medical care and treatment, which is concomitant to present study which incur huge medical cost [14]. In National Center for Chronic Disease Prevention and Health Promotion 1999,

Preventive care practices, in *Diabetes surveillance*, it has been showed that early detection of diabetes is important because initiating an early treatment of the disease may postpone complications. Besides an increased prevalence of diabetes, there is also an increase in the number of complications attributed to diabetes, which can affect every organ of the body. Poor glycemic control can lead to heart disease, stroke, blindness, kidney disease, amputations, and dental disease. This analysis will review journal articles and published sources on diabetes-related foot, oral, and eye complications, which strongly support the present study [15]. Diabetic retinopathy, the main contributor to blindness, is a term for certain abnormalities in the small blood vessels of the retina that are caused by diabetes. Early detection of diabetic retinopathy is essential since retinopathy is often asymptomatic. When first diagnosed, approximately 21% of people with type 2 diabetes show some retinopathy. People with type 1 diabetes tend to develop retinopathy after three to five years from the onset of diabetes [14]. One of the strongest predictors of developing retinopathy is the length of time an individual has had diabetes; the longer the duration, the greater the probability of developing retinopathy [4]. Besides routine eye exams, glucose control is recommended to prevent the onset of retinopathy. Although early detection and treatment of eye complications could prevent approximately 90% of new cases of diabetes-related blindness [16], many diabetics in the United States are not receiving the recommended preventive eye screenings [4]. This study is strongly support the present study.

Conclusion

Proper management with regular screening substantially reduces the expenditure related to care of patients with diabetic retinopathy and related complications even in a developing country. Strategies aimed at preventing DR and early detection of the onset of retinopathy complication will reduce medical costs in a substantial way. Timely management of patients with diabetes is both clinically astute and cost effective. It can increase survival and the interval without complications, and the cost effectiveness ratio will be able to compare favorably with many accepted healthcare programmes. This indicates that comprehensive care can reduce the burden of diabetic retinopathy even in a developing country. Future studies could also cast further light on the non-hospital costs of diabetic retinopathy complications. These findings support the common notion of the local health workers that diabetic retinopathy have become major economic and non-economic and public health problems among the subjects. Inadequate awareness regarding the control of diabetic retinopathy disease clearly indicate future directions to improve the health of those patients with type 2 diabetes and to undertake prevention programs that are culturally oriented, family centered, and community-based targeting healthful living. The study will provide macro-background for economic and clinical researchers to proceed further. Since there is no clinical and cost effectiveness analysis of the treatment of retinopathy complications from Diabetes, this will be a pilot and pioneer study in a poor country like Bangladesh where out of pocket expense of patients and resource constraint of providers can be addressed.

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