



## ASSESSING THE IMPACT OF COMPLICATIONS ON THE DIRECT MEDICAL COSTS OF TYPE 2 DIABETES MELLITUS OUTPATIENTS

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### ABSTRACT

**Purpose:** Type 2 diabetes is associated with a number of serious long-term complications, which are a major cause of morbidity, hospitalisation and mortality in diabetic patients. The purpose of the study was to assess the impact of complications on the costs of type 2 diabetes mellitus outpatients.

**Methods:** The study was done between May 2007 and September 2008. The recruited subjects were patients admitted into the Dr Sardjito Hospital for treatment of type 2 diabetes who failed with oral antidiabetic medications. Patients were divided into four broad categories defining their complication status in terms of no complications, one or more microvascular complications, one or more macrovascular complications or one or more of each microvascular and macrovascular complications. The prevalence of complications and associated costs were assessed prospectively for 6 months.

**Results:** In total, 84.35% of patients in type 2 diabetes mellitus had at least one complication, with 8.7% having microvascular only, 48.7% having macrovascular only and 28.7% of the total having both microvascular and macrovascular complications. Among the patients with microvascular complications, 67% had neuropathy, 17% renal damage, 10.6% ulcus diabetic, and 6.4% had retinopathy. Among the patients with macrovascular complications, 63.3% had hypertension, 29.2% dyslipidemia, 4.2% coronary heart failure, 1.7% ischemic heart disease, 0.8% hypertension heart disease and 0.8% had angina. In patients with both microvascular and macrovascular complications, the total cost of management was increased by up to 130% compared to those without complications.

**Conclusion:** Complications have a significant impact on the costs of managing type 2 diabetes mellitus. This study has confirmed that the prevention of diabetic complications will not only benefit the patients, but potentially reduce overall healthcare expenditure.

**Key words :** complication, type 2 diabetes mellitus, direct medical cost, cost analysis, Indonesia

### INTRODUCTION

Diabetes is a group of disorders characterized by high glucose levels that cause unique eye, kidney, and nerve complications and an increased risk for cardiovascular disease<sup>1</sup>. These factors contribute to an increased risk of illness and death which places a significant burden on health care system. The risk of cardiovascular disease, especially coronary heart disease, is two to five times higher in people with diabetes mellitus than in people without diabetes<sup>2</sup>. About 65% of deaths in individuals with type 2 diabetes are related to cardiovascular disease or stroke<sup>3</sup>.

Maintaining glycemic levels as close to the non-diabetic range as possible has been demonstrated to have a powerful beneficial impact on diabetes-specific complications, including retinopathy, nephropathy, and neuropathy. In type 2 diabetes, more intensive treatment strategies have likewise been demonstrated to reduced complications<sup>4</sup>. The management of diabetes alone renders considerable expenditure, however, macrovascular and microvascular complications are the major cause of healthcare costs<sup>5</sup>. The prevention of those diabetic-related long-term complications which make a significant contribution to the cost of diabetes is the major goal of the effective management of the disease<sup>6</sup>.

In the United States, management of chronic complications associated with diabetes, such as cardiovascular, renal and ophthalmic disease, accounted for approximately 27% of these expenditures. Diabetes care currently absorbs approximately \$1 of every \$7 US healthcare dollars. Most of the morbidity, mortality, and cost of diabetes care is a direct result of treatment of potentially preventable complications. Cost of care for those with diabetes is 4

times higher than for the population without diabetes<sup>7</sup>. Observations from managed care organizations in the United States suggest that annual management costs for people with diabetes are 1.5 to 2 times higher than those for people without diabetes. As diabetes-related complications develop and progress, management costs increase<sup>8</sup>. In the European CODE-2 study on type 2 diabetes costs, presence of both microvascular and macrovascular complications led to 3.5-fold increase in total direct medical cost when compared to diabetes without complications<sup>5</sup>. This increased use of resources is related to a broad range of factors including higher outpatient costs, higher pharmaceutical costs, higher rates of hospitalization, and longer hospital stays during admissions related to complications<sup>9</sup>. These complications substantially increase not only the economic burden for healthcare systems, but also the patient's risk for disability, death, and diminished quality of life<sup>10</sup>. The purpose of the study was to assess the impact of complications on the costs of type 2 diabetes mellitus outpatients.

### METHODS

The study was done between May 2007 and August 2008. The recruited subjects were patients admitted into the Dr Sardjito Hospital for treatment of type 2 diabetes. Random sampling technique was adopted to enroll the subjects into the study. The data collection was done by interviewing and reviewing the medical records and data obtained include socio-demographic details, diabetes and its complications, treatment details, and cost of outpatient care. Only direct medical costs, those directly related to delivery of the health care service, are included in the estimates reported here. Average per-patient total costs were estimated by

applying unit costs to the likely course of treatment for each complication.

For analysis, people were classified into four broad categories of complication status: no complications, one or more microvascular complication only, one or more macrovascular complication only, one or more of each of microvascular and macrovascular complications. The individual conditions and interventions defining microvascular and macrovascular complication status are detailed in Table 1. The macrovascular complications considered in this analysis are hypertension, hyperlipidemia, hypertension heart disease, congestive heart failure, angina pectoris, and ischemic heart disease. Microvascular complications include various levels of nephropathy, retinopathy, symptomatic neuropathy, and foot ulcers. While foot ulcers have been considered as neuropathic microvascular complications in this analysis, there is also a macrovascular component to these complications.

Patients who have visited the hospital at least six time were included in the study. A written informed consent was obtained from all the patients. The study was approved by the Ethics Committee of the Faculty of Medicine Gadjah Mada University, Indonesia. Expenditures for prescription drugs and physician services in 2008

were taken directly from corresponding database records. All expenditures are reported in 2008 US dollars.

Descriptive statistics was done to analyze the demographic details. Median with range was reported for cost details. Student's 't' test and Mann-Whitney U test were done wherever appropriate to determine the statistical significance between the groups. A p value of <0.05 was taken as statistically significant. The data was analyzed using SPSS (Statistical Package for Social Sciences) software version 15.0.

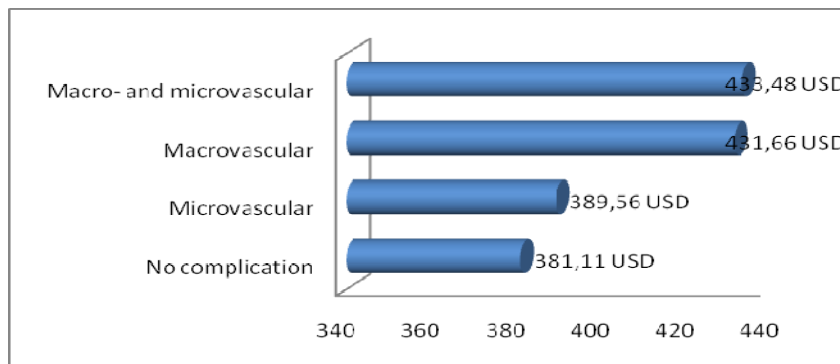
## RESULT

Of the total study subjects, 84.35% of patients in type 2 diabetes mellitus had at least one complication.

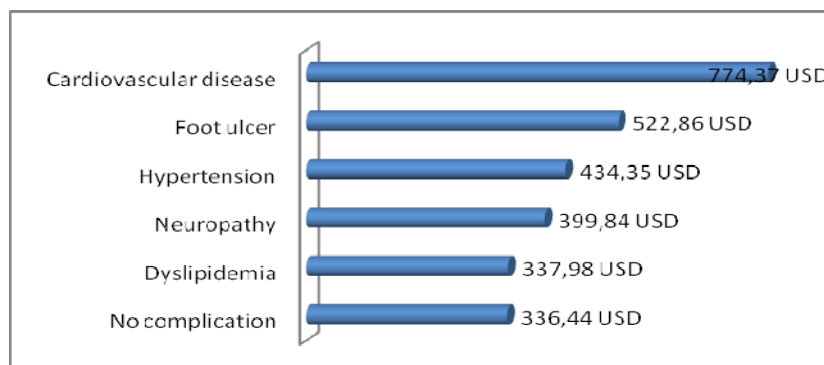
The prevalence of microvascular and macrovascular complications are shown in table 1. Of patients with microvascular complications, 67% had neuropathy, 17% renal damage, 10.6% ulcus diabetic, and 6.4% had retinopathy. Among the patients with macrovascular complications, 63.3% had hypertension, 29.2% dyslipidemia, 4.2% coronary heart failure, 1.7% ischemic heart disease, 0.8% hypertension heart disease and 0.8% had angina.

**Table 1: Clinical Characteristics of the Patients Studied**

Characteristics	Complication Category No complication	Macrovascular	Microvascular	Macro-and Microvascular
n (%)	15.65	54.78	5.22	24.35
Age (years) (mean±SD)	56.83±12.92	63.48±8.20	64.17±3.19	62.96±6.85
Male/Female (%)	55.55/44.45	50/50	53.97/46.03	39.29/60.71
Duration of diabetes (median)	10	11	10.5	11.5
Treatment (%)				
Insulin	72.22	58.73	83.33	39.29
Triple Oral therapy	27.78	41.27	16.67	60.71
HbA1c (%) (median)	7.9	7.7	8.7	9.4



**Fig. 1: Direct medical costs associated with classified of diabetes complications**



**Fig. 2: Direct medical costs associated with diabetes complications**

Table 1 shown that patients with poor glycemic control (HbA1c >9%) were more likely to have both micro and macrovascular complications than those with good glycemic control. Patients experiencing poorer glycemic control may have had diabetes for a longer amount of time and may have been suffering from long-term complications.

A patient with no complications was found to cost, on average, \$381.11 for 6 month in direct medical costs. The presence of microvascular and macrovascular complications led to 2.22 % and 13,26% increase in costs compared to patients with no complication, respectively (Fig 1). Those patients with both microvascular and macrovascular complications increased costs by 13.74% over those

without complications. Managing patients with both microvascular and macrovascular complications together represented a marked increase in expenditure.

Figure 2 indicated that macrovascular disease is the major component of these costs, and they are incurred much earlier than those due to managing microvascular complications. Our analysis found that macrovascular complications were associated with up to 130 % of the costs for outpatients treatment in patients for diabetes-related complications. People with 2 or more types of comorbidity had even higher health care expenditures (p=0.012). It appears that as the number of types of comorbidity increases, health care expenditures increase (Fig.3).

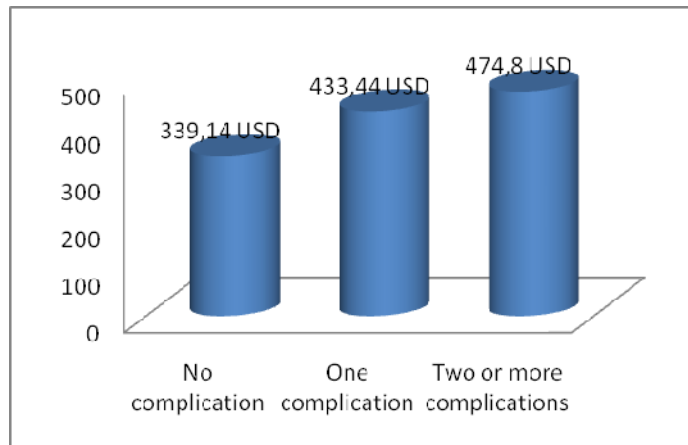


Fig. 3: Direct medical costs associated with the number of diabetes complications

## DISCUSSION

We studied the consumption of healthcare resources and the associated economic costs in a sample of patients with type 2 diabetes mellitus at the Dr Sardjito Hospital. The management of diabetes alone renders considerable expenditure, however, macrovascular and microvascular complications are the major cause of healthcare costs. From our study result, it is clear that the presence of complications has a substantial impact on the costs for managing patients with type 2 diabetes mellitus. An independent association was demonstrated between the total costs and the number of complications (p=0.012). Redekop et al. (2002) and Ballesta et al. (2006) demonstrated the association between the costs of the disease and the variables of age, the use of insulin, presence of macrovascular complication, presence of both macro- and microvascular complications, and hyperlipidemia<sup>11,12</sup>.

These findings of our study confirm that a large proportion of the costs associated with chronic complications of diabetes. These particular costs especially for cardiovascular complications due to costs associated with pharmacological treatment and with the diagnostic and therapeutic procedures for cardiovascular complications. The average state costs of cardiovascular complications were calculated to be \$774.37 per patient for 6 month. These included the cost of medications, physician visits, and monitoring cardiology tests. Congestive heart failure, ischemic heart disease, hypertension heart disease, and foot ulcers are associated with high resource use attribute to diabetes. Macroangiopathy, particularly cardiovascular disease, are the leading causes of morbidity and mortality in individuals with type 2 diabetes<sup>13,14</sup>. Data from a study in the United States indicated that renal and cardiovascular complications seem to be the most prevalent and were associated with particularly high costs. The greatest cost savings would be achieved by preventing major cardiovascular events<sup>15</sup>. Several plausible biological mechanisms have been proposed to explain a possible direct relationship between chronically elevated blood glucose levels and coronary heart disease. Glucose can react with many different proteins, causing structural alterations and subsequently impaired protein and tissue function.

Such alterations, including the formation of advanced glycation end products, may contribute to long-term complications in diabetes as well as to endothelial dysfunction, changes in arterial distensibility, plaque formation, and atherosclerosis<sup>14</sup>.

Macrovascular disease is predicted to be the major component of the costs accounting for over one third of the costs accrued over a lifetime from managing diabetes related complications. Therefore, reduction of the risks of macrovascular complications should also ease the costs of complications. Whether these results in net savings will depend on the cost of the treatment strategy used to achieve the lower risks. This strategy should address risk factors for cardiovascular disease such as smoking, high blood pressure, and hypercholesterolemia; it is not yet certain that improved glycemic control will also help, but recent epidemiological evidence suggests that macrovascular disease is related to postprandial glucose<sup>16,17</sup>.

Complications of microvascular include retinopathy, nephropathy, and neuropathy. Neuropathy occurred in 67% of the patients. Gordoys et al. (2003) reported that approximately 3.9% of people in the U.S. have been diagnosed with diabetes, and 50% have some degree of peripheral neuropathy. In the U.S. the total annual cost of treating distal symmetric polyneuropathy and its complications was \$10.91 billion<sup>18</sup>. Diabetic neuropathy is one of the major long-term complications associated with diabetes that can cause considerable morbidity and mortality<sup>19</sup>.

For renal disease treatment, our results yielded an aggregate population cost per person of \$433.48, much lower than for cardiovascular disease (\$774.37). Subjects without renal disease had higher average treatment costs than those without cardiovascular disease, presumably because the former group included a substantial complement of subjects with cardiovascular disease. Our estimates of the costs of nephropathy are much lower than a recent report of empirical estimates of the costs of renal disease in diabetes. Costs of renal disease were lower than average in subjects with less advanced cardiovascular disease, probably because the primary pharmacologic treatment for microalbuminuria and proteinuria was ACE-inhibitor therapy. In our staging algorithm,

ACE-inhibitor use was the single most common reason a subject was included in cardiovascular stage 1. Therefore, treatment of microalbuminuria and proteinuria could have added little to the cost of treating stage 1 cardiovascular disease. Despite the higher costs of renal disease in affected subjects, our results indicate that substantially more money would be saved on a population basis by preventing the development or progression of cardiovascular disease rather than renal disease. This is because late-stage cardiovascular disease is much more common than late stage renal disease.

Much of this cost is preventable through improved diet and exercise, prevention initiatives to reduce the prevalence of diabetes and its comorbidities and improved care for people with diabetes to reduce the need for costly complications<sup>20</sup>. Obviously, efforts to delay or avoid complications would be beneficial not only to the patient, but also to the family members and the health care system. The costs provided here give one piece of the economic analysis that will need to be performed to evaluate new interventional therapies for diabetes. As macrovascular disease costs arise early, it represents the major component of lifetime costs. Improving control of known risk factors for cardiovascular disease has an enormous potential for reducing the risk of developing complications and lowering health care costs associated with those complications. This study supports the initiatives by the National Diabetes Education Program to promote awareness of the benefits of optimizing blood pressure and cholesterol levels as well as blood glucose levels.

Several limitations of our study should be noted. First, we drew data from administrative health care databases, and, as such, relied on the accuracy and completeness of the records. Second, not all diabetes complications entered the model. It is possible that these complications do not independently contribute to direct medical costs. Finally, the costs in our model reflected only direct medical costs from the perspective of a hospital. The costs did not include patient out-of-pocket costs, direct non medical costs, indirect costs and intangible costs (eg. cost due to suffering).

In summary, our study indicated that diabetes complications have a substantial impact on total direct medical costs of type 2 diabetes mellitus. The prevention of type 2 diabetes-related complications will provide benefit to the patients as well as potentially reduce the overall healthcare expenditures. The present findings demonstrated that the burden of diabetes and its complications on the individual and on the health care system is significant.

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