



Economic Burden of Diabetic Tuberculosis Patients

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Authors' contributions

This work was carried out in collaboration between all authors. Author DMIA designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Author SASS managed the literature searches and reviewed the final draft. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aim: To assess the impact of diabetes mellitus (DM) on the cost of the tuberculosis (TB) treatment.

Study Design: Prevalence based cohort

Place and Duration of Study: Penang General Hospital, Hospital USM, and– Univesiti Malaya Medical Center; 2005 – 2008.

Methods: Study patients were placed in the TB only, DM only, or DM-TB groups, with each group including 200 patients. Information related to demographics, chronic disease comorbidity, duration of hypertension (HTN) and DM, and economic variables were obtained from the patients' medical files both at the beginning and end of the study period. The economic burden of DM-TB patients was assessed from hospitalization periods, frequency of clinic visits, and diagnostic requests.

Results: Durations of DM and HTN were 9.2 and 5.6 years, respectively, for the DMonly group compared to 5.3 and 1.1 years, respectively, for DM-TB subjects. For both diabetic groups, diabetes preceded HTN, with onset of HTN occurring approximately 4 years after patients were diagnosed diabetic. Approximately 86% of DM only subjects suffered additional comorbidity, and 44.5% had three or more coexisting chronic diseases compared to 56% and 11.4%, respectively, in the DM-TB group. The hospitalization period was 10.2 days for the DM-TB group compared to 7 and 4 days for the TB only

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and DM only groups, respectively; however, 43% of TB only subjects needed surgical intervention compared to 17% in the DM-TB group. The total cost was RM4530 (US\$1234.3) for the DM-TB group compared to RM3082.8 (US\$840) and RM6945.26 (US\$1892.40) for the TB only and DM only groups, respectively.

Conclusions: DM antedated HTN in our patients. Durations of both DM and HTN were longer for the DM only group. The number of diagnosed chronic diseases and overall treatment cost was higher in the DM-TB group compared to TB only group, but lower compared to the DM only group. The TB only group required the most surgical intervention.

Keywords: Tuberculosis; diseases burden; diabetes mellitus; cost; disease precedence; antedate; diabetes mellitus; hypertension; Malaysia.

1. INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*, and remains the leading cause of death from a bacterial infection. In 2011, TB claimed 1.4 million lives worldwide. [1] Malaysia is a country with an intermediate TB load (81 per 100,000 persons), and diabetes mellitus (DM) is quickly reaching an alarming level of 15.2% among those 18 years of age and older [2]. The TB load is also overwhelmed with the increasing rate of HIV co-infection, multiple drug resistant TB, homelessness, poverty, and illiteracy. The economics of all chronic diseases and diabetes in particular has become a matter of great interest due to increased life expectancy as well as changes in priorities of health care services that have taken place in many countries. The more market-oriented approach to health services has sharply affected its the rational distribution, [3], and thus people in low income brackets who cannot pay according to the market cost suffer from the inequality of health services [4]. DM and HTN coexist in many patients, and each one is considered as a risk factor for the other [5]. However, the relationship of the two conditions in terms of precedence and duration of coexistence are currently lacking.

There are reports that coexistence of DM and TB increases the complications and cost of treatment [6], but more specific studies related to burdens of patients having both TB and DM are lacking. We aimed to assess the impact of diabetes on the economic burden of TB, hoping that this study both highlights the magnitude of financial resources for patients with both DM and TB and improve proper TB treatment planning.

2. METHODS

This was a prevalence-based cohort study assessing the burden of patients with coexisting DM and TB. Details surrounding study centers, study approval, treatment outcome, and design are published elsewhere [7]. Our patients were selected from outpatient clinics at three teaching hospitals in Malaysia using a stratified random selection method. All subjects who were attending outpatient diabetic clinics from October 2004 to March 2005 were included in the selection. This six month's duration was based on length of appointments. TB patients were divided into diabetic patients and TB only subjects. For TB patients, because the data was not sufficient, the study period was not confined to that of DM (6 months), and was extended to include patients who were attending TB clinics from October 2004 till December 2005. Cases (DM-TB group) were compared separately with TB and DM only groups. Demographic data, chronic disease comorbidity, and economic variables were

collected from patients' medical records. DM and HTN duration were measured to identify which disease precedes the other and the effect on the disease burden. Cost-related variables were confined to direct medical costs, such as outpatient clinic visits, hospitalization, and study group diagnostics for a 2-year period, which is usually required for the diagnosis, treatment, and follow-up of TB cases. In addition, some cost-related information, such as service charges, was collected from hospital administrations and related departments. The cost was calculated for each patient by adding the cost of services, including diagnosis, medicine, hospitalization, and clinic visits (as shown in Table 3). The mean cost was used for all groups. The Malaysian Ringgit (RM) value in December of 2006 was used, where RM 3.67 equaled US \$1. Most charges were standard, as all study centers were governmental; patients only paid service charges for medicine (RM6) and hospitalization (RM3 per night). Some patients were subjected to hospitalization charges near market price (RM150 per day for stable patients, RM180 for intensive care patients); and clinic charges were RM70 for the first three visits, RM50 for the next three visits, and RM30 for any subsequent clinic visits. Data were processed using Statistical Package for Social Sciences (SPSS), version 11.5, and statistical significance was achieved when $p \leq 0.05$. Fisher's Exact Test was used for categorical variables with 2 x 2 contingency tables, and Pearson Chi square (χ^2) for data with larger contingency tables. Two tailed t-tests and Mann Whitney U tests were used to compare normally and non-normally distributed data sets, respectively. Multiple regression analysis was used to assess the strength and relation of variables accountable for total costs. The cost of TB only patients was adjusted for the age.

3. RESULTS

Information related to study centers, sampling procedure, inclusion and exclusion criteria, demographics, and smoking and substance abuse are described in a previous publication [7]. Two hundred subjects were selected for each group. Diabetic patients were stratified into 3 age groups. A total 1100 medical files of TB infected patients were reviewed; 510 were excluded. Two hundred diabetic TB patients were identified, and 200 non-diabetic TB patients were randomly selected from the remaining 390 patients. The study population contained 3 ethnic groups. The prevalence of Malays was 80, 62, and 42.9% in DM only, TB only, and DM-TB groups, respectively. There was a higher percentage of Chinese in the DM-TB group (37.1%) compared to the TB only and DM only groups (27.5 and 13%), respectively, while Indians represented 13.7, 10.5, and 7% of the DM-TB, TB only, and DM only groups, respectively. There was a higher percentage of males in the DM-TB group (72%) compared to the TB and DM only groups (58.3 and 45.5%), respectively. The age of the DM-TB patients was 55.1 years compared to 44.4 and 52.2 years for patients in the TB only and DM only groups, respectively. The average weight of the patients in the DM-TB group was 56.1 kg compared to 49.3 and 63.3 kg for patients in the TB only and DM only groups, respectively.

The duration of diabetes and hypertension were longer for the DM only group compared to the DM-TB group (9.2 and 5.6 vs. 5.3 and 1.1 years, respectively). The duration of DM was longer than hypertension, and diabetes mellitus antedated the onset of hypertension for approximately 4 years (Table 1). Approximately 28% of the DM-TB group was hypertensive compared to 68.5% of the DM only group and 12.5% in the TB only group ($P < 0.001$). Approximately 18% of patients in the DM-TB group exhibited dyslipidemia, compared to 71.5% in the DM only group and 4.5% in the TB only group. Approximately 86% of DM only subjects suffered additional comorbidity and 44.5% were diagnosed with three or more coexisting chronic diseases, compared to 56% and 11.4%, respectively, in the DM-TB group.

Only 37.6% of patients in the TB only group had additional comorbidity and 8.2% had three or more comorbidities. The mean number of chronic diseases at the beginning of the study period was 1.0 for DM-TB compared to 0.7 and 2.3 for the TB only and DM only groups, respectively (Table 1). The mean number of chronic diseases that developed during the study period was 0.1 for DM-TB compared to 0.08 and 0.26 the TB only and DM only groups, respectively. Hypertension, arthritis, and dyslipidemia occurred significantly more frequently in females and Malays ($P < 0.01$) (Table 2).

The mean hospitalization period was longer for DM-TB (10.2 days) patients and over 7 and 4 days for TB only and DM only patients, respectively. An equal frequency of clinic visits was seen for DM-TB and TB groups. Members of the DM only group visited the clinic most and incurred a higher cost for laboratory and medicine than the DM-TB group. The DM-TB group, however, had a higher number of laboratory requests and costs as well as more radiology requests compared to the TB only group. Approximately 43% of the TB only subjects needed surgical intervention, with only 17% of patients in the DM-TB group requiring intervention ($P < 0.01$). The DM-TB patients accumulated higher costs for chronic medication (RM1663.5 [US\$453.2]) compared to RM631.7 (US\$172.1) for the TB only group ($P < 0.01$), but less (RM5160 [US\$1406]) than the DM only group (Table 3). The overall total cost within the two year follow-up was lower for the DM-TB group (RM4530 [US\$1234.3]) compared to the DM only group (RM6945.26 [US\$1892.4]) ($P < 0.01$), but higher compared to both unadjusted and age adjusted TB only group (RM3082.8 [US\$840], 3650 [US\$994.5]; respectively) ($P < 0.01$). Multiple linear regression analysis showed that chronic medicines, frequency of clinic visits, laboratory requests, and hospitalization were mainly accountable for the total costs.

4. DISCUSSION

The DM only group exhibited a higher mean number of chronic diseases and longer duration of DM and HTN than the DM-TB group. Consistent with other studies [8,9], the number of patients with three or more comorbidities was also higher in our DM only group. Approximately 95.5% of Malaysian diabetic patients had microvascular complications [10], and Ramchurn et al. [11] showed that diabetes correlated with joint disorders. Approximately 30% of diabetic subjects experienced various types of musculoskeletal disorders [12]. Additionally; the number of comorbidities that developed during the follow-up period was higher for the DM only group, potentially as a result of a longer duration of diabetes in this group. This result matches that of Janghorbaniet al. [13], in which 20.8% of DM patients developed hypertension within a 2.9-year period. Diabetes is known to be more prevalent in older age groups [14], and because our DM-TB group encompassed older patients, shorter durations of HTN and DM were not expected for our DM-TB patients. The low prevalence of chronic diseases in the DM-TB group could be related to the shorter duration of diabetes in this group compared to the DM only group.

As mentioned previously, for both DM only and DM-TB groups, diabetes antedated hypertension by 4 years. Al-Haboriet al. [15] reported hypertension as a risk factor for type 2 diabetes mellitus; however, knowledge of their relationship in terms of precedence and duration in situations of comorbidity is lacking. The prevalence of HTN in our DM only group was 2.5 times higher than the 27.8% that represents the Malaysian general population [16] and 1.2 times of the 58.4% reported by Heydariat al. [17]. Moreover, Heydariat al. [17] assessed only newly diagnosed diabetic patients, while our subjects exhibited HTN for a longer period of time. Dyslipidemia was also higher in the DM only group, consistent with the longer duration of HTN in our patients. Heydariat al. [17] also reported a prevalence of dyslipidemia in 73.5% of their diabetic patient sample.

The DM-TB group showed a higher prevalence of chronic diseases, such as hypertension and dyslipidemia, more newly developed comorbidities, longer hospitalization, and longer duration of HTN compared to the TB only group. While the prevalence of HTN in the DM-TB group remained similar to the 27.8% of the general population, TB only group had less frequency, likely due to our subjects being younger (44.4 years) and underweight (49.2 kg), which is a hallmark of TB. Although TB only group had some cases that required longer hospitalization, but DM-TB patients were more frequently hospitalized.

Table 1. Prevalence of chronic diseases and duration of HTN and DM

Variables	Cases		Controls	
	DM-TB	TB	TB	DM
Diabetes				
Median duration (mean)	3 years (5.3)	Not applicable	Not applicable	8 years (9.2)
P-value (Mann Whitney)		Not applicable	Not applicable	$P^{++}<0.001$
Hypertension	N0. (%)	N0. (%)	N0. (%)	N0. (%)
Prevalence	56 (28)	25 (12.5)	137 (68.5)	
P- value (Pearson χ^2)		$P< 0.001$		$P^{++}< 0.001$
Median Duration (mean)	0.0 years (1.1)	0.0 (0.35)		3 years (5.6)
P-value (Mann Whitney)		$P<0.001$		$P^{++}<0.001$
Lipid Profile	N0. (%)	N0. (%)	N0. (%)	N0. (%)
Prevalence	36 (18)	9(4.5)	143 (71.5)	
P- value (Pearson χ^2)		$P<0.001$		$P^{++}<0.001$
Number of Comorbidities				
Median (mean)	1 (1)	0.0 (0.7)		2 (2.3)
P-value (Mann Whitney)		$P< 0.01$		$P^{++}<0.001$
Comorbidies Developed				
Median (mean)	0.0 (0.1)	0.0 (0.08)		0.0 (0.26)
P-value (Mann Whitney)		$P> 0.05$		$P^{++}<0.001$
Comorbidity Classes	N0. (%)	N0. (%)		N0. (%)
No comorbidity	85 (44)	121 (62.4)		28 (14)
1 Comorbidity	51 (26.4)	44 (22.7)		26 (13)
2 Comorbidities	35 (18.1)	13 (6.7)		57 (28.5)
3 Comorbidities	22 (11.4)	16 (8.2)		89 (44.5)
P-value (Fisher exact test)		$P<0.001$		$P^{++}<0.001$

P compares difference between DM-TB and TB only; P^{++} compares difference between DM-TB and DM only.

Females comprised the majority of the DM only group and also exhibited more frequent comorbidity. Additional reports highlight more chronic diseases in females [18,19]. In addition, Tsang et al. [20] reported increased chronic pain and anxiety-depression duality in females. Women are more inclined to report illness and utilize medical care services more than men [18,21]. The Malay race suffers from many chronic diseases, which could putatively be related to lifestyle variation.

Overall treatment costs were higher for DM-TB subjects compared to the TB only group. Both groups of TB patients (TB with or without DM) had numerous factors that are costly. Subjects of the TB only group exhibited more extra-pulmonary TB cases (TB of the spine, specifically), which made diagnoses problematic and increased the number of required operations, expensive radiology, and multidisciplinary consultations. On the other hand, the DM-TB group showed DM comorbidity with more severe TB pulmonary cases that required

increased hospitalization. However, the DM-TB group had more pulmonary TB patients, and these patients typically require radiological procedure and multidisciplinary interventions that are cheaper than those used for extra-pulmonary TB patients. Therefore, the impact of DM on TB is not clear. The cost of our TB treatment was higher than the numbers reported by Elamin et al. [22] (US \$86) and Aye et al. [23] (US \$396), possibly resulting from the expenditures of co-treating multiple diseases. The cost of chronic medication in our study groups accounted for 20, 34, and 74% of total costs for TB only, DM-TB, and DM only patients, respectively. This calculated cost was near the market rate, while Elamin et al. [22] assessed costs using either free or the lowest hospital charges. Our study period was also longer (24 months).

Table 2. Interrelation of certain variables among all study subjects¹

Variables	Arthritis	Hypertension	Dyslipidemia
Race and Chronic D			
Indian + others	1 (2.4)	12 (28.6)	13 (31)
Chinese	5 (5)	43 (43)	23 (23)
Malay	16 (6.2)	138 (53.5)	143 (55.4)
P-value (Fisher E.T)	P< 0.01	P< 0.01	P< 0.01
Gender and Chronic D	Arthritis	Hypertension	Dyslipidemia
Male	9 (3.9)	99 (42.1)	84 (35.7)
Female	13 (7.9)	94 (57)	95 (57.6)
P-value (Fisher E.T)	P< 0.0	P< 0.01	P< 0.01

¹This table does not compare differences between study groups, but instead shows the relationship between noted variables among study subjects.

DM only patients required higher treatment costs than those in the DM-TB group. Duration of hypertension and DM, body weight, number of coexisting diseases, clinic visits, lab requests, and medication amounts were all higher in the DM only group. The cost of medicine alone accounted for 79% of this total cost. Our findings are in agreement with other reports that found that medical expenditures were 1.7 times higher for patients diagnosed with diabetes for 5 years or more compared to the sum for patients who were diagnosed as diabetic for a shorter time period [24]. Patients who had both macro- and micro-vascular complications incurred 2.5 times higher costs compared to patients with no complications [8]. Lin et al. [25] reported both a higher hospitalization period (8.8 days) and frequency of clinic visits (35.8 times per diabetic patient per year).

Table 3. Costs related variables among study groups

Variables	Cases	Controls	
	DM-TB	TB only	DM only
Hospitalization Period			
Median (mean)	5 (10.2)	3 (7)	0.0 (4.1)
P-value (U test)		$P^* > 0.05$	$P^{**} < 0.001$
Clinic Visit Frequency			
Median (mean)	10 (11.55)	10 (11.6)	12 (13.8)
P-value (U test)		$P^* > 0.05$	$P^{**} < 0.001$
Laboratory			
Median Requests (mean)	20 (39.3)	17(21.2)	34(50.38)
P-value (U test)		$P^* < 0.01$	$P^{**} < 0.01$
Median Costs* (mean)	175 (265.56)	145(182.9)	281(338.9)
P-value (U test)		$P^* < 0.01$	$P^{**} < 0.01$
X- Rays			
Median Requests (mean)	7 (7.1)	5 (5.8)	2 (2.4)
P-value (U test)		$P^* < 0.01$	$P^{**} < 0.01$
Median Costs* (mean)	210 (302.8)	195 (317)	90 (191.3)
P-value (U test)		$P^* > 0.05$	$P^{**} < 0.01$
Surgical Operations			
Median (mean)	0.0 (0.17)	0.0 (0.43)	0.0 (0.15)
P-value (U test)		$P^* < 0.01$	$P^{**} > 0.05$
Costs of Medicines*			
Anti-TB drugs (mean)	256 (302.3)	258 (286.8)	Nil
P-value (U test))		$P > 0.05$	Nil
Cost Other medicines* (mean)	764 (1663.5)	0.00(631.7)	4810 (5160)
P-value (U test)		$P^* < 0.01$	$P^{**} < 0.01$
Total Costs*			
Median (mean)	2829(4530)	2197 (3082.8)	6143 (6945.26)
P-value (U test)		$P^* < 0.01$	$P^{**} < 0.01$
Age adjusted Cost* (TB only)	2829(4530)	2280 (3650)	-----

P^* compares the difference between DM-TB and TB only; P^{**} compares the difference between DM-TB and DM only. *Costs are in Malaysian Ringgit (1 US\$ = 3.67 Ringgit).

5. CONCLUSION

Females and Malays had more chronic disease comorbidities. DM antedated HTN by a mean time of four years. The DM only group suffered from an increased number of chronic diseases and longer durations of DM and HTN, more clinic visits, higher laboratory costs and medication, and higher overall total cost than the DM-TB group. The hospitalization period was longer for DM-TB compared to TB only and DM.TB only subjects required increased surgical intervention over the DM-TB group. Total cost was mainly dependent on chronic medication, frequency of clinic visits, and hospitalization. The DM-TB group showed DM comorbidity with more severe TB pulmonary cases that required increased hospitalization. However, the DM-TB group had more pulmonary TB patients, and these patients typically require less radiological procedure and multidisciplinary interventions than those used for extra-pulmonary TB patients. Therefore, the impact of DM on TB is not clear.

CONSENT

Not applicable.

ETHICAL APPROVAL

The study was approved by the Clinical Research Centre of Penang Hospital ((6 im.SL/CRC/HPP/05), the ethical committee of the Malaya Medical Centre (S13/05/12-2005), and the manager of the Hospital Universiti Sains Malaysia (HUSM/11/020).

LIMITATIONS

Patients' related information was retrieved from medical records. Missing data and wrong interpretation was possible.

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COMPETING INTERESTS

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