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Economic Burden of Diabetes Mellitus on Patients with Respiratory Failure Requiring Mechanical Ventilation during Hospitalizations

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A B S T R A C T

Objectives: To examine the economic burden of diabetes mellitus (DM) on medical expenditure among patients with respiratory failure (RF) requiring mechanical ventilation during hospitalization. **Methods:** We extracted the data from Taiwan National Health Research Insurance Database for those adult patients on their first hospitalization for RF requiring mechanical ventilation between 2004 and 2010. We examined associations between medical expenditure and the presence of comorbid DM. We performed independent t tests, chi-square tests, and multivariate linear regression analysis to identify factors associated with excess medical expenditure. **Results:** Of 347,961 patients hospitalized with first occurrence of RF requiring mechanical ventilation, 123,023 (35.36%) patients were documented to have a previous diagnosis of DM. Patients with RF and DM were sicker and consumed more health care resources than did patients with RF without DM. After adjusting for the specified covariates, mechanically ventilated patients with RF and DM consumed at least US $618 more of total inpatient medical expenditure than did patients with RF without DM. There were statistically significant interactions between age and DM on their total inpatient medical expenditure regardless of discharge status. **Conclusions:** DM was associated with more severe disease status and higher consumption of medical expenditure during hospitalizations among mechanically ventilated patients due to first occurrence of RF in Taiwan. These findings provide scientific evidence to facilitate appropriate resource allocation and formulate programs for higher quality of care in the future in Taiwan and other countries.
Keywords: diabetes mellitus, economic burden, hospitalization, respiratory failure.

Introduction

Mechanical ventilation (MV) in patients with respiratory failure (RF) is associated with an incremental cost of up to US $1500 per day in the United States [1,2]. Based on the National Health Insurance (NHI) report in Taiwan, the cost associated with MV-dependent patients with RF was approximately US $22,530 per year [3]. The MV utilization increased by approximately 180% from 1997 to 2004 in Taiwan [4]. Thus, the greater use of MV among patients with RF accounts for the large economic burden on limited resources of the health care system in Taiwan and other countries.

It is estimated that 15% to 25% of the patients with RF require prolonged MV because of difficult weaning [5,6]. Factors associated with difficult weaning in patients with RF included increasing blood urea nitrogen levels and lower comatose scores [7]. Furthermore, the increasing incidence of MV dependence was associated with the burden of comorbidities [8]. In particular, the increased incidence of MV among younger patients was associated with a higher burden of obesity, diabetes, or renal failure [8]. While diabetes mellitus (DM) was documented to be one of the most frequent complications for ventilator-dependent patients who were treated at long-term care hospitals [9], Cheng et al.'s study [4] indicated that DM was

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one of the leading diagnoses among patients with RF requiring MV.

Patients with DM consumed 4.3 times more health care costs than did patients without DM, and it accounted for 11.5% of the total health care cost in Taiwan [10]. Although those critically ill patients with DM were prone to develop more complications [11], these diabetic, critically ill patients had equal or even decreased mortality compared with those without DM [12,13]. As a result, decreasing mortality among critically ill patients might incur longer hospitalization and add on more economic burden either on the perspectives of health care providers and/or the Bureau of National Health Insurance (BNHI) in Taiwan. The aim of this study was to examine the economic burden due to DM among patients with RF requiring MV during hospitalization.

Methods

Data Sources

In Taiwan, the BNHI has contracted with 97% of hospitals since 1996 to ensure sufficient access to health care. Currently, the coverage of both population and hospitals is as high as 99%. The BNHI has proposed and implemented many strategies to ensure appropriate use of NHI resources in the hope of controlling the rapid growth of health care utilization and expenditures. For instance, the Integrated Delivery System (IDS) has encouraged hospitals to set up respiratory care centers and/or respiratory care wards. These step-down units provide high-quality, integrated care for patients with prolonged MV use and help with cost containment. Moreover, those sicker patients who consume more medical expenditure because of comorbid diseases and need long-term care (including RF with MV for 21 days or more) were qualified to be assigned with the catastrophic illness certificate (CIC). The co-payments for these patients are waived in accordance with NHI policy in Taiwan. Those patients with RF involved in the IDS programs or assigned with CIC were also evaluated for their excess medical expenditure.

This study used data from inpatient claims of the National Health Research Insurance Database, which covered all inpatient claims of the sampling insured Taiwanese population, during the study period of 2004 to 2010. The variables that were examined and evaluated included patients' demographic characteristics, disease status (e.g., primary and secondary admission diagnosis), and health care utilization (e.g., dates of admission and discharge, IDS, CIC, and hospital expenditure). The components of medical expenditure included all NHI-covered fees for diagnosis, laboratory tests, radiography services, therapeutic treatment, surgery, rehabilitation, blood products, hemodialysis, special medical supply, prescribed medications, and other services incurred during hospitalization. This study was exempt from the Institutional Review Board because the National Health Research Insurance Database contains only de-identified patient information and is publicly available through the proper application process.

Study Population

We evaluated beneficiaries aged 18 years or older who were hospitalized because of the first occurrence of RF during the years 2004 to 2010 on the NHI inpatient claim data. To minimize concern for data skewness, we excluded 7100 cases (2%) that were considered outliers because of extreme inpatient medical expenditure incurred during hospitalization.

Study Design

We conducted a population-based retrospective data analysis. For those included beneficiaries, the first occurrences of RF during hospitalizations in the years 2004 to 2010 were evaluated. We defined those patients with in-patient diagnoses *International Classification of Diseases, Ninth Revision, Clinical Modification* codes of 518.81, 518.82, 518.83, and 518.84 as patients with RF and those who had the *International Classification of Diseases, Ninth Revision, Clinical Modification* code of 250 as patients with DM. In our study, all patients with RF, either with DM or without DM, were ever mechanically ventilated during hospitalizations. We also evaluated the disease records regarding their dysfunctional organ systems during hospitalizations and grouped the systems into six categories (e.g., circulatory collapse, renal failure, hepatic failure, and coagulation defects). These categories were adapted from the results of expert panel discussions and modified definitions obtained from Marshall et al.'s and Gall et al.'s studies [14,15].

Those beneficiaries who lived in areas belonging to the first and fourth quartiles of population density in Taiwan were grouped into low and high urbanization, respectively. We used Charlson's comorbidity index to estimate disease burden and as a controlling variable for potential confounding [16]. We summed all claimed reimbursement expenditures that were associated with RF for total hospital expenditure during hospitalizations. We calculated the durations between admission and discharge dates during hospitalization as "length of stay (LOS)" and categorized the LOS into three levels. The medical expenditures were expressed in US dollars (US $1 = 31.64 New Taiwan Dollar in 2010). All the aforementioned variables were assumed to be related to medical expenditure that occurred in hospitals.

Specifically, discharge status in the NHRID was categorized as "recovered," "transferred to outpatients care," "deceased," "against-advice discharge," "critical against-advice discharge," "transferred to another hospital," and others. In Taiwan, the majority of citizens prefer to receive end-of-life care at home and so hospitals usually allow patients to be discharged under critical condition on the request of the patients' family. Therefore, we classified discharge status into two groups: alive and dead (including critical against-advice discharge).

Statistical Analysis

We used independent *t* tests and chi-square tests to analyze patients' sociodemographic characteristics, disease characteristics, their health utilization, and corresponding hospital characteristics among patients with first occurred RF with DM and without DM during hospitalization. As for the medical expenditure, it is expected to have some extreme values. Therefore, the truncated mean and the corresponding simple and multiple linear regression models were performed to assess the excess medical expenditure between patients with RF and DM and patients with RF without DM, stratified by their death status, after excluding 2% of the cases. Sensitivity analyses to include all cases were performed to confirm the robustness of all findings. The aforementioned variables of interest, including patients' characteristics, disease status, hospital settings, involvement of catastrophic illness status, and/or IDS, were expected to correlate with the consumption of medical expenditure through the consensus of focus group discussions. Thus, these variables were taken into account into different models when performing multiple regression analyses. Furthermore, the interaction effects of total hospital expenditure with age and DM were examined. The statistical significance level was set at a two-sided *P* value of less than 0.05. All analyses used the SAS software version 9.3 (SAS Institute, Inc., Cary, NC).

Results

Patient Characteristics

For the study period 2004 to 2010, the inpatient claims for 347,961 patients with RF were retrieved for further analyses. There were

123,023 (35.36%) patients documented to have a previous diagnosis of DM. The incidence of RF during hospitalization occurred mostly in persons aged 60 years or more. Patients with RF who had DM were more commonly men, had more comorbidities, and more dysfunctional organ systems than did those without DM (Table 1). Patients with RF and DM used more health care resources, hold CIC, had involvement in IDS programs, and were sicker (higher prevalence of various organ dysfunction) than did patients with RF without DM (Table 2).

Total Medical Expenditure during Hospitalizations

Regardless of being alive or dead on discharge, patients with RF and DM consumed significantly higher mean medical expenditure than did patients with RF but without DM . After adjusting for age, sex, hospital scale, urbanization of hospitals, number of comorbidities, and LOS (model 1), patients with RF and DM had significantly higher total medical expenditure (extra $1119 and $1469, respectively) than did their corresponding counterparts (Table 3). After the adjustment of aforementioned covariates in model 1 and those variables of CIC and dysfunctional organ systems, it was found that patients with RF and DM consumed more money (extra $682 for alive and extra $618 for dead) than did patients with RF without DM (in model 4). Compared with the adjustment of holding the CIC (model 1 vs. model 3 and model 2 vs. model 4), involvement in IDS programs was not associated with changes in medical expenditure among patients with RF and DM or patients with RF without DM. After additional adjustment of holding the CIC, models 3 and 4 explained more additional variance of total medical expenditure than did models 1 and 2, respectively. Patients with RF and DM who did not survive had higher medical expenditures than did those who were alive at discharge. The findings were opposed after controlling for holding the CIC.

After adjusting for the holding of CIC, age, sex, hospital level, urbanization, number of comorbidities, LOS, and the existence of dysfunction organ systems, all groups had the highest total medical expenditure at the age of 18 to 29 years (Fig. 1). Alive patients with RF without DM had decreasing medical expenditure as age increased. Dead patients with RF without DM had a similar trend before the age of 50 to 59 years, but the expenditure increases with aging again after the age of 80 years, but at a slightly reduced rate. There were significant interactions between age and DM, regardless of discharge status ($P_s < 0.001$).

Furthermore, findings of sensitivity analysis regarding distributions of patient characteristics and effects of DM and alive status on total medical expenditure during hospitalization by including all cases were similar to those obtained from excluding cases in the extreme 2%. The regression analysis findings were exactly the same.

Discussion

This study shows that mechanically ventilated patients with RF and DM had greater comorbidity, dysfunctional organs/systems, and consumed more health care resources than did patients with RF without DM. After adjusting for the corresponding covariates, it was found that patients with RF and DM consumed more total inpatient medical expenditure, regardless of discharge status, than did patients with RF without DM. The holding of CIC was associated with more consumption of total medical expenditure among either dead or alive patients with RF and DM.

The prevalence of DM in Taiwan has increased to 9.2% [17]. The corresponding medical expenditure for DM accounted for 4.5% of all outpatient expenditure of the NHI and 1.1% of hospitalization expenditure in 2008 [18]. Patients with DM had higher mortality than did the general population, especially among males [19]. While DM was documented to be one of the most common comorbidities among patients with long-term MV [9], this study demonstrated that patients with RF and DM were sicker, used more health resources, and consumed more total medical expenditure than did patients with RF without DM. This was consistent with evidence from the literature [4,10] but did not correspond with the evidence found in septic patients with DM who developed acute RF [20].

Furthermore, dead patients with RF and DM consumed an additional US $618 in medical expenditure during hospitalizations than did those without DM after multivariate adjustments. This additional inpatient expenditure for patients with RF and DM represents approximately 61% of total expenditure on health care per capita in 2007 in Taiwan (= US $618/1050, where US $618 was the additional medical expenditure during hospitalization for dead patients with RF and DM in Taiwan) [20], and 20% of the total cost of willing to pay to cure DM per

Table 1 – Comparisons in demographic and disease characteristics between patients with respiratory failure with and without DM (2004–2010).

Variable	Respiratory failure, n (%)			P
	Non-DM (n = 224,938)	DM (n = 123,023)	Total (N = 347,961)	
Age (y)				<0.001
18–29	6,064 (2.7)	277 (0.2)	6,341 (1.8)	
30–39	9,541 (4.2)	1,231 (1.0)	10,772 (3.1)	
40–49	18,411 (8.2)	5,076 (4.1)	23,487 (6.7)	
50–59	24,406 (10.9)	12,589 (10.2)	36,995 (10.6)	
60–69	29,745 (13.2)	22,635 (18.4)	52,380 (15.1)	
70–79	59,837 (26.6)	42,553 (34.6)	102,390 (29.4)	
≥80	76,934 (34.2)	38,662 (31.4)	115,596 (33.2)	
Sex				<0.001
Female	78,528 (34.9)	55,297 (44.9)	133,825 (38.5)	
Male	146,363 (65.1)	67,716 (55.1)	214,079 (61.5)	
No. of comorbidities	0.9 ± 1.0	1.4 ± 1.2	1.1 ± 1.1	<0.001
No. of organ/systems dysfunction*	2.2 ± 2.7	2.6 ± 2.8	2.3 ± 2.7	<0.001

DM, diabetes mellitus.
* Missing values include 57 persons for the category sex, 2 in hospital level, and 2 in urbanization. Some values are presented as mean ± SD.

Table 2 – Comparisons in health utilization and disease statuses between patients with respiratory failure with and without DM.

Variables	Non-DM (n = 224,937), n (%)	DM (n = 123,0220), n (%)	P
Existence of dysfunctional organ system			
Circulatory collapse	103,948 (46.2)	64,201 (52.2)	<0.001
Renal failure	87,736 (39.0)	56,712 (46.1)	<0.001
Hepatic failure	74,339 (33.1)	49,699 (40.4)	<0.001
Coagulation defects	74,733 (33.2)	49,780 (40.5)	<0.001
Central nervous system failure	75,099 (33.4)	50,127 (40.8)	<0.001
Acidosis	75,596 (33.6)	50,481 (41.0)	<0.001
Length of stay (d)	39.0 ± 82.3	48.2 ± 81.9	<0.001
Length of stay categorized into three levels			<0.001
Short (≤7 d)	57,695 (25.6)	24,293 (19.7)	
Intermediate (8–21 d)	65,367 (29.1)	33,698 (27.4)	
Long (>21 d)	101,876 (45.3)	65,032 (52.9)	
Holding catastrophic illness card during hospitalization	44,578 (19.8)	33,464 (27.2)	<0.001
Involved in Integrated Delivery System (IDS) during hospitalization	17,791 (7.9)	13,739 (11.2)	<0.001
Type of corresponding hospitals			<0.001
Medical center	84,532 (37.6)	39,947 (32.5)	
Regional hospital	96,155 (42.7)	54,316 (44.1)	
District hospital	44,250 (29.7)	28,759 (23.4)	
Urbanization of hospitals			<0.001
Low	16,899 (7.5)	9,365 (7.6)	
Moderate	44,812 (19.9)	23,717 (19.3)	
High	163,226 (72.6)	89,940 (73.1)	

DM, diabetes mellitus.

patient per year (= US $618/3066) in Taiwan [21]. Additional expenses used to manage every two patients with RF and DM compared with patients with RF without DM during hospitalizations in Taiwan could be better utilized to treat other conditions in Taiwan as in the other countries (i.e., Medicare patients' receiving surgical care due to peripheral arterial disease in the United States [US $1450 ± 106]) [22]. Other studies have demonstrated that patients with DM, who were older, had cardiovascular disease, neuropathy, or heart failure contributed to more diabetic and non–diabetic-related medical expenditure and deaths [19,23,24]. Therefore, such profound economic burden warrants increased effort to improve current diabetic care programs designed to prevent patients with DM from disease progression or hospitalization.

Patients hospitalized with RF commonly require MV and usually receive a complex and technically sophisticated level of care. In Taiwan, IDS programs provide high quality of integrated care for patients with prolonged MV use to ensure cost-effective

Table 3 – Multiple linear regression analysis for comparison in total medical expenditure (US $) between patients with and without DM, stratified by outcomes on discharge.

DM	Alive		Dead	
	Coefficient ± SE	Adjusted R^2	Coefficient ± SE	Adjusted R^2
Unadjusted	2297 ± 64	0.01	2798 ± 90	0.01
Model 1	1119 ± 55	0.33	1469 ± 74	0.38
Model 2	822 ± 51	0.41	1087 ± 70	0.45
Model 3*	855 ± 51	0.42	710 ± 64	0.54
Model 4†	682 ± 48	0.47	618 ± 63	0.55

Notes. Model 1: adjusted for age, sex, hospital level, urbanization, number of comorbidities, and length of hospital stay.
Model 2: adjusted for covariates in model 1 plus circulatory collapse, renal failure, hepatic failure, coagulation defects, acidosis, and central nervous system failure.
Model 3: adjusted for age, sex, hospital level, urbanization, number of comorbidities and length of stay, and catastrophic illness card (model 1 plus catastrophic illness card).
Model 4: adjusted for covariates in model 3 plus circulatory collapse, renal failure, hepatic failure, coagulation defects, acidosis, and central nervous system failure (model 2 plus catastrophic illness card).
DM, diabetes mellitus; IDS, Integrated Delivery System; SE, standard error.
* The cost coefficients as for the alive and dead patients reduced to US $831 ± 50 and US $701 ± 64, respectively, after these were also adjusted for IDS.
† The cost coefficients as for the alive and dead patients reduced to US $ 662 ± 48 and US $ 614 ± 63, respectively, after these were also adjusted for IDS.

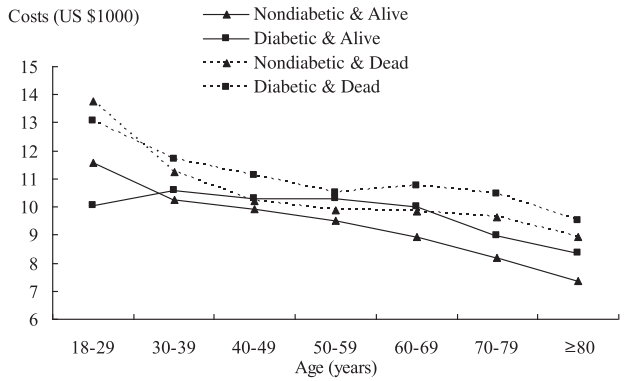

Fig. 1 – Comparison of total medical expenditure (US $) among patients with respiratory failure with and without DM after adjustments, stratified by status on discharge. ***Note.*** **The adjustment covariates included age, sex, hospital level, urbanization, number of comorbidities, length of hospital stay, existence of dysfunction systems, and holding the catastrophic illness card. DM, diabetes mellitus.**

utilization of medical resources [25]. Accordingly, the newly ventilator-dependent patients are allowed to stay up to 21 days in intensive care units and up to 42 days in respiratory care centers as per the health policy restriction in the IDS program. The implementation of IDS programs for patients with RF in Taiwan was successful [7], similar to programs developed in Italy [26]. Our results, however, showed more economic impact of holding CIC on the medical expenditure among patients with RF and DM during hospitalization, while the IDS program had a negligible impact on the inpatient medical expenditure. These findings corresponded with the phenomena that the BNHI had higher reimbursement rates for patients with CIC than did patients involved in IDS programs because these patients had greater disease severity and required more intensive care.

Although the NHI plays a stabilizing role in the society in Taiwan, the increasing incidence of catastrophic illnesses and RF would result in not only economic burden but also society burden while the population is aging. In 2008, there were 19,246 patients with CIC held due to long-term MV, representing the third leading cost for total medical expenditure and the second per capita cost among patients with CIC [18]. The claimed reimbursement of medical expenditure among patients with listed catastrophic illnesses (3.17% of all insurers) accounted for one fourth of all NHI expenditure [3]. Similar to other health care systems throughout the world, the issues of controlling costs, allocating available resources, enhancing the quality of care, improving beneficiaries' health, and ensuring equity of medical access for sicker patients and others in Taiwan remain.

Nevertheless, this study has some limitations. This study did not include outpatients and nonhospital costs, in terms of indirect cost, or other out-of-pocket co-payments. It is important to include these costs for evaluating the overall economic burden of RF due to DM even if the trend of impacts would not change significantly. This study focused on only those beneficiaries with their first occurrences of RF during hospitalizations in the years 2004 to 2010. In other words, those who had repeated visits to hospitals due to RF were excluded from further analysis. Thus, this study is applicable to only patients with DM or without DM during their first occurrence of RF in hospitals. From the NHI perspective, such patients with RF were considered very ill and are reimbursed for most of their medical expenditure because they need more intensive medical care in hospitals. As such, their outpatient expenditure was not the major concern when managing their RF. Furthermore, the lack of laboratory data and severity scores (e.g., the Acute Physiology and Chronic Health Evaluation II) and the use of diagnostic practice by the *International Classification of Diseases, Ninth Revision, Clinical Modification* codes may not reflect the disease severity. The detailed data on the utilization of MV were not included. The variability in respiratory care models in different medical settings might be the issue. The holding of CIC and involvement in IDS programs for each patient, however, would be key elements to ensure similarity of care models.

With the large sample size in this study, the statistically significant results might be due to the occurrence of type I error. Thus, the extent and scale of each variable or coefficient would be more beneficial to be interpreted but not the significant levels.

Last, the distribution of medical expenditure was still skewed to the right after removing 2% of cases and the corresponding testing of normality (one sample Kolmogorov-Smirnov) was rejected ($P < 0.05$). The sensitivity analyses to include all cases for all findings did not change the results at all. Although the excess medical expenditure during hospitalization was the major concern from NHI and providers' perspectives in this study, we performed multivariate regression analyses after excluding 2% of extreme values. Using generalized linear model of log-transformed approach, as Morales et al. [27] and Pasquale et al. [28] did, solves the problems of having skewed data of cost. The interpretation of the exponentiated coefficient β for diabetes status is the ratio of the expected geometric mean of costs for patients with DM over the expected geometric mean for patients without DM. Different analysis methods, including generalized linear model, ordinary least squares using linear regression, median quantile regression, Winsorizing, or propensity score case matching, would either overestimate or underestimate the extrapolated cost on adjusting for the key variable or not [29]. There was no conclusion, however, on which approach is better off. The goodness of fit for data using ordinary least squares linear regression might not be perfect. The interpretation of mean medical expenditure, however, might be easier than the relative value of cost after transforming it back to exponential value from log values. Specifically, the value of medical expenditure is understood by clinicians and general health policy makers who have no economic background as in the other population study to describe the determinants of health care expenditure and associated factors in Korea [30]. Ideally, further analyses using more appropriate approaches might be needed to verify the results in this study.

Conclusions

The presence of DM as a comorbidity significantly affects disease status and increases hospital medical expenditures among mechanically ventilated patients due to the first occurrence of RF in hospitals. It is beneficial to understand the extent of economic burden of DM and its impact on mechanically ventilated patients due to RF in Taiwan. This information can be used to help develop and implement sound public health strategies for programs aimed at improving DM management and reducing the large health care burden in Taiwan in the future.

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