EVALUATION OF DIABETES MELLITUS AND ITS COMPLICATIONS AS CONTRIBUTING CAUSES OF MORTALITY IN A GENERAL HOSPITAL (2016–2019)

Avaliação do diabetes mellitus e suas complicações como causa associada ao óbito, no período de 2016 a 2019, em um hospital geral

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ABSTRACT

Objectives: To evaluate diabetes mellitus (DM) as the underlying and contributing cause of death, as well as its main comorbidities in patients who died at Hospital Edmundo Vasconcelos (HEV). **Methods:** This is an observational and retrospective study. We analyzed all death certificates at HEV from January 2016 to June 2019. Of these, 26 certificates were excluded. We evaluated sociodemographic characteristics, the prevalence of DM, and its macro and microvascular complications. The same variables were reviewed in the electronic medical records of patients. **Results:** No significant associations were detected between the sociodemographic variables and the prevalence of DM. According to the electronic medical record, we found that 138 individuals had DM, but only 77 of these had a death certificate that mentioned the presence of this disease. Diabetic patients were also more likely to develop coronary artery disease, peripheral arterial disease, and hypertension. **Conclusion:** DM was listed in the death certificate, either as the underlying or associated cause, in 18.5% of deaths, while the medical records showed a prevalence of 33.3% among deceased patients. This discrepancy underscores the underestimation of DM's contribution to mortality in death certificate data.

Keywords: diabetes, mortality, death certificate.

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INTRODUCTION

The World Health Organization (WHO) defines diabetes mellitus (DM) as a syndrome with multiple etiologies resulting from either a deficiency of insulin or an inability to perform its functions effectively. Insulin, a hormone produced by pancreatic β cells, is crucial for carbohydrate metabolism, as it facilitates the transport of glucose into cells to be converted into energy. A lack of insulin or resistance to its action leads to elevated blood glucose levels, resulting in hyperglycemia[1].

In 2021, over 537 million people worldwide were estimated to be living with DM, with approximately 90% of cases being type 2 DM[2]. In Brazil, the prevalence of DM is particularly concerning as the country undergoes epidemiological transitions, with chronic diseases related to aging, including DM, becoming increasingly prominent in public health[3].

Morbidities associated with DM are often due to a combination of disease duration and poor glycemic control. Following diagnosis, achieving glycemic control is the primary goal of treatment, as it can help prevent or delay both acute and chronic complications, improve quality of life, and reduce mortality[1,4].

Despite being a significant and growing health problem worldwide, approximately 75% of cases of DM occur in developing countries, including Brazil, where the prevalence of DM is expected to rise over the coming decades[2]. Additionally, DM is the third leading cause of premature mortality, surpassed only by systemic arterial hypertension and tobacco use[4]. Thus, DM is extremely important for public health, given its high prevalence and resulting macrovascular (such as cardiovascular, cerebrovascular, and peripheral vascular diseases) and microvascular complications (including retinopathy, nephropathy, and neuropathy).

Currently, the Brazilian Institute of Geography and Statistics (IBGE) and the Mortality Information System (SIM) of the Brazilian Ministry of Health, which was established in 1975, collect mortality data for the Brazilian population. Although SIM serves as the primary source of mortality data in Brazil and has expanded its scope significantly over the years, challenges remain in enhancing data quality, mainly due to the inadequate completion of the Death Certificate (*Declaração de Óbito* - DO), the system's standard document. The DO consists of three self-copying, sequentially prenumbered copies provided by the Ministry of Health and distributed by State and Municipal Health Departments according to a standardized nationwide flow[5].

DM can be recorded on the DO in three ways: in part I, as either an underlying cause of death or an antecedent condition, and in part II, as a condition that contributed to death but did not result in the underlying cause listed in part I6. However, mortality statistics are based solely on the underlying cause of death, which the WHO defines as "the disease or injury that initiated the chain of pathological events that led directly to death, or the circumstances of the accident or violence that produced the fatal injury[7]." While the underlying cause of death is a valuable indicator for public health, studying this variable alone does not capture the impact of other conditions that may have contributed to the death, such as DM[8,9].

Thus, analyzing mortality through multiple causes, rather than only the underlying cause, is essential, as most deaths result from a multicausal pathological process. Understanding all diseases and complications present at the time of death enables a more comprehensive profile of the population's health. Moreover, analyzing mortality due to multiple causes offers valuable insights for public health professionals, as it provides a richer dataset that better reflects disease prevalence within the population[10].

DM is estimated to contribute to 14.5% of global mortality from all causes—a number greater than the combined deaths from infectious diseases such as HIV/AIDS, tuberculosis, and malaria4. However, accurately estimating DM-related mortality remains challenging, as approximately one-third of countries lack quality epidemiological data on DM. Moreover, where data exists, mortality due to DM is often underestimated due to frequent omission of this diagnosis on death certificates. Possible reasons for such an omission include the physician's unawareness of the patient's DM diagnosis prior to death, a low suspicion of DM's contribution to death, or physical space limitations on the DO[6]. As a result, when only the underlying cause of death is considered, diabetes ranks between the 4th and 8th leading cause of death. However, studies analyzing multiple causes of death have shown that the actual number of DM-associated deaths may be up to 6.4 times higher[4]. This suggests that the contribution of DM to overall mortality is significantly underestimated when only underlying causes are assessed[6].

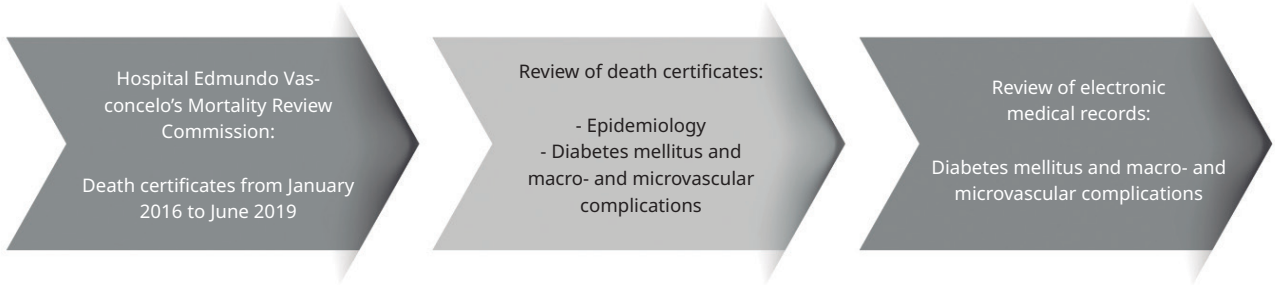
In this context, the primary objective of this study is to evaluate DM as both an underlying and contributing cause of death in patients who died between January 2016 and June 2019 at Hospital Edmundo Vasconcelos (HEV) in São Paulo, Brazil. Additionally, the study aims to analyze the presence of DM-related comorbidities, including macrovascular and microvascular complications such as coronary artery disease (CAD), cerebrovascular disease, peripheral arterial disease (PAD), diabetic retinopathy (DR), nephropathy, and neuropathy, in this patient group. By examining these factors, the study seeks to assess the extent to which DM-related mortality may be underestimated when it can be considered both an underlying and an contributing cause of death.

METHODS

This observational, retrospective study was conducted based on death certificates issued by HEV. The study sample includes patients who were hospitalized at HEV and died between January 2016 and June 2019. We analyzed all DOs from this period obtained through the hospital's Mortality Review Commission. Based on these DOs, we reviewed electronic medical records to identify the presence of DM in the patients' histories and/or as a primary diagnosis, as well as its major macrovascular and microvascular complications, including CAD, stroke, PAD, DR, diabetic nephropathy, and neuropathy and assessed their impact on the primary outcome (mortality).

All medical records were reviewed to account for cases where DM may not have been listed as the underlying or contributing cause of death on

FIGURE 1 - Flowchart describing the study's methods.



the DOs despite the presence of this comorbidity. Additionally, we collected sociodemographic data such as sex, race, age group, profession, education, and marital status. We examined a total of 440 DOs, excluding three of these due to incomplete data, and 23 pertained to patients referred to the Death Verification Service (Serviço de Verificação de Óbitos - SVO), which uses different documentation, potentially resulting in interpretation difficulties due to inconsistent information.

We performed descriptive statistics for all variables. For categorical variables, we used measures of complete cases, frequency, percentage, and cumulative percentage. For continuous variables, such as age, we used measures of complete cases, mean, standard deviation, maximum, and minimum.

The inclusion criteria for this study encompassed all deaths occurring at HEV during the specified period. Exclusion criteria included patients referred to the SVO or Legal Medical Institute (Instituto Médico Legal—IML) and those for whom complete information could not be obtained from the electronic medical records or DOs. **Figure 1** provides a flowchart illustrating the process performed in this study to analyze these deaths.

Descriptive statistics were obtained for all variables. For categorical variables, we reported counts, frequencies, percentages, and cumulative percentages. For continuous variables, such as age, we calculated the number of complete cases, mean, standard deviation, maximum, and minimum values.

To investigate whether DM is underestimated as a cause of death, we analyzed the frequency of various conditions potentially associated with DM (DR, diabetic nephropathy, neuropathy, CAD, PAD, and stroke) in patients with and without a DM diagnosis. We used a contingency table for this analysis and applied the Chi-square (χ^2) Association Test with Fisher's Correction, appropriate for cases with cell frequencies below 5. Statistical significance was set at 5% ($p < 0.05$).

The objective of this analysis was to determine whether the frequencies of specific causes of death differ between patients with and without DM. If no significant association is found, it suggests that the observed frequencies vary by chance. Conversely, a significant association would indicate that a DM diagnosis influences the distribution of these causes of death. We calculated the Odds Ratio (OR) to assess this possible association. When calculating the OR was not feasible, such as when variables had more than two categories, we interpreted the association based on the relative frequencies in the contingency table. Lastly, to determine whether DM was accurately identified in medical documentation, we compared the diagnosis in the DOs with that in the medical records, using the contingency table and the χ^2 test.

The project was approved by the Ethics Committee of the HEV/Fundação Instituto de Moléstias do Aparelho Digestivo e da Nutrição under the number 23949019.5.0000.0090/2019.

RESULTS

The study sample consisted of 440 individuals, with 26 excluded based on the criteria described above, resulting in a final sample of 414 patients. The mean age of the participants was 73.5 years (see **Table 1**), and 53% were women.

Regarding race, 82.8% were white, 7.5% were Asian, and 5.1% were Black (see **Table 2**). Regarding marital status, 46.8% were married, and 31.4% were widowed. Additionally, 28.9% of the sample had completed higher education.

Among diabetic patients identified in their medical records, 55.7% were male, and approximately 25.4% had

TABLE 1 - Age of deceased patients at Hospital Edmundo Vasconcelos in São Paulo, Brazil, between January 2016 and June 2019.

	AGE RANGE	STANDARD DEVIATION
Age	0,5 -105	18,26

Source: death certificates.

TABLE 2 - Race of deceased patients at Hospital Edmundo Vasconcelos in São Paulo, Brazil, between January 2016 and June 2019.

RACE	NUMBER OF PATIENTS	PERCENTAGE (%)
White	342	82.81
Asian	31	7.51
Black	21	5.08
Brown (*Pardo*)	16	3.87
Native-Brazilian	0	0
Unknown	3	0.73

Source: death certificates.

TABLE 3 - Diagnosis of Diabetes Mellitus according to different sources of data.

	ELETRONIC MEDICAL RECORD		
DEATH CERTIFICATES	**NO**	**YES**	**TOTAL**
Yes	2	75	77
No	274	63	337
Total	276	138	414

Source: death certificates and electronic medical records.

completed higher education. No significant associations were found between sociodemographic variables and the presence of DM ($p > 0.05$).

Considering only the DOs, DM was mentioned anywhere in the certificate of 77 patients (18.6%). Among these cases, CAD showed a statistically significant association ($p < 0.01$), with an Odds Ratio (OR) of 3.10 (95% CI = 1.52 to 6.19), indicating a 3.10 times greater likelihood of CAD in diabetic patients. A similar trend was observed for PAD, with a statistically significant χ^2 value ($p < 0.01$) and an OR of 3.83 (95% CI = 1.50 to 9.54), suggesting a 3.83 times greater likelihood of PAD in patients with DM. Additionally, diabetic patients were found to be 7.79 times more likely to have hypertension as a comorbidity (95% CI = 4.38 to 13.99).

DR was not documented in any cases, while nephropathy had a prevalence of 1.9% within the sample, although its etiology was undetermined in all cases. Diabetic neuropathy had a prevalence of approximately 0.7%.

A review of medical records revealed that 138 patients (33.3%) in the sample had a diagnosis of DM, compared to only 77 patients whose DO indicated DM, as shown in Table 3. This difference suggests that in 14.8% of cases, DM was not included in the DO despite being present in the patient's medical history.

Among the 138 patients with DM identified in the medical records, 19.1% had CAD as a complication, 15.9% had experienced at least one stroke (unspecified if ischemic or hemorrhagic), and 9.9% had been diagnosed with PAD.

In this analysis, the association between DM and CAD was statistically significant ($p < 0.01$), with an OR of 2.81 (95% CI = 1.66 to 4.81), indicating a 2.81 times greater likelihood of CAD in diabetic patients. A similar trend was found for PAD, with an OR of 4.53 (95% CI = 2.20 to 9.73), reflecting a 4.53 times higher likelihood of PAD in those with DM. The likelihood of stroke was also elevated in patients with DM, with an OR of 1.99 (95% CI = 1.12 to 3.52). Additionally, diabetic patients were 4.96 times more likely to have hypertension as a comorbidity (95% CI = 3.09 to 8.12).

Regarding microvascular complications, DR was not documented in the medical records of any patients. On the other hand, nephropathy was documented in 9.2% of patients, although the renal disease's etiology was unclear in 4.8% of cases. Diabetic neuropathy was identified in only 1.9% of cases.

DISCUSSION

Significant issues exist regarding the reliability and validity of cause-of-death information on DOs. These challenges stem from diagnostic inaccuracies, variations in causal interpretation, and identifying the conditions that contributed to death[8]. Additionally, the Brazilian DO provides only four lines for part I and two lines for part II, which can restrict space, particularly for patients with multiple chronic conditions, such as many patients with DM. As a result, other conditions, including hypertension, dyslipidemia, and chronic kidney disease, may compete for space on the DO due to the lack of a clear hierarchy among these comorbidities.

Consequently, DM is frequently omitted from DOs, as demonstrated in this study's sample, where DM was recorded in only 18.6% of cases on DOs, compared to 33.3% in medical records. This finding is even lower than that reported in a U.S. study by McEwen *et al.*[6], who documented DM in 39.0% of the death certificates analyzed, though DM was listed as the cause of death in only 10% of cases. That study concluded that death certificates underestimate the prevalence of diabetes among deceased patients, resulting in a biased representation of the causes of death for individuals with DM. In our study, however, the prevalence of DM in medical records was closer to that found on death certificates analyzed by McEwen *et al.*

Unfortunately, mortality statistics based solely on death certificates fail to reflect the actual mortality rate due to DM[12]. In another study by McEwen *et al.*[13] focusing on patients with type 1 DM, the disease was mentioned in any part of the death certificate in only 46% of cases and listed as the cause of death in just 16%. In another sample that included patients with both type 1 and type 2 DM, McEwen *et al.*[6] found an association between the likelihood of DM being mentioned on the death certificate and factors such as insulin use and disease duration,

although no significant differences were noted between DM types. In our study, however, it was not possible to identify insulin-dependent diabetics or determine disease duration, as many medical records listed only the DM diagnosis without details on treatment or duration of the disease. This limitation restricts our ability to accurately detail the characteristics of patients whose DM diagnosis is reported on the DO and compare them to those not mentioned in their death certificates.

Chronic complications of DM are increasingly common as the incidence of this metabolic disorder rises. In our study, macrovascular complications were noted in 24.1% of medical records, whereas microvascular complications were documented in only 9.4%. This disparity may stem from a tendency not to investigate or document microvascular diseases, compared to macrovascular diseases such as CAD and cerebrovascular disease, as these conditions are often linked to acute events and death. These findings differ from those of Santos *et al.*[14], who reported a prevalence of microvascular complications in 53.8% of patients with type 2 DM, significantly higher than in our study. However, it is essential to note the different patient profiles in the two studies: while Santos *et al.* conducted telephone interviews with patients registered with the Diabetic Association of Maringá and Region (ADIM), this study evaluated patients who had recently died.

In our study, no cases of DR were reported, which contrasts with existing literature showing that the natural progression of DM generally involves the development of microvascular complications across multiple sites simultaneously. However, in clinical practice, retinal changes, for example, do not necessarily imply concurrent renal impairment, and vice versa. Studies, however, indicate that when diabetic nephropathy is present, it is common to find some degree of DR in the same patient[15].

Our study also found that 19.1% of diabetic patients had CAD as a complication of DM (classified as ischemic cardiomyopathy). CAD is known to be a complex condition influenced by multiple inflammatory, metabolic, and genetic factors. Extended follow-up in the Diabetes Control and Complications Trial (DCCT) demonstrated a 57% reduction in cardiovascular mortality with intensive glycemic control during the initial study years[16]. This association appears relevant, as diabetic patients in our sample were found to be 2.81 times more likely to be diagnosed with CAD compared to non-diabetic patients.

Our results indicated a 4.96-fold higher likelihood of hypertension in diabetic patients compared to those without DM. This finding aligns with previous studies that reported a 2.4-fold increased prevalence of hypertension in diabetic patients. This association is significant, as hypertension is linked to various acute cardiovascular events, which are the leading cause of death in patients with type 2 DM4. It is worth noting that the stronger association observed in this study could be attributed to the sample consisting of recently deceased patients who likely had more severe conditions.

In summary, our study supports the hypothesis that data recorded on death certificates underestimates the contribution of DM to overall mortality. Furthermore, diabetic patients in our study exhibited a higher likelihood of macrovascular complications, such as CAD and PAD, as well as hypertension. However, this trend was not observed for microvascular complications, possibly due to limited investigation or documentation of these conditions in the medical records of critically ill patients. For instance, DR was not reported in any cases, suggesting that its prevalence, like that of DM, is underestimated.

To improve the reliability of death certificate data, a potential solution would be to add a dedicated field for recording major comorbidities, such as DM, hypertension, and smoking, regardless of their direct causal relationship with death[17]. Without such an intervention, death certificates will remain an unreliable source for estimating the association between DM and various causes of death. As a result, death certificates will not accurately measure DM's impact on life expectancy.

CONFLICT OF INTEREST

The authors attest they have no conflict of interest to declare.

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