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# Mortality Patterns in Patients with Diabetes Mellitus at a Nigerian Tertiary Hospital: A 10-Year Autopsy Study

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## Abstract

**Objectives:** Diabetes mellitus (DM) is a global health problem with associated high morbidity and mortality. This study was a retrospective review of post-mortem examination findings of hospitalised patients with DM for causes of death. **Materials and Methods:** A retrospective, cross-sectional autopsy review of all the patients with DM in our hospital between January 2008 and December 2017 was conducted. The causes of death were classified into cardiovascular, cerebrovascular, acute diabetic emergencies, infection, cancers and unnatural deaths. The demographic data and clinicopathological parameters were extracted, and the data were analysed using the SPSS software version 23. **Results:** A total of 1092 cases of autopsy were done within the study period, of which 91 cases were on patients with diabetes accounting for 8.3%. Infections with sepsis were the major cause of death, accounting for 51.6% followed by cardiovascular diseases (16.5%), cancers (14.3%), acute diabetic emergencies (6.6%) and cerebrovascular accidents (6.6%), with renal complications and road traffic accidents accounting for 2.2% each. Patients' age ranged from 31 to 84 years, with a modal age of 57 years. There was a male predominance with a male-to-female ratio of 1.5:1. Systemic hypertension co-morbidity was statistically significantly more common in patients aged 60 and above ( $P = 0.035$ ). The most common lesion observed in the kidneys was benign nephrosclerosis (43.2%). **Conclusions:** This study suggests that majority of our patients with diabetes mellitus die from infections with attendant sepsis. Older patients appear to have co-morbid systemic hypertension. Patient education on infection prevention and prompt treatment might be life-saving.

**Keywords:** Autopsy, diabetes mellitus, Ibadan, mortality

## INTRODUCTION

Diabetes mellitus (DM) is one of the chronic diseases that frequently cause significant morbidity and mortality in patients.<sup>[1]</sup> DM is a serious chronic disease that can alter an individual's quality of life. There is an increase in the prevalence of diabetes in Africa, with an estimated prevalence of 1% in the rural areas and 5%–7% in the urban sub-Saharan Africans.<sup>[2]</sup> The prevalence in Nigeria has also risen over time, and this could be due to increase in awareness and presentation in hospitals.<sup>[3,4]</sup> The prevalence of diabetes in Nigeria varies between rural and urban cities and between geopolitical zones. The north-west zone has the lowest prevalence of 3%, whereas the south-south zone has the highest prevalence of 9.8%.<sup>[3]</sup> The risk factors associated with diabetes in Nigeria include urbanisation, unhealthy dietary habits, physical inactivity and advancing age.<sup>[3]</sup>

The management of diabetes is life-long and is expensive. Most patients have to pay from their pockets due to the weak health insurance system of the country.<sup>[5]</sup> This has contributed in some ways to poor drug compliance and lower quality of life.<sup>[6]</sup>

The most common cause of death in patients with diabetes has been reported in some Nigerian studies to be DM emergencies, cerebrovascular diseases and diabetic foot.<sup>[1,7,8]</sup> Mortality is higher in male patients, those with strokes and diabetic foot ulcers.<sup>[7]</sup> Most of these studies derived their information from death certificates, with no indication on what proportion of the deceased had post-mortem examination. In a retrospective review of autopsy cases of patients with diabetes by Gibson and Char in West Indies, infectious disease was responsible for the

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majority of deaths.<sup>[9]</sup> Understanding the exact complications in patient with diabetes leading to death will help in policy decisions to reduce such mortality statistics. There are multiple studies in the developed nations establishing the complications of diabetes that resulted in mortality.<sup>[10-12]</sup> There is a paucity of autopsy-based studies in Nigeria showing the pattern of mortality among patients with diabetes. The objective of this study is to review the causes of death in patients managed for DM and to determine the pattern of distribution of such fatal pathologies.

## MATERIALS AND METHODS

This was a 10-year (January 2008–December 2017) retrospective review of post-mortem records of patients with DM managed in our institution and who had post-mortem examination in the Department of Pathology, University College Hospital, Ibadan, Oyo State, Nigeria. All autopsies were performed after obtaining consent from the deceased's relatives and all were complete and performed using standard methodology.

This study was conducted in accordance with the Helsinki Declaration on research ethics maintaining confidentiality and dignity of patients. Patient's name or other unique identifiers were not used in this study. Data such as cause of death, kidney lesions present, age, sex and presence of co-morbidity such as hypertension were extracted from the post-mortem records, and the clinical details, including the diagnosis of DM, were extracted solely from the clinical summary in the archived post-mortem reports. The causes of death were classified into cardiovascular (including ischaemic heart disease, myocardial infarction and pulmonary embolism), cerebrovascular, acute diabetic emergencies, infections, cancers and unnatural deaths (adapted from Gibson and Char<sup>[9]</sup>). The data were analysed using the IBM SPSS Statistics (version 23; IBM Corporation, Armonk, New York) and expressed as frequencies, median, means and mode, and the Chi-square test statistics were used to determine the associations between categorical variables.  $P \leq 0.05$  was considered statistically significant.

## RESULTS

During the study period, 1092 autopsies were performed, and 91 cases were on patients with diabetes accounting for 8.3% of these cases. Systemic hypertension was co-morbidity in 62.6% of the cases. Infections with sepsis was the major cause of death, accounting for 47 (51.6%) followed by cardiovascular diseases (15, [16.5%]), cancers (13, [14.3%]), acute diabetic emergencies (6, [6.6%]) and cerebrovascular accidents (6 [6.6%]), with chronic kidney diseases and road traffic accidents accounting for (2 [2.2%]) each [Figure 1]. Foci of infection include urinary tract (17 cases), lungs (11 cases), skin and soft tissues (8 cases), gastrointestinal tract (6 cases), heart (2 cases), brain (2 cases) and puerperal sepsis (1 case). Patients' age ranged from 31 to 84 years, with a modal age of 57 years. Those aged 60 and above had a higher incidence of death from cancers and cardiovascular diseases,

whereas those aged <60 years had a higher incidence of death from cerebrovascular accidents [Figure 2]. There was male predominance with 60.4% of the study population. The most common lesion seen in the kidneys was benign nephrosclerosis (43.2%) [Table 1]. Systemic hypertension co-morbidity was significantly more common in patients aged 60 and above [ $P = 0.035$ ; Table 2]. The majority of the causes of cardiovascular-related deaths were heart failure (53.3%), coronary heart diseases (33.3%), myocarditis (6.7%) and pericarditis (6.7%). Cerebrovascular diseases were mainly haemorrhagic (66.7%). Histomorphology of the coronary artery in the diabetic patient aged 60 and above showed severe coronary atherosclerosis [Figure 3] and that of the kidney revealed nodular glomerulosclerosis, arteriosclerosis and global sclerosis [Figure 4]. The specific cancer types seen in this study are shown in Table 3.

## DISCUSSION

Due to decline in requests for post-mortem examinations, not all patients who died from DM had autopsy. However, the cases we studied give an idea of the mortality patterns of patients dying from DM. The most common cause of death is from infectious diseases, with sepsis from multi-organ

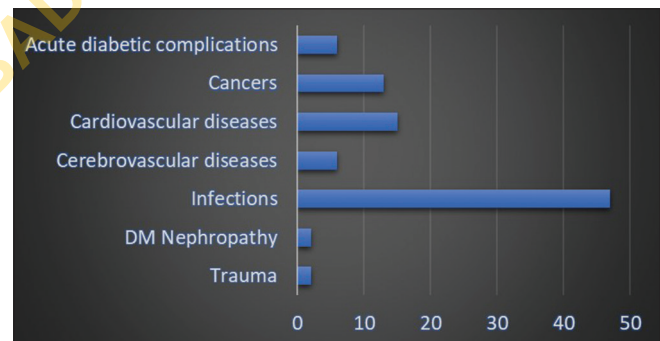


Figure 1: Bar chart showing the frequency of the causes of deaths

Table 1: Microscopic lesions seen in the kidney

Kidney lesions present	Frequency (%)
Acute tubular necrosis	3 (4.2)
Benign nephrosclerosis	32 (43.2)
Chronic pyelonephritis	3 (4.2)
Cortical cysts	4 (5.6)
Malignant nephrosclerosis	3 (4.2)
Microabscesses	4 (5.6)
Normal	24 (33.3)
Plasmacytoma nodules	1 (1.4)

Table 2: The age distribution of a co-morbidity (systemic hypertension)

Systemic hypertension	Age <60 (%)	Age 60 and above (%)
Yes	19 (50)	38 (71.7)
No	19 (50)	15 (28.3)

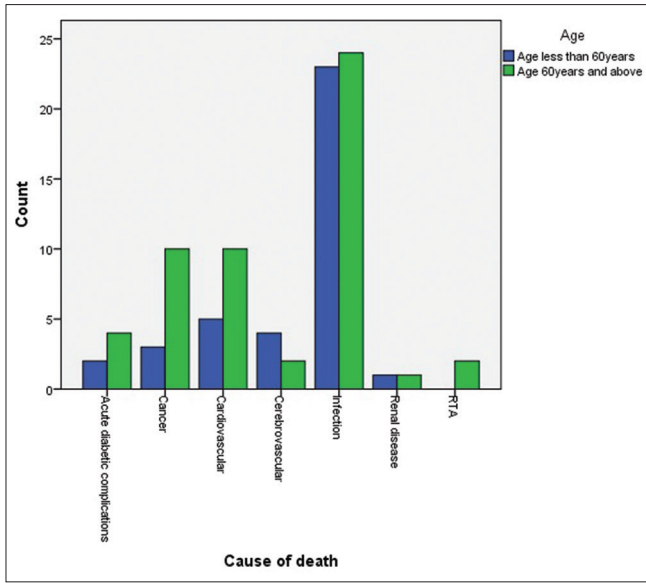


Figure 2: Bar chart showing causes death distribution with age

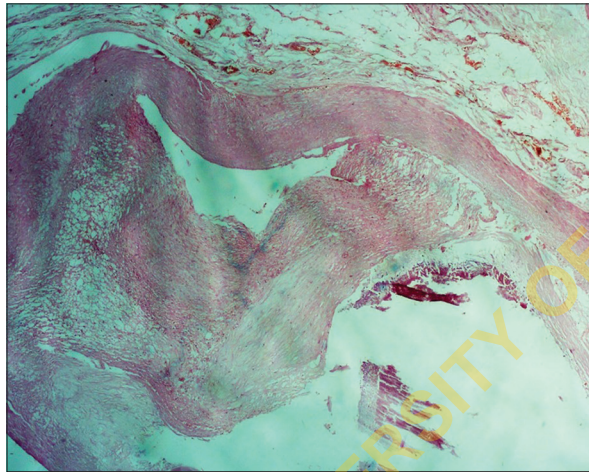


Figure 3: Section showing severe coronary atherosclerosis (H and E, x100)

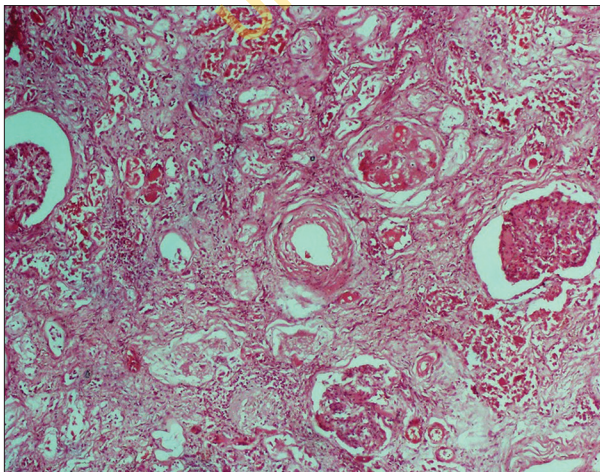


Figure 4: Section of a kidney showing nodular glomerulosclerosis, arteriosclerosis and global sclerosis (H and E, x100)

Table 3: The distribution of cancers in diabetic mellitus patients

Type of cancer	Frequency
Bronchogenic carcinoma	2
Cervical carcinoma	1
Laryngeal carcinoma	1
Pancreatic carcinoma	1
Cholangiocarcinoma	1
Colonic carcinoma	1
Craniopharyngioma	1
Gastric adenocarcinoma	1
Glioblastoma	1
Hepatocellular carcinoma	1
Prostate carcinoma	1
Multiple myeloma	1
Chronic lymphocytic leukaemia	1

failure being the major finding in infectious cases. Pneumonia, pericarditis and meningitis were other infections resulting in demise. Our finding is similar to the findings by Gibson and Char<sup>[9]</sup> in West Indies, a developing country like ours. These differ from most studies from developed countries that showed that cardiovascular diseases are the major cause of death in patient with diabetes.<sup>[10,11,13]</sup> Cardiovascular diseases are the second most common cause of death in our own study, and this observed difference might be accounted for by the relative poorer hygienic conditions in our environment. Previous non-autopsy studies from Nigeria show that the most prevalent causes of deaths in diabetics are diabetic emergencies, stroke and diabetic foot syndrome.<sup>[1,7,8]</sup> Deaths from infection or outright sepsis did not rank high in these studies that are based largely on death certificates. We think that much attention is not paid to the underlying factors that would have potentiated the acute diabetic emergency seen during presentation. Infections can be responsible for deterioration in glycaemic control with consequent acute presentation and fatality.<sup>[14,15]</sup> In the autopsy study by Lam, in Hong Kong, infection is the second most common cause after cardiovascular causes, with tuberculosis being the most common infection.<sup>[16]</sup> In our study, there was only one case of tuberculosis. There is the possibility that cases of known tuberculosis were not sent for post-mortem examination by the managing physicians. DM predisposes patients to immunosuppression with increased risk of having severe infections due to impaired immunity.<sup>[17,18]</sup> These infections lead to sepsis with multi-organ failure and consequent death.<sup>[16]</sup>

Cardiovascular diseases in the present study presented mainly with heart failure followed by coronary heart diseases. This differs from the study by Joron *et al.* that showed coronary artery disease to be the most common cause of cardiovascular disease in diabetics.<sup>[13]</sup> Furthermore, the lower incidence of ischaemic stroke was observed among the cerebrovascular diseases, with haemorrhagic stroke occurring much more frequently in the present study. Again, this contrasts with the

finding by Joron *et al.* who found near equal proportions of haemorrhagic and ischaemic stroke.<sup>[13]</sup> It is possible that fewer number of the cases dying from ischaemic reasons come to the autopsy room as the mortality are usually less acute and dramatic.<sup>[19]</sup>

Microscopic kidney lesions are relatively common but are not always significant enough to cause death. Diabetic nephropathy is attributed as the cause of death in 2.2% of our cases, whereas benign nephrosclerosis is the most common microscopic change seen in these patients' kidneys and this is similar to the report of the finding by Gibson and Char in West Indies. This value is lower in proportion when compared to the 8%–16% reported by Joron *et al.* in Canada and a WHO multinational study by Morrish *et al.*<sup>[10,13]</sup>

Malignant neoplasms are significant causes of mortality in patients with diabetes and are much more common in the elderly age group.<sup>[20]</sup> DM has been associated with increased risk for the breast, endometrium, bladder, liver, colorectal and pancreatic carcinomas and decreases the risk for prostate carcinoma.<sup>[20,21]</sup> The cancers seen in this study included cervical carcinoma, lung adenocarcinoma, cholangiocarcinoma, hepatocellular carcinoma and laryngeal carcinoma, and these differ from DM-associated malignancies highlighted previously.<sup>[20,21]</sup> There is no mesenchymal cancer observed in this review. Increased prevalence of carcinomas in diabetic patients has been shown by previous studies looking at the patterns of death at autopsy.<sup>[9,16]</sup> Our study did not show any relationship of the incidence with any of the malignant tumour, although Lam in his study observed an unusual high incidence of endometrial cancers among diabetics.<sup>[16]</sup>

Hypertension as a co-morbidity is significantly associated with older age which is similar to the epidemiology of hypertension in the general population. The coexistence of DM and systemic hypertension occur so frequently that it is thought that they share similar risk factors and that DM is a risk factor for systemic hypertension, although some patients usually develop hypertension before DM.<sup>[22,23]</sup> The presence of systemic hypertension in a diabetic patient is associated with higher incidence of complications and mortality, suggesting a potentiating effect on DM morbidity.<sup>[23]</sup>

## CONCLUSIONS

This study suggests that the majority of our DM patients die from infections with attendant sepsis. Older patients tend to have co-morbid systemic hypertension more often. Patient education on infection prevention and prompt treatment might be life-saving.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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