

MORTALITY AMONG CHILDREN AND YOUNG ADULTS WITH TYPE 1 DIABETES MELLITUS IN GHANA, A TEN-YEAR REVIEW

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ABSTRACT

Introduction: Acute complications of diabetes, particularly diabetic ketoacidosis (DKA) and hypoglycemia, can be fatal if misdiagnosed and hence not appropriately managed. This study was a 10-year mortality audit in children, adolescents, and young adults with T1DM attending the Pediatric and Adolescent Diabetes Clinic, Komfo Anokye Teaching Hospital, Kumasi, Ghana. **Methods:** A mortality audit consisting of a review of the medical records of participants and verbal interviews with caregivers and physicians in other hospitals who also attended to some participants just before death. The period spanned from January 2012 to December 2021. **Results:** A total of 14 patients out of 355 died within the 10 years giving a mortality rate of 3.9%. Seventy-one-point four percent (71.4%) were females. The mean age at diagnosis was 12.9 ± 5.2 years (Range: 8-14 years). The mean duration of diabetes before mortality was 7.4 ± 2.7 years (Range: 2-13 years). The mean age at death was 19.7 ± 3.8 years (Range: 15-28 years). Up to 50% of the participants died in district and teaching hospitals while the other 50% died at home. The identified causes of death included DKA, chronic renal failure, and osteosarcoma for those who died in hospitals. **Conclusion:** Mortality among children and young adults with T1DM occurred at all levels of health care with misdiagnosis of DKA as a significant cause. Most of the children and young adults with diabetes died at home and specific causes of death could not be found.

Keywords: Children, Misdiagnosis, Mortality, Type 1 diabetes mellitus, young adults

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is a chronic metabolic disease that results from the autoimmune destruction of beta cells of the pancreas leading to an absolute lack of insulin which results in persistent hyperglycemia (Kahanovitz et al., 2017). Children and adolescents with T1DM, therefore, need to be given exogenous insulin for life (Kahanovitz et al., 2017; Malik et al., 2014). If insulin is given well to achieve good glycaemic control, short- and long-term complications can be avoided (Malik et al., 2014) and quality of life improved. Although there has been significant improvement in the management of T1DM since insulin was discovered in 1921 (McKay et al., 2021), access to insulin in Africa remains precarious. So there is usually poor glycaemic control among children and adolescents with T1DM in Africa (Ngwiri et al., 2015; Noorani et al., 2016) resulting in the development of early complications and premature mortality.

Children, adolescents and young adults with diabetes attending Paediatric and Adolescent Diabetes Clinic (PADC) at Komfo Anokye Teaching Hospital (KATH) have access to free insulin since 2013 under the auspices of Life For A Child (LFAC), Australia, although access to insulin for children with T1DM who seek medical care in other health facilities in Ghana under National Health Insurance Scheme (NHIS) remains precarious as NHIS only pays for a part of the cost of insulin. As a result, the patients have to pay for the difference. Many families with children and young adults living with diabetes in Ghana live in extreme poverty (Fobil et al., 2010; Ghana Poverty Assessment., 2019), and so are unable to afford the difference in the cost of insulin and so the affected children and adolescents may not inject appropriate doses and at right frequencies. This can result in poor glycaemic control which could lead to complications including mortality.

Management of T1DM involves a multidisciplinary approach with the pediatric endocrinologist being the focal team player. The other team members include a diabetes nurse educator, psychologist, dietician, and the caregiver of the child or adolescent. Since 2008, the Paediatric Endocrinology Training Centres for Africa (PETCA) with secretariats in Nairobi, Kenya, and Lagos, Nigeria (Odundo et al., 2016; WDF., 2013) have trained many pediatric endocrinologists working in their respective countries across Africa. As a result, children and adolescents with diabetes are now being diagnosed, managed, and supervised to ensure good glycaemic control to avoid or minimize short- and long-term complications. Although insulin, glucometers, strips, insulin syringes, and lancets are supplied free of charge to children and young adults with T1DM who seek medical care at PADC, KATH, some of the patients are not able to afford transportation (Fobil et al, 2010) to come for regular appointments. This compels them to seek care at hospitals closer to them where medical care for T1DM may not be optimum (Kratzer J., 2012). Misdiagnosis of diabetes and its consequences in Ghana have been documented across all levels of health care, especially at the primary and secondary levels (Ameyaw, E., & Ameyaw, R., 2017; Ameyaw et al., 2017; Fobil et al., 2010), with some hospitals registering 100% mortalities.(Ameyaw et al., 2017).

Diabetic ketoacidosis (DKA) is a life-threatening emergency and can be fatal if not promptly recognized and immediately managed (Ameyaw et al., 2017; Ameyaw et al., 2017). Misdiagnosis of DKA would result in the administration of the wrong treatment, which could result in further complications such as cerebral edema and possible death (Ameyaw, E., Asafo-Agyei, SB., 2017; Poovazhagi, V., 2014; Rosenbloom AL, 2010). Children and adolescents with diabetes have more than 8-fold increased risk of sudden cardiac death compared to their counterparts without diabetes. (Lyng et al., 2019) Tu et al., (2008) in a retrospective review of the autopsy report in children, adolescents, and young adults with T1DM in Australia found the causes of death to include cardiovascular, respiratory, gastrointestinal diseases, infections, and acute complications of diabetes such as DKA and hypoglycemia. Severe hypoglycemia is suspected to be the cause of death in 4–10% of children and adolescents with T1DM. Severe hypoglycemia in patients with T1DM mostly occurs in the night when there is inhibition of counter-regulatory hormones such as cortisol, adrenalin, noradrenalin, and glucagon and results in no compensation for hypoglycemia. This mechanism can induce arrhythmias causing sudden unexpected death. (Lyng et al., 2019; Urakami T., 2020)

This study looked at mortality among children and young adults with T1DM over a 10-year period in Ghana.

METHODS

Study design: A mortality audit was done among fourteen children and young adults with T1DM who were attending PADC at KATH, Kumasi, Ghana who died during supervised and follow-up care between January 2012 and December 2021. This included a review of medical records of patients and verbal interviews with physicians and other health workers who also attended to them just before death. Caregivers of all the participants were also interviewed. The lead author traveled to three health facilities and two homes of participants and conducted interviews with the attending physicians and the caregivers respectively. Physicians and caregivers who could not be contacted physically were interviewed via telephone.

Study Site: All the patients were registered at the PADC, KATH, Kumasi, Ghana. KATH is a tertiary hospital that serves as the main referral center for the northern sector and the middle belt of Ghana, consisting of about twelve of the sixteen regions of Ghana. The PADC is the first Paediatric and Adolescent Clinic to be organized in Ghana. It is organized by two paediatric endocrinologists and two diabetes nurse educators. Patients are followed up in the clinic by appointment system. Patients who default on their appointments are tracked via telephone calls to remind them to come for their impending review.

A case was defined as a child, an adolescent, or a young adult diagnosed with T1DM and attending PADC, KATH, Kumasi who died during the course of follow-up care between January 2012 and December 2021. T1DM was diagnosed in a child or an adolescent or a young adult with clinical features suggestive of diabetes such as polyuria, polydipsia, polyphagia, poly nocturia, skin infections such as tinea, recurrent vaginal candidiasis and

random plasma glucose of ≥ 11.1 mmol/L or fasting plasma glucose of ≥ 7.0 mmol/L, physical examination findings of wasting, lack of acanthosis nigricans as well as low insulin and C peptide levels.

Inclusion criteria: All patients with T1DM diabetes who died natural death during the 10 years.

Exclusion criteria: Patients whose death could not be related to diabetes and its complications were excluded such as suicide.

Names of health facilities and towns and physical features that could lead to the identification of participants were kept anonymous.

Ethical consideration

The Institutional Review Board of KATH reviewed and approved the study, with reference number KATH IRB/AP/153/20. The study was done in accordance with ethical standards. All participants signed a detailed informed consent form before the collection of data. Participation in the study was entirely voluntary. Anonymity was ensured so that no participant could be traced or identified.

Data Collection

A structured questionnaire was used to collect participants' socio-demographic and clinical data. Data were gathered from physicians and health workers who attended to children, adolescents, and young adults with diabetes who had been registered at KATH and died during the course of their follow-up care and treatment either at KATH or at other health facilities.

Statistical analysis

Socio-demographic and clinical data such as age, sex, duration of diabetes, place of death, and cause of death were recorded using a structured questionnaire and transferred onto excel spread sheet and further transported to Stata SE 17.0 (StataCorp, Texas 77845, USA) for analysis. Variables were represented as means, standard deviations, ranges, and percentages with simple diagrams and tabulations.

RESULTS

Fourteen (14) deaths out of a total number of three hundred fifty-five (355) children and young adults with T1DM occurred within the 10-year period, yielding a mortality rate of 3.9%.

Table 1: Sociodemographic characteristics

Variable	N	%
Sex		
Male	4	28.6
Female	10	71.4
Age at diagnosis		
8-13	11	78.6
14-19	1	7.1
20-25	2	14.3
Age at death		
15-19	8	57.1
20-24	4	28.3
25-28	2	14.3

Females consisted of 71.4%. At diagnosis, 78.6% of the participants were between 8 and 13 years of age and at death, 57.1% were between 15 and 19 years of age.

Table 2: Clinical and social characteristics

Variable	N	%
Causes of death (n=14)		
DKA	5	35.8
CRF	1	7.1
Osteosarcoma	1	7.1

Unknown causes	7	50.0
Place of death		
Hospital	7	50.0
Home	7	50.0
Type of hospital (n=7)		
District hospital	4	57.1
Teaching Hospital	3	42.9
Misdiagnosed as (n=4)		
Cerebral malaria	3	75.0
Meningitis	1	25.0

DKA: Diabetic ketoacidosis, CRF: Chronic renal failure.

Up to 50% of the participants died at home and no definite cause could be assigned after thorough interviews with their caregivers. Most hospitalized participants died because of misdiagnosis of DKA. They were misdiagnosed and managed as cerebral malaria or meningitis. The mean age at diagnosis was 12.9 ± 5.2 years with a range of 8 to 14 years old. The mean duration of morbidity before mortality was 7.4 ± 2.7 years. The mean age at death was 19.7 ± 3.8 years with a range of 15 to 28 years.

DISCUSSION

In this study, the mortality rate among children and young adults with T1DM over the 10-year period was 3.9%. This was lower than what was found in Kenya by Musoma et al., (2020) where they found a mortality rate of 6.9%. Our study spanned a period of ten years and we followed patients both in the outpatients and at the emergency units when they came in an acute disease or in any complication while the study of Musoma et al., (2020) spanned over five years and looked at the outcome of patients with DKA at the emergency unit. Shimelash et al., (2023) in another five-year study in Ethiopia which considered mortality in children with DKA found a mortality rate of 10%. This study was over a period of ten years and it looked at all causes of mortality.

The age range at diagnosis was 8-14 years with 78.6% of them being between 8 and 13 years old (Table 2). This could be possibly due to the fact that tight glycaemic control needed to avert complications and mortality was not achieved in younger patients which could be attributed to factors such as unpredictable adolescent behavior, lack of supervision by parents and caregivers, difficulty with transportation to come to the clinic for insulin and other

supplies. (Ghana Poverty Assessment., 2019; Ngwiri et al., 2015; Noorani et al., 2016) The causes of mortality in seven of the patients (50.0%) could not be identified because they died at home and the parents and caregivers could not describe the immediate processes and features of the patients at the time of death. This is similar to a study done in Cameroun by Katte et al., (2022) where 71.7% of children with T1DM died outside the hospital and 24.5% of them the cause could not be determined. According to an oral report from the parents, these participants (50%) were relatively well on the day before death. They all died in their sleep. They were all on insulin as prescribed in dosage and regularity. So it is more likely they died of sudden cardiac death from arrhythmias due to severe hypoglycemia. (Lynge et al., 2019; Tu et al., 2008) In the Australian study by Tu et al., (2008) they did autopsies for even those who died at home so they could assign specific diagnoses. However, in Ghana, autopsy is hardly done for people who die at home hence our inability to get specific diagnoses for those who died at home. Of the other 50.0% who died at hospitals, 28.6% (4/14) occurred at district hospitals and they all died of DKA while the remaining 21.4% (3/14) died at a Teaching Hospital. All those who died at district hospitals had DKA but they were all misdiagnosed and wrongly managed as cerebral malaria and meningitis (Table 2). DKA is a major cause of death among children and adolescents with T1DM in Africa (Katte et al., 2014; Shimelash et al., 2023). In Ghana, mortality due to DKA is so high that in some district hospitals, it can be 100% because of misdiagnosis and mismanagement. (Ameyaw et al., 2017) The clinical features of DKA can mimic infections such as cerebral malaria, meningitis, typhoid fever, pneumonia, gastroenteritis, etc (Kratzer., 2012; Misra et al., 2011) which are rather more common in Ghana than DKA. Therefore, misdiagnosis of DKA is possible and probably more common than reported. Indeed, misdiagnosis of diabetes in children and adolescents occurs at all levels of health care in Ghana (Ameyaw et al., 2017; Kratzer., 2012). A child with DKA misdiagnosed as cerebral malaria or meningitis would rather be treated as such and dextrose is part of the initial supportive management and the patient would worsen and could result in mortality (Misra et al., 2011).

One of those who died at a Teaching Hospital had DKA, was correctly diagnosed but potassium was entirely omitted in the management, and that resulted in mortality. DKA results in loss of potassium through urine (Carlotti et al., 2013; Rosenbloom AL., 2010) and further loss after insulin treatment has been initiated and so potassium replacement is important to avoid hypokalemia (Carlotti et al., 2013; Rosenbloom AL., 2010). Skeletal muscles including cardiac muscles are vulnerable to hypokalemia resulting in cardiac arrhythmias including ventricular fibrillation, as well as muscle weakness, cramps and finally paralysis and death (Kjeldsen K., 2010; Rosenbloom AL., 2010). One patient died from osteosarcoma with lung metastasis and pleural effusion. Osteosarcoma is an aggressive cancer that metastasizes to other parts of the body and has a high recurrence rate even after adequate chemotherapy (Taran et al., 2017). Patients with T1DM have been reported to have an increased risk of cancer, more particularly in females. (Feodoroff et al., 2024) Our patient was a 22-year-old female who initially complained of pain and swelling in the left humerus which was finally diagnosed as osteosarcoma with lung metastasis. However, it cannot be inferred that this patient developed osteosarcoma as a result of type 1 diabetes mellitus. The third patient who died in a Teaching Hospital had chronic renal failure (CRF). CRF is common in children and adolescents with T1DM particularly those with prolonged poor glycemic control (Rivetti et al., 2023).

Limitations of the study

This study was primarily a one-center study with a small sample size. Hence, the results cannot be generalized. However, the observation and outcome have identified gaps in clinical practice and this can help in improving the management of T1DM at all levels of health care in resourced-constrained regions.

CONCLUSION

Mortality among children and young adults with T1DM occurs at all levels of health care with misdiagnosis as a major cause. Mortality at home is worrisomely high. More awareness about T1DM should be done at the community level so that children with T1DM will be identified and sent to health facilities for confirmation of diagnosis, treatment, and follow-up. Frequent continuous professional developments and update courses should be organized for all health workers in Ghana so that the right diagnosis and management of T1DM and DKA can be done at all levels of health care or appropriately referred. Caregivers and children and adolescents with T1DM should be counseled and encouraged to take the right doses of their insulin, eat appropriately, and do regular exercise to maintain target glycaemic values to avoid getting into DKA. They also be taught about how to recognize hypoglycemia and treat it.

Conflicts of Interest

The authors declare no conflicts of interest.

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