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REVIEW

Using Clinical Vignettes to Understand the Complexity of Diagnosing Type 1 Diabetes in Sub-Saharan Africa

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Abstract: Lack of awareness, access to insulin and diabetes care can result in high levels of morbidity and mortality for children with type 1 diabetes (T1DM) in sub-Saharan Africa (SSA). Improvements in access to insulin and diabetes management have improved outcomes in some settings. However, many people still present in diabetic ketoacidosis (DKA) in parallel to misdiagnosis of children with T1DM in contexts with high rates of communicable diseases. The aim of this study was to highlight the complexity of diagnosing pediatric T1DM in a healthcare environment dominated by infectious diseases and lack of adequate health system resources. This was done by developing clinical vignettes and recreating the hypothetico-deductive process of a clinician confronted with DKA in the absence of identification of pathognomonic elements of diabetes and with limited diagnostic tools. A non-systematic literature search for T1DM and DKA in SSA was conducted and used to construct clinical vignettes for children presenting in DKA. A broad differential diagnosis of the main conditions present in SSA was made, then used to construct a clinician's medical reasoning, and anticipate the results of different actions on the diagnostic process. An examination of the use of the digital based Integrated Management of Childhood Illness diagnostic algorithm was done, and an analysis of the software's efficiency in adequately diagnosing DKA was assessed. The main obstacles to diagnosis were low specificity of non-pathognomonic DKA symptoms and lack of tools to measure blood or urine glucose. Avenues for improvement include awareness of T1DM symptomatology in communities and health systems, and greater availability of diagnostic tests. Through this work clinical vignettes are shown to be a useful tool in analyzing the obstacles to underdiagnosis of diabetes, a technique that could be used for other pathologies in limited settings, for clinical teaching, research, and advocacy.

Keywords: type 1 diabetes, underdiagnosis, sub-Saharan Africa, clinical vignette

Introduction

It is estimated that there are currently 9 million people with type 1 diabetes (T1DM) worldwide.[1] A general increase in cases of T1DM is observed worldwide, with an annual rate increase of approximately 3%, predominantly in people under 15 years of age.[2] Africa accounts for 8% of prevalent cases of T1DM.[1] However, the epidemiological situation of T1DM in sub-Saharan Africa (SSA) is very poorly understood, as estimates are based on a small number of old studies.[3,4] In addition people with T1DM in sub-Saharan Africa face a number of challenges in terms of diabetes management.[5,6] These relate to both the overall socio-economic context of this region as well more specific health challenges related to access to the delivery of diabetes care and insulin. Sub-Saharan Africa includes over 70% of low-income countries (LMIC), with fragile healthcare systems that already bear a heavy burden of mortality linked to infectious diseases.[7]

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Health systems also need to contend with an estimated 70 to 80% increase in the prevalence of type 2 diabetes by 2050 in the sub-Saharan Africa,[8] of which 44% of cases are currently undiagnosed.[2]

Delayed diagnosis of diabetes, combined with a lack of awareness among the general public and healthcare staff, not only exacerbates the complications associated with chronic hyperglycemia, but is of particular concern for T1DM, where delayed diagnosis and access to care can rapidly lead to diabetic ketoacidosis (DKA), which may be fatal.[9] In high income countries (HIC), mortality from DKA is estimated at less than 1%, whereas studies carried out in sub-Saharan Africa estimate a mortality rate of over 40% on initial presentation.[8] The rate of DKA at first presentation in sub-Saharan Africa is extremely high, ranging from 20% to 100% depending on the study.[10–12] Several authors suggest that the main cause of mortality in children with T1DM is under-diagnosis of the condition.[13,14] Atkinson and Ogle,[15] assert that:

> the most common cause of death for a child with type 1 diabetes is more likely to be mortality from ketoacidosis that has been mistakenly managed as an infection or other disorder.

DKA is the result of the combination of a relative or absolute insulin deficiency and an increase in counter-regulatory hormones including glucagon, catecholamines, growth hormone, and cortisol. The latter induce a state of glycogenolysis, gluconeogenesis, lipolysis and proteolysis that worsens hyperglycemia and dehydration, leading to ketoacidosis and plasma hyperosmolarity. If left untreated, profound dehydration and metabolic acidosis, potentially aggravated by concomitant sepsis, can lead to death.

The classically recognized signs and symptoms of DKA include polyuria, polydipsia, and weight loss; tachypnea with a Kussmaul breathing pattern; nausea, vomiting, and abdominal pain (which may mimic an acute abdomen) and ultimately impaired consciousness and coma. This spectrum of signs and symptoms overlaps with those of other more common conditions in SSA, such as infections and malnutrition, and can make clinical suspicion of DKA difficult.

Given the increased DKA mortality and likely under-diagnosis of T1DM in SSA, the aim of this study was to explore the reasons for under-diagnosis and to suggest possible improvements by observing the clinical course of using vignettes of fictitious cases of DKA in the epidemiological and health system context of Burkina Faso.

Methodology

Different clinical vignettes of children in moderate DKA were developed. A vignette is a description of a clinical situation that a clinician may encounter in real life, intended for training and reflexion.[16] These vignettes included detailed descriptions of the symptoms, signs and potential laboratory results for a fictitious patient. These were created using a non-systematic review of existing literature on the epidemiology of T1DM and DKA in Africa on PubMed. This was complemented by examining reports from the International Diabetes Federation (IDF), International Society for Pediatric and Adolescent Diabetes (ISPAD) focusing first on the pathophysiology of T1DM and DKA, its symptomatology and risk factors, and recommendations for the management of DKA. From this review, three initial vignettes of children with moderate to severe DKA were established, according to the ISPAD classification.[17] The age of the hypothetical patients, as well as the symptoms and signs presented, classified by physiological system, are based on eight retrospective studies of T1DM and DKA cases hospitalized in countries in the African region, focusing on patients' symptomatology prior to diagnosis.[10,11,18–23] Laboratory values shown are the disturbances that ISPAD classifies as "moderate to severe" in a DKA.[24]

These vignettes were then compared with clinical practice observed during six weeks of fieldwork during the summer of 2018 at the Charles de Gaulle Pediatric University Hospital, in Ouagadougou, Burkina Faso. Burkina Faso's healthcare system is organized in a pyramidal structure, with primary health care centers run by community health workers, clinics and peripheral hospitals in the middle staffed with general practitioners and surgeons, and university hospitals at the tip. This country faces a high infant mortality (42.6/1000 < 1 years, 81.6/1000 < 5 years in 2015), linked to the heavy burden of malaria, as well as malnutrition. Malaria prevalence in children under 5 is estimated at 46%, with a case-fatality rate of 1.4%.[25–27] The IDF estimates that there are 254 people with type 1 diabetes aged 0–19 years.[2] There are no national statistics on the actual prevalence of T1DM. The pediatric endocrinology consultation at the University Hospital Yalgado, in Ouagadougou, monitored 91 children in 2019, the majority of whom were reported being diagnosed with severe DKA.

During this period, unstructured meetings took place with a pediatric endocrinologist, ten children, and their care givers from the T1DM pediatric consultations, during a diabetes education session, with collection of their testimonies concerning the diagnosis and difficulties of day-to-day treatment. Observation of the work of clinicians working in the pediatric emergency department of the Charles de Gaulle Pediatric University Hospital shed light on the functioning of the healthcare system, assessment and treatment habits in emergency situations, and resources available.

Based on clinical pediatric reference textbooks,[28,29] a broad pediatric differential diagnosis of the main complaints of 2 of the 3 vignettes created (dyspnea/abdominal pain) was established. The most significant clinical elements for the diagnosis found in the literature search were noted, either from specific sources (meningitis,[30–34] malaria,[35–39] pneumonia,[40,41] enteric fever,[42] appendicitis[43,44]), or general textbook references,[28,29] with an assessment of sensitivity, specificity of said clinical elements if present. The basic medical examinations necessary to confirm or deny the diagnosis were added. When such information existed, their prevalence in Burkina Faso was added.[25,26] The vignettes and differential diagnosis were then validated by external experts specialized in tropical medicine and pediatrics, from Democratic Republic of Congo, USA and Switzerland, including co-authors (SK and JC) on this paper. In addition, using existing records from the emergency department at the Charles de Gaulle Pediatric University Hospital, the initial vignettes were adapted to reflect different "real-life" challenges actual children diagnosed with T1DM had faced. In the development of the vignettes the presence or absence of certain diagnostic tools in Burkina Faso, such as tools to measure blood or urine glucose or ketones, was also included in the clinical pathway. With these elements, and the assessment and treatments habits seen during field work, it was possible to establish a differential diagnosis, and create a hypothesis of the clinician's hypothetico-deductive process.

For each differential diagnosis, the presence or absence of identification of symptoms in the vignette was included, enabling the likelihood of a given diagnosis to be established. This process resulted in a more restricted differential diagnosis, which can be easily investigated via the list of complementary examinations required by each differential diagnosis previously outlined. Once this process was completed, it was possible to consider the patient's complete clinical course, with the impact of each clinician's decision and laboratory results on their prognosis. More broadly, the assessment of the patient's journey from home to diagnosis has been evaluated, with a search for the various obstacles to proper care. For the purpose of this exercise the identification of traditional symptoms of polyuria/polydipsia and weight loss were excluded.

The third case (impaired consciousness) went through another process. This case was presented to a computer algorithm based on Integrated Management of Childhood Illness (IMCI),[45–47] a project currently being deployed in certain regions of Burkina Faso to guide community health workers without advanced medical training in their management, and observed the treatment suggestions offered by the algorithm, as well as their impact on the patient's prognosis.

Results

The first part of the literature search focused on DKA symptomatology and its risks factor and identified six articles on inaugural T1DM and DKA clinical presentation in SSA.[10,11,18,20,22,48] The most frequent symptoms noted outside the classical symptoms (polydipsia 70–98%, polyuria 40–100%, loss of weight 50–82%, asthenia 50–70%) were respiratory distress/ tachypnea (10–90%), abdominal or nausea and vomiting (0.2–50%), and altered state of consciousness (37–90%), and fever in 7–10% (Appendix 1).

Three articles were found regarding the risk factors of DKA.[12,49,50] The risk factors for DKA at diagnosis, were mainly based on data from HICs, and identified low socioeconomic status, lack of health insurance, delayed treatment and misdiagnosis. In one review, almost 40% of children with DKA were seen at least once by a physician in the period preceding diagnosis, illustrating the degree of difficulty of clinical suspicion.[12] Another study found that DKA frequency is inversely associated with gross domestic product, latitude and background incidence of type 1 diabetes.[49]

Based on this literature search, three vignettes were created, illustrating cases of moderate to severe DKA (Appendix 2). Vignette A and B are summarized in Figure 1. Vignette A is that of an 8-year-old girl, brought to hospital because of a deterioration in general condition with labored breathing. The hypothetical management, presented in vignette A (Figure 2), shows that after a physical examination, the working diagnostic hypothesis, which is based on the differential diagnosis developed in Appendix 3, includes pneumonia, meningitis, sepsis of undetermined origin, malaria, or severe anemia (Appendix 3). The practitioner then performs a baseline biological workup and chest X-ray, while

Abbreviated vignettes (*Appendix* 2, pathological features only)		
	Case A	**Case B**
History	An 8-year-old girl with no medical history, is brought in by his mother for respiratory distress at a regional medical center. She describes an episode of upper respiratory tract infection with antibiotic treatment at the community health center 10 days ago.	A 13-year-old boy presents to the regional hospital with diffuse abdominal pain and vomiting.
Constant	RR 50/min, HR 150/min, Temp. 36.6 C, moderate dehydration, irritable child	HR 90, RR 30, Temp 36.7. Slight dehydration
Status	Normal breath sound with deep breathing. The rest of the examination is non-contributory.	Diffuse periumbilical abdominal pain without guarding or rebound tenderness. The rest of the examination is non-contributory.

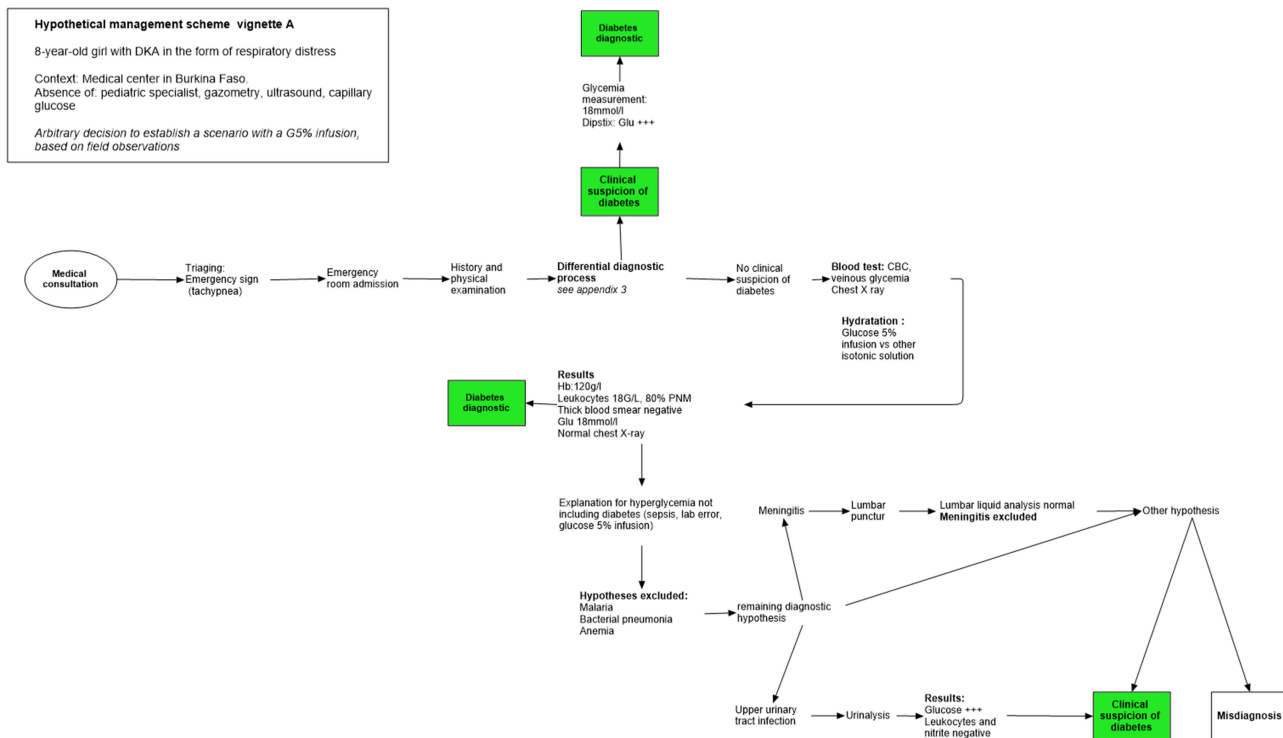**Figure 1** Abbreviated description of vignettes.

Figure 2 Hypothetical management scheme vignette A - DKA in the form of respiratory distress.

starting hydration (Glucose 5% versus other isotonic fluids). Laboratory results would be expected to show an inflammatory syndrome with hyperglycemia and a chest X-ray within normal limits, raising the suspicion of DKA, or sepsis of undetermined origin, needing further investigation. At the end of the process, two options are possible: a correct

diagnosis of DKA, or a mistaken/incomplete diagnosis of an infectious event, leading to a significant delay in management, or death, with an obvious risk of deterioration in the event of glucose infusion.

Child B is a 13-year-old boy presenting to a hospital with abdominal pain and vomiting. After an examination, the working diagnosis includes gastroenteritis, infectious colitis, appendicitis, typhoid fever, or sickle-cell crisis. (Appendix 4) Two possible diagnostic pathways are possible depending on the clinician's assessment. Outpatient investigations may be possible, with a delay inherent in the tests and a risk of DKA deterioration, or inpatient work-up. After a biological workup without major abnormality, in the absence of any suspicion of diabetes, the clinician could decide on conservative care with antibiotic therapy, or surgical care, both of which would result in delayed management with a significant risk of complications and death, as shown in Figure 3.

In both cases, the hypothetical management generated by these differential diagnoses and additional investigations assume that DKA is not part of the clinician's primary differential diagnosis. The frequent absence of capillary glycemia, linked to a lack of resources, limits its regular/systemic use, and makes blood glucose testing a deliberate act by the clinician, implying pre-existing clinical suspicion. This highlights the difficulty of diagnosing DKA in the absence of awareness or recognition of the pathognomonic symptom triad of diabetes, and the life-threatening danger associated with delayed diagnosis of diabetes. Intravenous glucose infusions were routinely given during clinical care witnessed in Burkina Faso for the prevention of hypoglycemia associated with severe malaria, which would be an aggravating and potentially confounding factor in cases of DKA.

Child C is a 4.5-year-old, in hypovolemic shock, consulting in a community health center for altered consciousness. Clinical examination reveals poor general condition, severe dehydration (>10%) with tachypnea and fruity breath. A thorough history could have revealed weight loss with polyuria/polydipsia for two weeks, and lethargy over the past 48 hours. This vignette was used to observe the effectiveness of an IMCI-based computer algorithm in the diagnosis and management of DKA.[47] The flowchart Figure 4 describes the steps performed on the software with the clinical
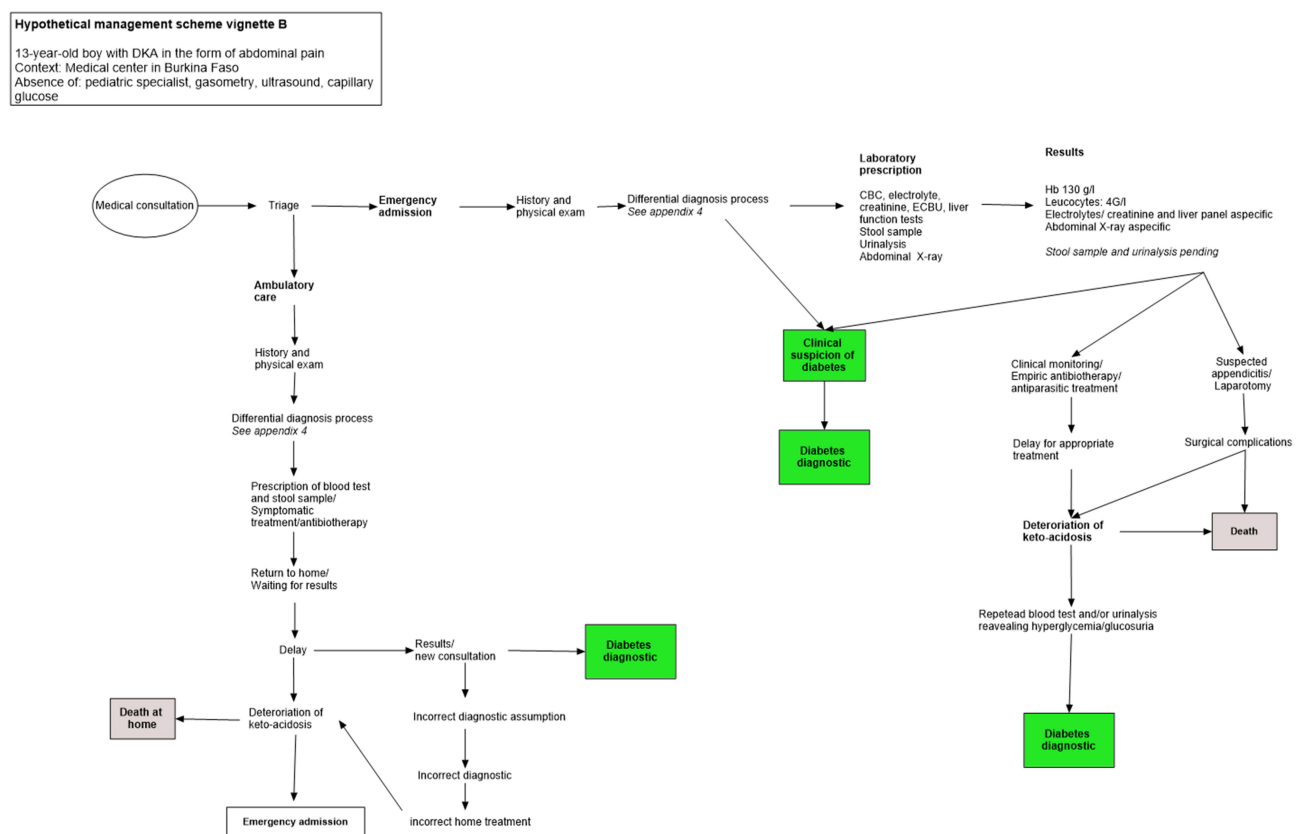

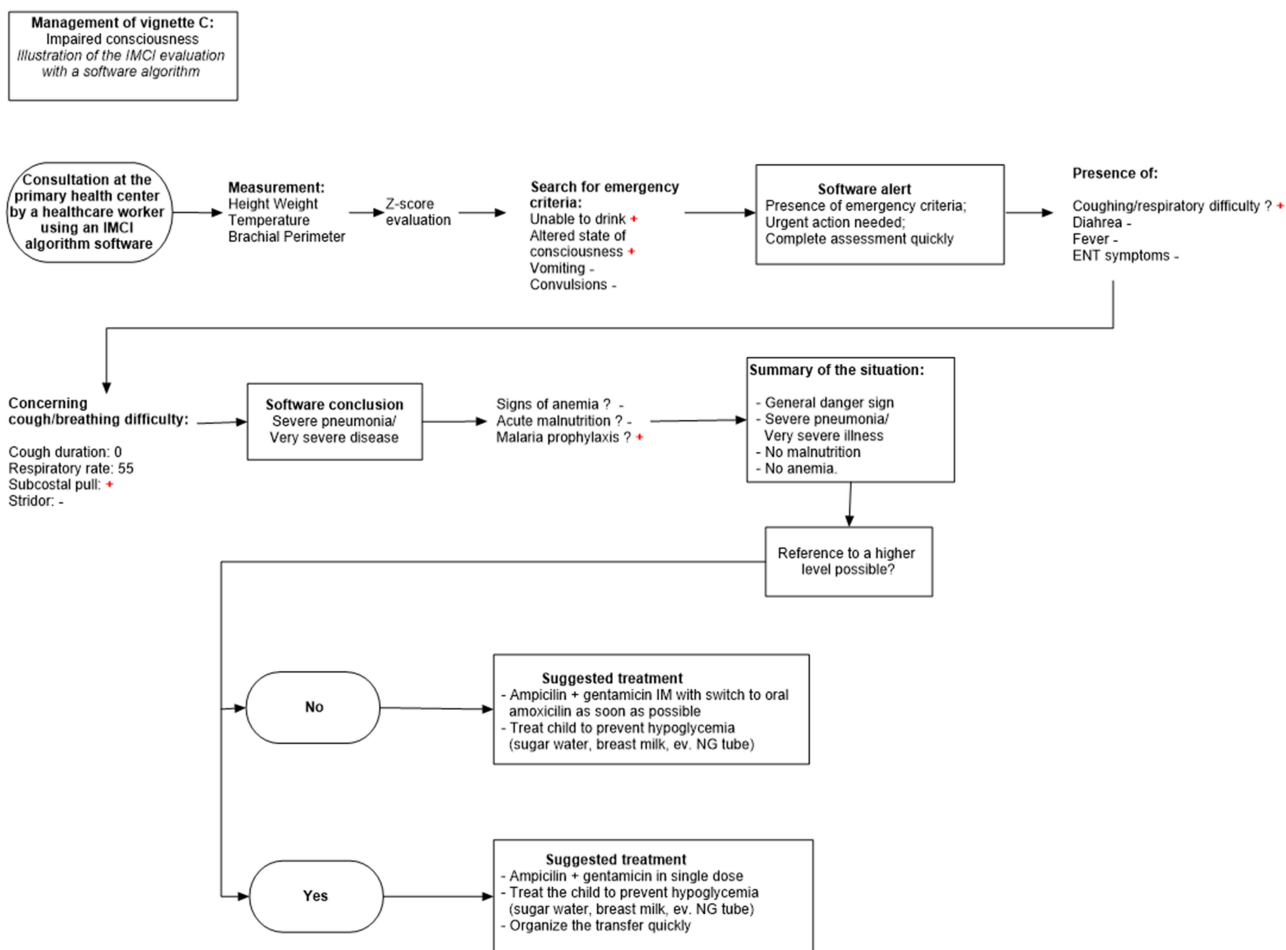**Figure 3** Hypothetical management scheme vignette B - DKA in the form of abdominal pain.

Figure 4 Hypothetical management scheme management of vignette C – impaired consciousness.

elements for Child C. The computer algorithm makes two proposals, depending on the possibility of transfer, involving broad-spectrum antibiotic therapy and oral sugar intake. These proposals are based on the high frequency of infectious and parasitic etiology, as well as the danger of hypoglycemia in this population, but would consequently exacerbate DKA.

Discussion

The aim of this study was to highlight the complexity of DKA diagnosis in SSA using clinical vignettes. These vignettes demonstrate that the vast differential diagnosis of DKA is overly complex due to the intrinsic variability of DKA's clinical presentation, the variability in disease presentation across age groups from toddler to adolescent, the low prevalence of T1DM in sub-Saharan African contexts, the high prevalence of other conditions with similar modes of presentation and symptomology, the lack of awareness, clinical suspicion, and training on T1DM, and the lack of access, or limited access to simple diagnostic tools like capillary glucose, making systematic screening impossible. In this context, a high degree of suspicion is required for an early diagnosis. The vignettes also allow for the identification of the key places where the diagnosis of T1DM is missed.

The presence or absence of diagnostic equipment (dipstick, capillary glucose, blood gases) in each vignette is based on observation in the field in Burkina Faso. Access to, or lack of diagnostic tools, some of which are absent in the cases illustrated, may alter the potential management of these cases. Easy access to capillary blood glucose can make a diagnosis of diabetes obvious, if used. However, in the absence of systematic capillary blood glucose monitoring, it is the practitioner's clinical suspicion that allows a diagnosis to be made, regardless of the tools used.

More generally, this work has demonstrated that clinical vignettes with their hypothetical management can be used as tools in the multi-level analysis of the causes of under-diagnosis of rare pathologies, highlighting expected and unexpected obstacles to the management of these conditions. These can also serve as demonstrations and arguments for better management of these diseases, as well as accessible and cost-effective training tools in the medical training of the countries concerned.

From a clinical perspective in the SSA context, it might be imagined that the implementation of diagnostic algorithms, as an aid to healthcare staff, would improve survival of children presenting in DKA. However, the IMCI algorithm used in vignette C proved deleterious to the patient. Theoretically, the introduction of an item looking for the cardinal signs of T1DM is possible but has its challenges. These algorithms are based on the local burden of disease and adapted to the level of training of health workers. Adding an item looking for signs of T1DM could be considered but would need to balance this with treating the most common, rapidly fatal diseases in these areas. Similarly, discontinuing the systematic use of glucose infusion will certainly be detrimental to a majority of patients in the epidemiological context of SSA. An easier solution might be to add glucose check in the algorithm.

In looking at these vignettes from a more global perspective, based on the biopsychosocial model, there is a need to contextualize these barriers to diagnosis within the wider barriers to access to healthcare. In 1994, Thaddeus and Maine[51] described the "Three delays model (deciding to seek care, accessibility to care, quality of care)", initially used in public health to study maternal mortality, and since applied to other public health issues. This same concept can be applied to T1DM in SSA, as shown in Figure 5.

The care process begins at home, in the child's environment and, in the pediatric context more specifically, in their family. In SSA the use of traditional healers as a first point of provision of healthcare should also be considered. The first task is to observe symptoms and seek care, before even taking the diagnostic steps described above. In the case of DKA, the "atypical" clinical presentation, which may mimic or exist in parallel with more common diseases, may lead to a delay in seeking care, as the symptoms encountered are not those most frequently experienced by parents compared to other childhood pathologies in tropical environments (cough, fever, diarrhea). Numerous factors can influence the decision to seek care, including economic factors (consultation costs, transport, treatment, loss of earnings, etc.).[38,52] The perception of the health system, the family's previous experiences and their health literacy are also important parameters.

Figure 5 Hypothetical global management scheme for vignettes A and B.

The next barrier, access to care facilities, encompasses broad socio-economic issues, such as geographical distance from the place of care and the patient's ability to travel, which are not specific to T1DM.[53] The third barrier, quality of care, includes first and foremost the diagnosis. This study demonstrated the complexity of diagnosing DKA in a resource-poor environment, in view of the wide range of differential diagnoses and in the absence of simple diagnostic equipment. If the diagnosis is made, optimal management of the condition remains a major challenge, as DKA is often associated with severe electrolyte and infectious disorders. As these challenges are present in many LMICs this approach and its findings might be relevant in providing insights into similar contexts with weak health systems and high rates of infectious diseases in children.

In the long term, the survival of children with T1DM depends on increased awareness of the condition, its symptoms and presentation, and access to insulin, diagnostics, and appropriate follow-up. In Burkina Faso, treatment costs can represent 500% of the average annual salary of the lowest economic classes, with a very low number of specialized facilities for diabetes care provision.[5] At the time of the field study, the only two official health facilities for the management of T1DM were in Ouagadougou and Bobo-Dioulasso, the country's two largest cities.

Some improvements in the management of T1DM in SSA are due to an increase in the number of trained endocrinologists,[14] and follow-up programs and access to insulin via philanthropic associations.[23,54,55] More generally, several public health measures could contribute to a reduction in T1DM mortality in LMICs, such as awareness campaigns for the general public and healthcare personnel which are known to be effective in decreasing the percentage of DKA in HICs,[56,57] and improved access to blood or urine glucose testing in health facilities.[54] These are theoretically relatively simple measures, but practically, are complex due to the size of the territories and the costs involved.

Limitations

A generalization to the entire African continent is obviously not possible based on this approach, but the hypothetico-deductive process in this work was an attempt to recreate the thinking of a clinician faced with children presenting in DKA. It was deliberately decided to exclude identification of the pathognomonic triad of polyuria/polydipsia and weight loss from the elements given in the vignettes, given that in clinical reality, we postulate it is highly possible that these symptoms are not systematically recognized, reported by the patient, or specifically sought by the clinician, as shown in Appendix 1. This assumption needs to be formally assessed by further studies. This choice also made it possible to consider a broader differential diagnosis in the process described, to create a worst-case scenario. Other management pathways exist, shortening or nullifying the delay in diagnosis, but were not presented in this article. The cases presented here are fictious, and it's important to note that DKA management, or mismanagement were not observed during fieldwork.

Conclusion

The challenge of diagnosing T1DM in low-resourced health systems remains a significant barrier to improving care. Mortality at initial presentation for these children is driven by health system, economic and global health factors. These include facilities lacking the appropriate equipment to appropriately diagnose this condition, trained staff, challenges in accessing the health system, absence of universal health coverage, high rates of poverty and the high burden of communicable diseases in children. However, with persisting barriers to access to insulin, self-monitoring equipment and other resources, a comprehensive approach is needed to decrease the mortality and morbidity of T1DM in low resource settings, by ensuring access to proper diagnosis as well as continuous quality management. The use of these clinical vignettes offers an interesting approach to disentangle the complexity of diagnosing T1DM and allows for recommendations to be formulated. Based on this work, a health system response to the challenges presented above would need to include increased availability of diagnostic tools and increased awareness of T1DM symptomology in communities and health systems.

Disclosure

The authors report no conflicts of interest in this work.

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