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Clinical pattern of childhood Type 1 (insulin-dependent) diabetes mellitus in the Sudan

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Summary. During a 10-year period, 101 children with Type 1 (insulin-dependent) diabetes mellitus were admitted to the Department of Paediatrics of the University Hospital in Khartoum, Sudan. The age distribution of the patients showed a steady increase from age one to ten years followed by a sharper increase around puberty. A higher number of cases were diagnosed during the cooler compared to the warmer months of the year ($p < 0.05$). Family history of Type 1 diabetes was reported in 14.9% of patients. Diabetic ketoacidosis was a presenting symptom in 82 patients (81.2%) and 93 patients (92.1%) have had at least two documented episodes of ketoacidosis during the follow-up period. Almost all patients were treated with bovine insulin given as a single dose per day. An initial remission period was not observed in any of the patients. Four years after diagnosis, the average daily dose of insulin used by the patients was greater than 2.0 U/kg body weight and the mean HbA_{1c} was 13.4% (reference value 5.3–6.7%). Seventeen patients (16.8%) were known to have died during 399 person-years of observation resulting in a mortality rate of 42.6 per 1000 person-years of follow-up. Another 29 patients (28.7%) for no apparent reason did not attend a follow-up examination after discharge from hospital. Some of these patients might have died in other hospitals or at home. The study emphasizes the need for urgent measures to increase public awareness of diabetes and to improve methods of case-finding and management of diabetic patients.

Key words: Type 1 (insulin-dependent) diabetes mellitus, ketoacidosis, mortality, child, Africa.

Type 1 (insulin-dependent) diabetes mellitus in childhood has been considered uncommon in African populations [1, 2], and little information on its clinical course is available [3–6]. We have recently documented a high prevalence (0.95 per 1000) of Type 1 diabetes in Sudanese children 7–14 years of age [7]. The purpose of this paper is to present the clinical features of the diabetic children admitted to the Department of Paediatrics at University Hospital in Khartoum, Sudan, during a 10-year period. There are five hospitals with paediatric units in Khartoum. The paediatric unit at University Hospital has 20% of the total number of beds allocated to these units. Diabetic children have equal chances of admission to any of these units by virtue of the admission system which has a strict rotational schedule. University Hospital was chosen because it has a good registration and record-keeping system.

Subjects and methods

Data were collected retrospectively for all diabetic children diagnosed at or before the age of 15 years, who were admitted to the Department of Paediatrics at Soba University Hospital in Khartoum from 1 January 1977 to 31 December 1986. Patients are usually referred from the Children's Emergency Hospital in Khartoum and from community health centres. Few patients are referred from private clinics and from physicians at other institutions. Diabetic children in Khartoum are routinely admitted to hospital at the time of diagnosis for initiation of insulin therapy and stabilization of metabolic control. After discharge from hospital, they are usually seen at the out-patient clinic every 2 months if their metabolic condition is stable and satisfactory and more frequently if it is not well controlled. Those patients with a persistently poor metabolic condition and those presenting with complications are re-admitted to hospital. Clinical records, including complete medical and family history, thorough physical examination, appropriate laboratory data and notes on each follow-up visit have been carefully kept on all diabetic subjects. Haemoglobin A_{1c} had been measured for most of the patients at the time of diagnosis and at 6 month-intervals after that. Ketoacidosis was diagnosed on clinical grounds in acutely ill patients with impaired consciousness, dehydration, acidotic breathing, hyperglycaemia and glucose and acetone in the urine. Partial remission was defined as a period free from clinical symptoms of diabetes with an insulin requirement of less than $0.5\ U \cdot kg^{-1} \cdot day^{-1}$ and absent or minimal glucosuria for more than 4 weeks [8]. Diabetic nephropathy was diagnosed on clinical grounds in patients with persistent proteinuria in the absence of other known renal disease, which was excluded by history, urine culture, plain abdominal radiographs and sometimes intravenous urography. Renal biopsy is not normally available. Patients were considered hypertensive if the

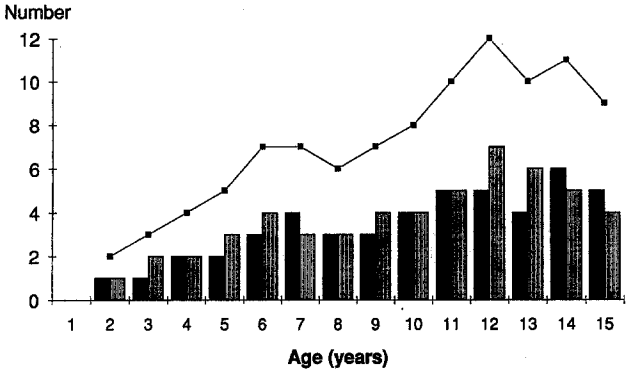

Fig. 1. Age at diagnosis of Type 1 (insulin-dependent) diabetes mellitus in children in Khartoum, Sudan (1977–1986); Boys (▬), Girls (▭), Boys and Girls (—■—)

blood pressure was consistently above the 95th centile value for age according to the American Task Force standards [9]. Neuropathy was diagnosed if sensation was absent in the feet or if the patient had mononeuropathy or autonomic neuropathy. The eyes were examined for cataract and the fundi for retinopathy with dilated pupils and whenever feasible patients were referred to an ophthalmologist. In those who died in hospital, cause was determined clinically as autopsy was not possible due to cultural reasons.

Statistical analysis

The arithmetic means and standard deviations were calculated for quantitative variables and the statistical significance of seasonal trends was tested by the method described by Roger [10].

Results

The hospital records of 101 children with Type 1 diabetes have been traced. All patients fulfilled World Health Organisation criteria for diagnosis of Type 1 diabetes in children [11]. Patients were prone to ketoacidosis and required insulin for survival. Day of diagnosis was defined as the day when the first insulin injection was given. In this group, there were 53 girls and 48 boys giving a male:female ratio of 0.91:1. The mean age at diagnosis was 9.9 years (10.1 for boys and 9.8 for girls). Fourteen patients became diabetic before the age of 6, the youngest at the age of 15 months, 37 between ages 6 to 10 years and 50 after the age of 10 years. The most common age at diagnosis was 12 years in girls and 14 years in boys (Fig. 1). Duration of symptoms before diagnosis ranged from 3 days to 6 weeks with a median of 18 days. A seasonal variation in the month of diagnosis of the disease was observed in both sexes (Fig. 2). Fewer diabetic children were diagnosed during the summer months, May to August, compared with the cooler months of the year, November to February ($p < 0.05$).

Eighty-two children (81.2 %) presented with ketoacidosis and the rest showed rapid onset of the classical symptoms of polyuria, polydipsia and weight loss. At the follow-up examination 93 patients (92.1 %) had experienced at least two documented episodes of severe ketoacidosis and 19 (18.8 %) had experienced severe hypoglycaemia.

Because there were no local standards, growth and pubertal development were assessed in all patients using the American National Center for Health Statistics growth charts [12] and Tanner staging of pubertal development [13]. Nine patients (8.9 %) five boys and four girls had stunted growth (below the 5th centile of height for age and sex). Two of these patients were typical diabetic dwarfs (Mauriac syndrome) with delayed sexual maturation and hepatomegaly. None of those patients was obese and none of them showed any of the known features of malnutrition-related diabetes mellitus [11, 14].

Most of the patients were treated with bovine insulin, using a mixture of short- and long-acting, taken as a single daily dose 30 min before breakfast. Porcine insulin is not used because of religious and social reasons. Only thirty-nine patients (38.6 %) reported as having refrigerators at home to store the insulin while the rest of the patients stored the insulin at room temperature usually in the moist sand under the family's water jar. Some families kept the insulin frozen and thawed it before each use. Home blood glucose monitoring was not used and even simple urine glucose testing was not performed regularly.

At diagnosis, the average daily dose of insulin required to achieve reasonable metabolic control was 1.2 $U \cdot kg^{-1} \cdot day^{-1}$ (range 0.8–1.6), but 4 years after clinical onset the insulin requirement was raised to 2.1 $U \cdot kg^{-1} \cdot day^{-1}$ (range 1.8–2.5). The level of HbA_{1C} of this group of patients ranged between 10.6–16.7 % with a mean of 13.4 % (reference values 5.3–6.7 %). A transient remission phase, the so-called honeymoon period, has not been observed in any of the 101 subjects.

The total number of diabetes-related hospital admissions in this group of children, excluding the first admission after diagnosis, was 203 during 10 years. The most common reason was stabilization of metabolic control. There were 167 admissions due to ketoacidosis, 12 admissions due to severe hypoglycaemia and 51 due to concomitant infections. Four patients have had tuberculosis, 18 urinary tract infections and 29 suffered from falciparum malaria, acute pneumonia and pyogenic infections. Duration of hospitalization for patients in the initial admission ranged from 11 to 30 days (mean 21 days) and for sub-

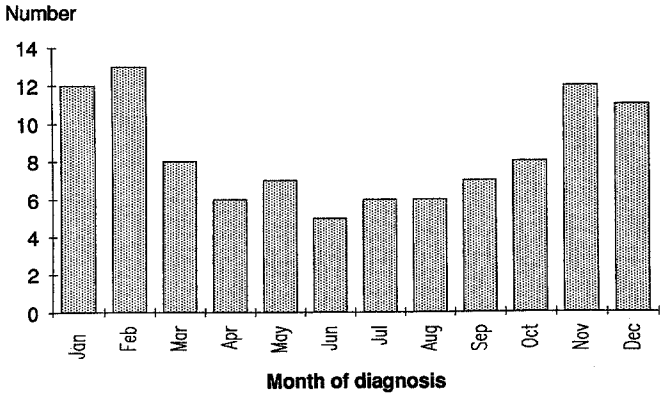

Fig. 2. Month of diagnosis of Type 1 (insulin-dependent) diabetes mellitus in children in Khartoum Sudan (1977–1986)

Table 1. Long-term complications of Type 1 (insulin-dependent) diabetes mellitus in Sudanese children in relation to the duration of the disease

Duration (years)	Patients	Nephro-pathy	Neuro-pathy	Retino-pathy	Cataract	LJM
0–5	62	1	0	0	0	1
6–10	34	5	3	2	2	7
>10	05	3	2	2	1	3
Total	101	9	5	4	3	12

Values given are the number of diabetic patients. LJM, Limited joint mobility

sequent admissions, duration of their stay ranged from 6 to 82 days, with a mean of 27.4 days.

Other endocrine diseases seen in these patients were hypothyroidism in seven patients (6.9 %), six girls (two of them were sisters) and one boy, and two patients with hyperthyroidism and one with Addison's disease. This latter patient also had vitiligo and achlorohydria.

Seventeen patients (16.8 %) were known to have died in 399 person-years of observation resulting in a mortality rate of 42.6 per 1000 person-years of observation. Thirteen deaths were due to ketoacidosis, one was due to hypoglycaemia and the rest were due to acute pneumonia, tuberculosis and renal failure. Another 29 patients (28.7 %) for no apparent reason did not attend a follow-up examination after discharge from hospital. We have tried to trace this group of children, but it proved impossible. Some of these patients might have died in other hospitals or at home.

A history of known Type 1 diabetes in a close relative was reported by 15 (14.9 %) patients. This relative was the father in eight cases, the mother in three and a sibling in four. Information about parental consanguinity was not available. Information about the effect of the disease on the families and other social aspects could not be deduced from the records. However, 19 patients (18.8 %) were reported to have had discontinued their schooling because of the disease. The long-term complications of Type 1 diabetes, related to the duration of the disease, in this population is summarized in Table 1.

Discussion

The clinical presentation of childhood diabetes observed in this study is in accordance with classical symptoms of Type 1 diabetes [15]. None of our patients exhibited the features of either Type 2 (non-insulin-dependent) diabetes of the young [16] or malnutrition-related diabetes mellitus [14]. The age distribution of the patients showed a steady increase from age one to ten years before demonstrating a sharper increase around puberty.

The pattern of seasonal variation observed in the month of clinical onset of the disease is consistent with our previous report [17] though it is less striking in the present study. A higher number of patients were diagnosed during the cooler months of the year compared to the warmer ones. This finding is consistent with global reports from both Northern and Southern hemispheres [18–21] and has been cited as evidence of a possible role for environmental factors in the aetiology of Type 1 diabetes [22].

The data on the occurrence of diabetes in the families of children with Type 1 diabetes in this series is in agreement with most of the published reports [23–25].

The vast majority of our patients (81.2 %) had diabetic ketoacidosis at the time of diagnosis. Almost all of them at follow-up examination reported as having had two other episodes of ketoacidosis. These figures appear to be greater than the highest figures documented in the medical literature [26–31]. This finding reflects the severity and the seriousness of the disease in our population. It could be explained in part by a delay in seeking medical attention or a delay in making the correct diagnosis. Children presenting with diabetic coma in Africa are likely to be investigated and empirically treated on the lines of cerebral malaria or meningitis before the correct diagnosis is suspected [32]. A serious extrapolation of this observation is the speculation that many children with Type 1 diabetes in Sudan do die before being identified as having diabetes.

There was a poor prognosis of diabetes in this group of patients reflected in the high mortality and morbidity. The mortality and default rates demonstrated in this study can also be expressed as a 5-year mortality of approximately 20 %, and mortality and loss to follow-up of approximately 50 %. A similar finding was reported from Tanzania [33], whereas in developed countries 70% of Type 1 diabetic patients survive 30 years or more after diagnosis [12]. These figures may highlight the inadequate facilities available for care of children with Type 1 diabetes in developing countries.

Both acute and chronic complications of diabetes were prevalent in our patients and their short-term metabolic control was poor as shown by the high average daily dose of insulin and the high concentration of HbA_{1C}. This finding was not surprising because these children do not always have insulin. Even when insulin is available, most of those patients lack the knowledge and the means to keep it potent and effective in the warm tropical environment. In hospital, insulin is distributed free of charge to all patients. On the market, one vial of insulin costs approximately 7.0 US dollars. Before 1989 insulin was not on the essential drug list of the Ministry of Health in Khartoum. This has jeopardized the continuity of its supply for many years. Unfortunately, even after the inclusion of insulin in the essential drug list, the health planners in a large populous country like Sudan are striving to maintain the primary health care activities with a small allocated budget and have very little, if any, resources for importing insulin. A similar situation has been reported from other African countries [34, 35]. Other factors which might have contributed to the poor metabolic condition of these children included the use of non-purified bovine insulin in a non-physiologic dose regimen, food shortages and irregular dietary habits, attempts at traditional healers, ignorance because of lack of diabetes education and the absence of organized diabetes care. The average daily dosage of insulin used 4 years after diagnosis is astonishingly high and probably reflects the occurrence of insulin resistance due to poor metabolic control and impure bovine insulins.

The high frequency of hospital admissions and the long duration of stay observed in this study were potentially preventable. Ketoacidosis, hypoglycaemic episodes, as well as long-term complications could be reduced significantly by a diabetes care service and education programme. Hospital-bed occupancy by diabetic patients has been reduced by as much as 66 % when improved ambulatory care facilities were provided [36, 37].

In conclusion, this study indicates that childhood Type 1 diabetes is a serious disease in Sudan with severe acute onset and rapid progression towards death or disability. More efforts are therefore required to increase public awareness and to improve patient detection and management. An efficient national diabetes care programme is urgently needed to reduce both the human misery and the burden on the fragile health economy in the country.

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