

Pattern of presentation in type 1 diabetic patients at the diabetes center of a university hospital

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BACKGROUND AND OBJECTIVES: Diabetes mellitus (DM) is a major health problem worldwide. This study aimed to investigate the pattern of presentation and complications of pediatric diabetes.

DESIGN AND SETTING: Retrospective study of children treated at a diabetes clinic at a university hospital for diabetes over 12-year period.

PATIENTS AND METHODS: We collected data on the age at onset, sex, clinical presentation, duration of symptoms before diagnosis, and partial remission rate that were obtained from the hospital medical records, the National Diabetes Registry, and the statistics department.

RESULTS: Of 369 diabetic children, most (n=321) children had polyuria (92%) 321/369=87% as the presenting symptom; other symptoms included polydipsia (310 patients, 88.8% 310/369=84%), weight loss (292 patients, 83.9%), nocturia (240 patients, 68.8% 240/369=65%), diabetic ketoacidosis (DKA) (174 patients, 49.9% 174/369=47.20%), and abdominal pain (172 patients, 49.3% 174/369=46.6%). Presenting symptoms were missing in 20 files, so the percentages were calculated among 349 patients. Most patients had acute diabetic complications such as hypoglycemia (222 patients, 62%) and DKA (88 patients, 38.1%, but none had severe complications such as coma and cerebral edema. Chronic complications included retinopathy (4 patients, 1.3%), neuropathy (2 patients, 0.6%), coronary heart disease (2 patients, 0.6%), and nephropathy (1 patient, 0.4%).

CONCLUSION: The pattern of presentation of type 1 diabetes has changed as the incidence of DKA has decreased; unlike in previous studies, DKA was not the most common presenting symptom in this study. Chronic complications of diabetes, such as retinopathy, neuropathy, coronary heart disease, and nephropathy are mostly rare but still present. These complications might be prevented by achieving better awareness of the need for glycemic control.

Diabetes mellitus (DM) is a major health problem worldwide. Current studies have revealed a definite global increase in the incidence and prevalence of diabetes, with the World Health Organization (WHO) projecting that there will be almost 221 million cases in the year 2010 and up to 285 million cases in the year 2025.¹ It is the fourth or fifth leading cause of death in most developed countries.^{1,2} Although this increase is mainly expected in type 2 diabetes, a parallel increase in childhood diabetes, including type 1 and 2 diabetes, has been reported.³ DM in children has previously been considered rare in African and Asian populations.⁴⁻⁸ The WHO Diabetes

Mondiale (WHO DIAMOND) project group has reported a worldwide increase in the incidence and variation (over 400-fold) of type 1 diabetes, with the highest occurring in Finland (over 45 per 100 000 children under the age of 15 years) and the lowest in parts of China and Fiji.⁹

DM in children in Saudi Arabia has not been studied well and further studies are needed.¹⁰ Little local information on the disease is available, and most cases reported have been of type 2 DM.¹¹ The epidemiology and characteristics of DM, particularly insulin-dependent DM, are not known in the Saudi community, and only a small amount of data is available.¹¹ Moreover,

Table 1. Characteristics of pediatric diabetic patients attending the diabetes center at a university hospital (1993-2005) (n=369).

| | Percent (n) | Mean (SD) | Median (range) |
|---|-------------|--------------|----------------|
| Age (years) | | | |
| <5 | 13 (3.5) | 3.39 | 4 |
| 5-10 | 100 (27.1) | 7.76 | 8 |
| 11-15 | 159 (43.1) | 13.08 | 13 |
| >15 | 97 (26.3) | 14.56 | 15 |
| Total | 369 (100) | 12.3 (4.03) | 13 (2-18) |
| Duration of DM (years) | | | |
| <5 | 218 (60.2) | 2.42 | 2 |
| 5-10 | 114 (31.5) | 7.67 | 7 |
| 11-15 | 25 (6.9) | 12.7 | 13 |
| >15 | 5 (1.4) | 16 | 16 |
| Total | 362 (100) | 4.6 (3.7) | 4 (0.08-16) |
| Family history of DM | | | |
| Positive | 260 (73.7) | | |
| Negative | 93 (26.3) | 1.26 (0.4) | 1 (1-2) |
| Total | 353 (100) | | |
| Duration of symptoms before diagnosis (days) | | | |
| <15 | 134 (58.5) | 8.27 | 7 |
| 15-30 | 53 (23.5) | 27.08 | 30 |
| 31-60 | 23 (10.0) | 56.74 | 60 |
| 61-90 | 10 (4.4) | 87.3 | 90 |
| >90 | 9 (3.9) | 261.67 | 270 |
| Total | 229 (100) | 30.9 (53.8) | 14 (1-365) |
| Daily dose of insulin (units) | | | |
| <26 | 129 (36.3) | 16.98 | 18 |
| 26-50 | 151 (42.4) | 37.4 | 38 |
| 51-75 | 59 (16.6) | 59.97 | 58 |
| >75 | 17 (4.8) | 84.88 | 82 |
| Total | 356 (100) | 36.0 (19.7) | 37 (2-106) |
| Duration of partial remission ("honeymoon" phase) (days) | | | |
| ≤30 | 14 (66.7) | | |
| >30 | 7 (33.3) | 50.67 (59.0) | 30 (4-210) |
| Total | 21 (9.1) | | |

the data confirm the need to develop a national registry and the need for further epidemiological research.¹² Furthermore, adolescents are not examined in pediatric clinics, and they do not receive adequate attention in adult clinics.¹³

Saudi Arabia is a unique country among developing nations in view of its excellent economic status and relatively low literacy rate, particularly among mothers, in addition to the cultural and religious background, which might influence the management of diabetes.¹⁴ The presentation of type 1 diabetes in Saudi children seems to differ from that in children from Western countries.¹⁵ The most common clinical sign is diabetic ketoacidosis (DKA), which is observed in 67.2% of the patients.¹¹ DKA is the most serious presenting symptom of type 1 DM. The frequency and severity of DKA at presentation vary significantly worldwide.¹⁶ In Saudi Arabia, studies have revealed that DKA is present in 55% to 77% of the DM cases.^{15,17} Ketoacidosis is the most common presenting symptom of childhood DM in this region.¹⁸

This study presents some of the epidemiological and clinical features and complications of childhood DM as recorded in the Diabetes Center at King Abdulaziz University Hospital, Riyadh, Saudi Arabia. The Diabetes Center receives patients from Riyadh District and suburban areas; in addition, it is a tertiary care center that receives referred patients from different cities in the country. The objective of this study was to investigate the pattern of presentation of pediatric diabetes in patients enrolled in the diabetes center of a university hospital and to review the complications of diabetes in the study group.

PATIENTS AND METHODS

All diabetic children who were enrolled in the study from among those treated at the King Abdulaziz University Hospital over a 12-year period from 1993 to 2005. Vital data for the study were extracted from several sources, including hospital medical records, the National Diabetes Registry, and the statistics department. The data were extracted by an experienced physician under the strict supervision of the author, who also checked for the consistency and completeness of the extracted data. The recorded information included the age at onset, sex, nationality, consanguinity, clinical presentation, duration of symptoms before diagnosis, and partial remission rate (which was defined according to the criteria of the International Study Group of Diabetes in Children and Adolescents as a period of freedom from clinical symptoms of diabetes with insulin requirements of <0.5 units/kg/day and absent or

minimal glycosuria for more than 4 weeks). During this study, type 1 diabetes was predominantly diagnosed on the basis of the clinical and biological features. Polyuria, polydipsia, weight loss and fatigability were the principal clinical features for diagnosis. Significant hyperglycemia was taken into account as a biological feature according to the National Diabetes Data Group criteria of fasting blood glucose of >140 mg/dL (>7.7 mmol/L), 2-hour postprandial blood glucose level of >200 mg/dL (>11.1 mmol/L), and glycosuria with or without ketonuria.

Both clinical and biological features were included in the diagnosis of DKA. Clinical features such as vomiting, abdominal pain, moderate-to-severe dehydration, and stupor, in addition to hyperglycemia with blood glucose levels exceeding 15 mmol/L, ketonuria and metabolic acidosis with a bicarbonate level of <15 mmol/L, played significant roles in determining DKA. The chronic complications such as retinopathy, nephropathy and neuropathy were identified by ophthalmic findings indicative of retinopathy, persistent microalbuminuria, and abnormal nerve conductions, respectively. Data analyses (chi square tests, Fischer exact test) were performed using the statistical packages STATA, R, and Minitab.

RESULTS

Of the 369 diabetic patients, 159 (43.1%) patients were between 11 and 15 years of age. The age groups 6-10 years and >15 years consisted of a similar number of patients—100 (27.1%) and 97 (26.3%) patients, respectively. Only 13 (3.5%) patients were less than 5 years old. The mean (standard deviation) age was 12.3 (4.0) years with a range of 2-18 years (Table 1). Of the enrolled patients, 175 (47.4%) were male and 194 (52.6%) were female. The study group included 324 (87.8%) Saudi patients and 45 (12.2%) patients of different Arab nationalities. A positive family history of DM was recorded in 260 (73.7%) patients, including both type 1 and type 2 diabetes patients. The overall mean (SD) duration of diabetes was 4.6 (3.7) years. There were two major peaks of age at diagnosis, one at the age of 7 years and the other at 11 years, with a sharp drop after the age of 11 years; the curve almost reached a plateau at the age of 18 years (Figure 1). Most patients (134 patients, 58.5%) had a less than 15 days duration of symptoms before diagnosis. The duration of symptoms before diagnosis ranged from 1 to 365 days, with a median of 14 days (Table 1). The mean total insulin intake was 36.0 units/d, with a range of 2-106 units/d and a median of 37 units/d. Partial remission was observed in 21 (9.1%) patients (Table 1). Numbers of patients by age group, duration of diabetes, family history, diabetic complications, and

were above 17 years of age at the time of diagnosis, and these were the oldest patients in this study. Two peaks [peaks of age at time of diagnosis?] were observed, one as early as at 12 days of age in a case that was diagnosed in another hospital and referred to the Diabetes Center of King Abdulaziz University Hospital. Three patients

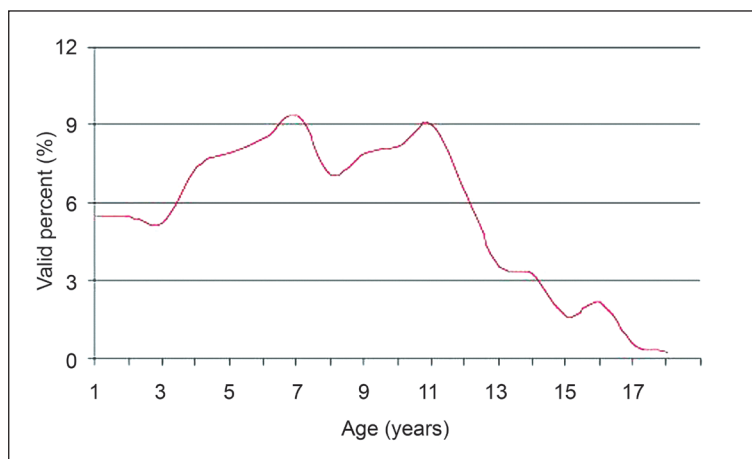


Figure 1. Distribution curve of age of diagnosis pediatric patients attending the diabetes center at a university hospital (1993-2005).

Table 2a. Sex of pediatric diabetic patients by age group.

| Age group (years) | Male (n) | Female (n) |
|-------------------|--------------------|------------------|
| <5 | 6 | 7 |
| 5-10 | 47 | 53 |
| 11-15 | 72 | 87 |
| >15 | 50 | 47 |
| Total | 175 (47.4%) | 194 (52%) |

Total number of patients, 369. P=.8 sex vs age group.

Table 2b. Sex and age group by duration of diabetes.

| Duration of diabetes | Sex ^a (n) | | Age group (years) ^b | | | |
|----------------------|----------------------|------------|--------------------------------|-----------|------------|-----------|
| | Male | Female | <5 | 5-10 | 11-15 | >15 |
| <5 | 114 | 104 | 13 | 85 | 88 | 32 |
| 5-10 | 47 | 67 | 0 | 13 | 60 | 41 |
| 11-15 | 8 | 17 | 0 | 0 | 10 | 15 |
| >15 | 2 | 3 | 0 | 0 | 0 | 5 |
| Total | 171 | 191 | 13 | 98 | 158 | 93 |

Total number of patients <369 because duration of diabetes was missing in file. ^aP=.092 sex vs. duration, ^bP<.001 age group vs duration.

duration of partial remission by the other variables are presented in **Tables 2a, 2b, and 2c**.

The most frequent presenting symptoms were polyuria, polydipsia, weight loss, nocturia (**Table 3**) while DKA was present in about half (**Table 3**). Because of missing data, not all information on all patients was available. The data on fatigability was available for 231 patients; fatigability was observed in 179 of these 231 patients. The less frequent symptoms included fever, obesity, delayed wound healing, vomiting, loss of consciousness, and diarrhea; a history of preceding illness was also less frequent. Ten (4.3%) patients of the studied cohort were asymptomatic. Most patients had acute diabetic complications such as hypoglycemia, and DKA (**Table 4**). None of the patients had severe complications such as coma and cerebral edema. Chronic complications included retinopathy, neuropathy, coronary heart disease and nephropathy.

DISCUSSION

Among the patients in the study, diabetes was diagnosed as early as at 12 days of age in a case that was diagnosed in another hospital and referred to the Diabetes Center of King Abdulaziz University Hospital. Three patients

were above 17 years of age at the time of diagnosis, and these were the oldest patients in this study. Two peaks in age at time of diagnosis were observed, one at 7 and the other at 11 years of age. In a study by Salman et al, the age at onset ranged from 7.5 months to 12 years, with a peak at around 5-7 years and 11-14 years, respectively. The second peak in this study was observed to occur in the age range similar to that reported by Abdullah (10-13 years), while the first peak was observed to occur slightly earlier (4-6 years).^{19,20} In the study by Abdullah, the youngest patient was 6 months old at diagnosis.

The present study showed a female preponderance, with 194 (52.6%) females versus 175 (47.4%) males; such a female preponderance was also observed in the series conducted by Salman et al, wherein 53.6% of patients were female. On the contrary, the series conducted by Abdullah showed a male preponderance, with a male-to-female ratio of 1.3:1; this ratio is similar to the ratios observed in the UK, Denmark and India.^{19,20} In this study, the duration of symptoms before diagnosis was 1-35 days with a median of 14 days as compared to a duration of 2-60 days with a mean of 18.2 days in the series conducted by Salman et al.

Table 2c. Sex, age group and duration by family history of diabetes, diabetic complications and duration of partial remission.

| | Sex (n) | | | Age group (years) | | | | | Duration (years) | | | | |
|---|-----------|----------|------|-------------------|----------|-----------|----------|------|------------------|----------|----------|----------|------|
| | Male | Female | P | <5 | 5-10 | 11-15 | >15 | P | <5 | 5-10 | 11-15 | >15 | P |
| Family history | | | | | | | | | | | | | |
| Positive | 123 | 137 | | 7 | 76 | 109 | 68 | .324 | 152 | 86 | 17 | 4 | .277 |
| Negative | 47 | 46 | | 6 | 22 | 41 | 24 | | 62 | 21 | 7 | 1 | |
| Total | 170 | 183 | | 13 | 98 | 150 | 92 | | 214 | 107 | 24 | 5 | |
| Diabetic complications (acute and chronic) | | | | | | | | | | | | | |
| Hypoglycemia | 106 | 116 | .899 | 7 | 64 | 102 | 49 | .242 | 135 | 67 | 17 | 3 | .265 |
| Diabetic ketoacidosis | 32 | 56 | .01 | 1 | 13 | 51 | 23 | .003 | 43 | 37 | 7 | 1 | .015 |
| Retinopathy | 3 | 1 | .262 | 0 | 0 | 4 | 0 | .173 | 2 | 2 | 0 | 0 | .859 |
| Neuropathy | 0 | 2 | .173 | 0 | 1 | 1 | 0 | .818 | 0 | 1 | 1 | 0 | .075 |
| Coronary heart disease | 0 | 2 | | 0 | 0 | 1 | 1 | | 1 | 1 | 0 | 0 | |
| Nephropathy | 0 | 1 | .343 | 0 | 0 | 0 | 1 | .315 | 0 | 0 | 1 | 0 | .002 |
| Duration of partial remission ("honeymoon phase") (days) | | | | | | | | | | | | | |
| ≤30 | 6 | 8 | .727 | 0 | 6 | 8 | 1 | .258 | 12 | 3 | 0 | 0 | .614 |
| >30 | 6 | 1 | | 0 | 0 | 4 | 1 | | 6 | 0 | 0 | 0 | |
| Total | 12 | 9 | | 0 | 6 | 13 | 2 | | 18 | 3 | 0 | 0 | |

Total number of patients <369 because all the variables were not recorded for every patients in the file. So for some patients some of the data were missing.

The most common clinical presentations in the present study were polyuria (92%) and polydipsia (88.8%). In the study by Salman et al, DKA was the most common clinical presentation and was observed in 74 (67.3%) patients; while in the present study, DKA was observed in 49.9% of the patients. In the study by Abdullah, 55% of the patients presented with DKA. Studies in Malaysia revealed a figure (48%) similar to that in the present study, while studies in Philippines and India revealed figures of 63% and 20%-40%, respectively.^{6,21,22} DKA is considered uncommon in Japan and Indonesia.^{23,24} DKA was observed in 49.9% of the patients in this se-

ries; thus DKA was less common in this study than in other local studies, such as those by Salman et al (DKA was observed in 67.2% of the patients) and Abdullah (DKA observed in 55% of the patients). This difference may be explained by a higher level of awareness among parents and improvement in health services with early diagnosis.

The partial remission rate in this study was only 9.1%, which is lower than the rates observed in the studies by Abdullah (32%) and Salman et al. (30.9%). It correlates to those studies in relation to age group; none of the patients below 5 years of age had any episode. Partial

Table 3. Symptoms of pediatric diabetic patients on presentation at the diabetes center according sex, age group, and duration of symptoms.

| Presentation | No. (%) | Sex | | | Age (years) | | | | | Duration of symptoms before diagnosis (days) | | |
|-----------------------|------------|------------|------------|------|-------------|-----------|------------|-----------|-------|--|-----------|------|
| | | M | F | P | <5 | 5-10 | 11-15 | >15 | P | <30 | >30 | P |
| Polyuria | 321 (92) | 157 (44.9) | 164 (46.9) | .039 | 12 (3.4) | 95 (27.2) | 136 (38.9) | 78 (22.3) | .012 | 195 (191.1) | 19 (8.9) | .054 |
| Polydipsia | 310 (88.8) | 139 (39.8) | 171 (48.9) | .005 | 10 (2.9) | 83 (23.8) | 138 (39.5) | 79 (22.6) | 0.000 | 177 (91.2) | 17 (8.8) | .066 |
| Weight loss | 292 (83.9) | 164 (47.1) | 128 (36.8) | .009 | 10 (2.9) | 75 (21.6) | 131 (37.6) | 76 (21.8) | .012 | 168 (90.3) | 18 (9.7) | .093 |
| Fatigue | 179 (77.5) | 82 (35.5) | 97 (41.9) | .051 | 9 (3.9) | 46 (19.9) | 85 (36.8) | 39 (16.9) | .472 | 107 (91.4) | 10 (8.5) | .548 |
| Nocturia | 240 (68.8) | 111 (31.8) | 129 (36.9) | .460 | 7 (2) | 60 (17.2) | 110 (31.5) | 63 (18.1) | .670 | 132 (91.0) | 13 (9.0) | .130 |
| DKA | 174 (49.9) | 70 (20.1) | 104 (29.8) | .001 | 8 (2.3) | 50 (14.3) | 87 (24.9) | 29 (8.3) | .025 | 177 (93.6) | 12 (6.3) | .027 |
| Abdominal pain | 172 (49.3) | 71 (20.3) | 101 (28.9) | .001 | 7 (2) | 49 (14.0) | 73 (20.9) | 43 (12.3) | .123 | 96 (88.9) | 12 (11.1) | .805 |
| Polyphagia | 91 (39.4) | 39 (16.9) | 52 (22.5) | .397 | 3 (1.3) | 21 (9.1) | 42 (18.2) | 25 (10.8) | .341 | 54 (91.5) | 5 (8.5) | .076 |
| Dehydration | 81 (35.1) | 35 (15.2) | 46 (19.9) | .402 | 6 (2.6) | 21 (9.1) | 40 (17.3) | 14 (6.1) | .430 | 48 (92.3) | 4 (7.7) | .408 |
| Anorexia | 78 (33.8) | 31 (13.4) | 47 (20.3) | .541 | 5 (2.2) | 19 (8.2) | 39 (16.9) | 15 (6.5) | .679 | 50 (92.6) | 4 (7.4) | .694 |
| Fever | 105 (30.1) | 43 (12.3) | 62 (17.8) | .263 | 4 (1.1) | 29 (8.3) | 48 (13.8) | 24 (6.9) | .641 | 58 (85.3) | 10 (14.7) | .392 |
| Delayed wound healing | 42 (18.3) | 12 (5.2) | 30 (13.1) | .228 | 0 | 9 (3.9) | 24 (10.5) | 9 (3.9) | .896 | 25 (92.6) | 2 (7.4) | .971 |
| Vomiting | 52 (14.9) | 22 (6.3) | 30 (8.6) | .513 | 3 (0.9) | 12 (3.4) | 24 (6.9) | 13 (3.7) | .326 | 36 (90) | 4 (10) | .008 |
| Preceding illness | 24 (6.9) | 12 (3.4) | 12 (3.4) | .994 | 0 | 5 (1.4) | 14 (4.0) | 5 (1.4) | .190 | 13 (92.9) | 1 (7.1) | .399 |
| Loss of consciousness | 21 (6) | 9 (2.6) | 12 (3.4) | .326 | 1 (0.3) | 5 (1.4) | 9 (2.6) | 6 (1.7) | .56 | 12 (92.3) | 1 (7.7) | .508 |
| Diarrhea | 10 (4.3) | 7 (3.0) | 3 (1.3) | .076 | 2 (0.9) | 2 (0.9) | 5 (2.2) | 1 (0.4) | .004 | 5 (100) | 0 | .649 |
| Asymptomatic | 9 (4.3) | 7 (3.0) | 2 (0.9) | .837 | 0 | 4 (1.7) | 1 (0.4) | 4 (1.7) | .352 | 5 (83.3) | 1 (16.7) | .312 |

Data are n (%). Presenting symptoms were missing in 20 files, so the percentages were calculated among 349 patients.

Table 4. Diabetic complications (acute and chronic).

| | |
|------------------------|-----------|
| Hypoglycemia | 222 (62) |
| Diabetic ketoacidosis | 88 (23.8) |
| Retinopathy | 4 (1.3) |
| Neuropathy | 2 (0.6) |
| Coronary heart disease | 2 (0.6) |
| Nephropathy | 1 (0.4) |

Data are n (%).

remission is considered more common when diabetes is diagnosed in older children and teenagers, and most patients in the present study were diagnosed when they were less than 11 years of age (**Figure 1**); this might explain the low rate of partial remission observed in this study. The lower incidence of DKA may further explain the low rate of partial remission.

A positive family history of both types (1 and 2) of diabetes was observed in 73.7% of the patients in this study; this figure is higher than that reported in the study by Abdullah (56.7%). DM occurs significantly more frequently in the parents and siblings of diabetics than in those of the control population.^{25,26} In the study by Salman et al., both the consanguinity rate and family history of type 1 and 2 diabetes were higher than those reported in the literature and also in

a similar local study.²⁵⁻²⁹

The treatment of DM in children requires the provision of a comprehensive, well-coordinated and continuous service. This is best achieved by teamwork. Adolescents or "young adults" in Saudi Arabia and in some other non-Western countries are not examined at pediatric clinics and do not receive adequate attention at adult clinics. Studies of the microvascular complications in non-insulin-dependent DM patients suggest that the onset of these complications occurs at least 4-6 years before clinical diagnosis. Evidence shows that strict glycaemic control prevents microvascular complications.³⁰

In summary, the incidence of DKA was lower than that reported in previous studies; in addition, unlike in previous studies, DKA was not the most common clinical presentation. This difference is due to better awareness and early diagnosis. Additionally, the partial remission rate was lower, which indicates early diagnosis. Although chronic complications are uncommon in children, retinopathy, neuropathy, coronary heart disease and nephropathy have been observed; this necessitates an awareness among physicians, caretakers and patients about the importance of early diagnosis and strict control of DM. The incidence of family history was higher than that reported previously, which can be explained by the higher rate of consanguinity in the Saudi community. This observation indicates the need for further genetic studies of DM in the Saudi population.

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