Relationship of Family History with Sex and Age in Newly Diagnosed Children with Insulin Dependent Diabetes Mellitus in the Western Province of Saudi Arabia

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Abstract

We aimed to determine the magnitude of positive family history (FH) of IDDM among 1st and 2nd degree relatives of newly diagnosed children with IDDM throughout 4 years study and evaluation of its relationship with sex and age in western province of Saudi Arabia.

Methods: Data were collected from medical records of 119 newly diagnosed patients with IDDM 69 females (58%) and 50 males (42%) with Age ranged between 1 month and 12 years at diagnosis, who were followed-up at the outpatient endocrinology clinic throughout 4 years study from beginning of 2005 till the end of 2008. These data included sex, age at initial diagnosis, parental consanguinity and family history (FH) of other diabetic relatives of 1st, 2nd degrees including parents, siblings, uncles/aunts, cousins and grandparents. In addition, patients' clinical data suggestive of associated autoimmune disorders and FH of affected members with autoimmune disease were also looked for. Patients' historical data were obtained by a detailed questionnaire of family members; who were mostly the two parents.

Results: It was noted that females had got suffering usually at a mean of 1 year or more older than males. Moreover, it was noted that the closer the relationship of diabetic family members to the diabetic child, the earlier age at initial clinical presentation. FH of diabetic 1st degree relative (parents and siblings) with IDDM was 26.1% in females and 24% in males. Strong FH with affected more than one 1st degree relative with IDDM was reported in 10.1% of females versus 2mal% in es. Sex differences as regard for age at initial diagnosis and family members affected with diabetes (IDDM or NIDDM) were non-significant by different statistical methods while for autoimmune disorders in the family members, it was highly significant more frequent in the female side while absent in male side.

Key Words: Family history – Sex and age in newly diagnosed children – IDDM.

Introduction

INSULIN-dependent diabetes mellitus (IDDM) or type I diabetes is a worldwide occurrence disease of childhood with genetic, environmental and familial risk factors [1]. It was recently suggested that there is a tendency of the rising incidence of IDDM [2]. It is commonly known that there is a higher risk of similarly affected relatives of patients with IDDM. According to some reports in families of these patients the incidence of non-IDDM (NIDDM) is also higher [3].

Setting:

Pediatric diabetic Clinic of king Abdulaziz university hospital at Jeddah western Province, Saudi Arabia).

Aim of the study:

Our study aimed to determine the magnitude of positive family history (FH) of IDDM among 1st and 2nd degree relatives of newly diagnosed children with IDDM throughout 4 years study and evaluation of its relationship with sex and age in western province of Saudi.

Patients and Methods

Data were collected from medical records of 119 newly diagnosed patients with IDDM, following-up at the outpatient endocrinology clinic throughout 4 years study from beginning of 2005 till the end of 2008. These data included sex, age at initial diagnosis, parental consanguinity and family history (FH) of other diabetic relatives of 1st 2nd degrees including parents, siblings, uncles/aunts, cousins and grandparents. In addition, patients' clinical data suggestive of associated autoimmune disorders and FH of affected members with autoimmune disease were also looked for. Patients' historical data were obtained by a detailed questionnaire of family members; who were mostly the two parents. Data were considered accurate
when same information were obtained by more than one physician at several clinic visits and when there was no disagreement with the data recorded before in the medical files. Data were analyzed by Chi-Square, ANOVA and t-tests.

**Results**

One hundred and nineteen patients; 69 females (58%) and 50 males (42%) were included. Age at diagnosis ranged between 1 month and 12 years. 21% of both sexes had ages below 4 years (18.8% of females and 28% of males). The mean age at diagnosis was 6.9 years for females and 6 years for males with overall mean was 6.5y. Positive FH of at least one diabetic member of 1st, 2nd degree relatives (type I or II diabetes) was reported in 73.9% of females and 68% of males. In case of diabetic females, the order of frequency was grandparents (29%), siblings (24.6%), cousins (17.4%), father (8.7%) and mother (4.3%). In case of diabetic males, the affected family members were Grandparents (30%), father (16%), siblings (16%), uncles/aunts (8%), cousins (8%) and mother (2%). All diabetic siblings and cousins, 42.9% of diabetic fathers, 75% of diabetic mothers and 20% of diabetic grandparents had IDDM. The rest of family members had NIDDM. About 34.5% of our subjects had at least one family member among 1st and 2nd degree relatives affected with IDDM (25.2% and 20.2% respectively) with female diabetics had more prevalence compared to males (36.2% and 32% respectively). In females, siblings (24.6%) followed by cousins (17.4%) were the most reported affected relatives and fathers were more noticed than mothers to have IDDM (2.9% Vs. 1.4%). In case of male diabetics, siblings were the most frequently affected relatives (16%) followed by grandparents (10%), then fathers and cousins (each 8%) with mothers only 2%. As a total, FH of diabetic 1st degree relative (parents and siblings) with IDDM was 26.1% in females and 24% in males. Strong FH with affected more than one 1st degree relative with IDDM was reported in 7.2% of females and 8% of males. In diabetic children having ages below 4 years, 1st degree relatives affected with IDDM represented 36% (30.8% in females and 41.7% in males) and 2nd degree relatives represented 28% (30.8% in females and 25% in males). Preceding or co-incidence of one or more of autoimmune disorders was reported in 10.1% of females versus 2% in males. Positive FH of autoimmune disorder was 13% in females versus nil in males. These disorders included in descending frequencies, thyroiditis, vitiligo, alopecia and hypoparathyroidism. Consanguinity up to 2nd degree was reported equally in 42% of both females and males. At diagnosis, for patients with FH of diabetic 1st degree relatives with or without other relatives; the mean age was 6.5 years for females and 5.5 years for males while for patients with FH of only diabetic 2nd degree relatives, the mean age was 7.2 years in females and 5.7 years for males and for patients with negative FH, the mean age was 7 years in females and 6.9 years in males. Sex differences as regard for age at initial diagnosis and family members affected with diabetes (IDDM or NIDDM) were non-significant by different statistical methods while for autoimmune disorders in the family members, it was highly significant more frequent in the female side.

| Table (1): FH of IDDM in 1st and 2nd degree relatives of diabetic children. |
|-----------------|-----------------|-----------------|
|                  | Male            | Female          | Total            |
| Father           | 4               | 2               | 6               |
| Mother           | 1               | 1               | 2               |
| Sibling          | 8               | 17              | 25              |
| 1st degree relative | 12             | 17              | 25              |
| Cousin           | 4               | 12              | 16              |
| Uncle/Aunt      | 1               | 3               | 4               |
| Grandparent      | 5               | 3               | 8               |
| 2nd degree relative | 8             | 16              | 24              |
| Both 1st & 2nd degree relatives | 4             | 9               | 13              |

FH of type 1 diabetes in relatives of the diabetic children

Fig. (1)
Several international published reports handled IDDM profile in relation to sex, age and family history. In our area, a proper registry system for documentation of all cases of IDDM has not yet fully developed; but in fact, our hospital as a main patient attending/referral center for pediatric patients, is considered as a convenient place that could give a satisfactory idea about profile of IDDM in our area.

During the 4 years of the study course, females were more frequently affected with IDDM than males (1.4: 1). Positive FH of IDDM was noticed to be higher in females than in males particularly among 2nd degree relatives though non-significant difference was reported. It was apparent that siblings of diabetic children were the most frequently affected family members with IDDM particularly in females. This was not apparent to be significantly related to close parental consanguinity which is less than the overall parental consanguinity rate of our diabetic children (36% Vs. 42%) and this is a part of the continued trend of consanguineous marriage in the area as an inherent property of gulf cultural marital traditions. It was also noticed that the number of affected fathers with IDDM are twice as affected mothers and they are more related to males rather than to females.

The above mentioned figures are more or less differing from some other reports as a previous Saudi study [4] which reported that first degree family history was positive for IDDM in 28% in both sexes, (compared to 25.2% in our study) and among these cases, siblings accounted for 26%, fathers 2% and mothers none (compared to 21%, 5% and 1.7% respectively in our study). In an Austrian study [5], 5.8% of the diabetic children had at least one parent with IDDM and the prevalence of IDDM in fathers (3.9%) was higher compared to mothers (1.9%); the figures that are near to our results. In an old Swedish study [6] (1985) it was reported that 12.8% of the probands had a first degree relative with IDDM, which is about a half of our figure and it was twice as common that this relative was a father as a mother, which agreed with our findings. Also, Harjutsalo V, et al. [8] reported that the age-corrected risk for IDDM, is statistically significantly higher as much as twice in fathers (10.26 ± 1.75%) than in mothers (5.28 ± 1.49%). In another report by Svensson J et al. [9] it was found that in 9.7% of families of IDDM, one of parents was also reported to have same type of diabetes (compared to 6.7% in our study) and in 0.2% of families both parents had IDDM.
same study, 2.3% of the diabetic families had a sibling with IDDM, which is much less than our figure (21%). In another study [10], it was found that affected girls with IDDM were more likely to have a father with IDDM than affected boys which is contradicting to our results.

It was noted that females had gotten suffering usually at a mean of 1 year or more older than males. Moreover, it was noted that the closer the relationship of diabetic family members to the diabetic child, the earlier age at initial clinical presentation. Lower ages at diagnosis were observed when a diabetic male had affected fathers with IDDM; the mean was 2.6 years Vs. 7 years in those with FH of fathers with NIDDM. Males with affected siblings, whatever parents were healthy or affected, had mean age of 6.6 years at diagnosis. In females, the lowest ages at diagnosis, were observed when there were affected siblings; the mean age was about 5.8 years. It was also noted that diabetic children of both sexes younger than 4 years old, had higher incidence of positive FH of IDDM among both 1st and 2nd degree relatives (36% and 28% respectively Vs. 22.3% and 18.1% in those older than 4 years age). This finding was little more in relatives of diabetic males particularly among the 1st degree. Positive parental consanguinity per se, even of 1st degree; does not differ significantly than negative parental consanguinity as regard to relation to the initial age of presentation. The above mentioned findings may be partially agreed with the report of Bienisz J [1] who suggested that familial IDDM patients have a younger age at onset than non-familial patients supported by the fact that children with disease onset in the 0-4 year age-range were more likely to have an affected father than were children who were older at onset and similar although weaker associations were seen in mothers and siblings.

Associated and/or positive FH of autoimmune disorders is almost confined to diabetic females in our study (23.2% Vs. 2% in males), the finding that is matching with the preponderance of autoimmune disorders in females as generally agreed in other reports particularly with thyroid disorders and alopecia Areata [11,12]. Mean age at diagnosis for these children, was higher (9.5 years) compared to other diabetic children without present or family histories of autoimmune disorders (6 years) meaning that no tendency for earlier presentation as with FH of IDDM.

It could be concluded from the above data that FH of IDDM among relatives of newly diagnosed diabetic children is so pronounced that it actually exceeds what reported in many world areas and there are some remarkable differences between both sexes as regard for ages at clinical presentation and its relationship with the frequencies of IDDM among 1st and 2nd degree relatives that are variably agreed with other reports.

References