Singapore Med J 1998; Vol 39(8):359-362

The Incidence of IDDM in Singapore Children

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ABSTRACT

Objective: To determine the incidence of insulin dependent diabetes mellitus (IDDM) in children 0-12 years of age in Singapore, which has a population of 2.9 million.

Methods: The primary source was a 2-year phone and mail survey of doctors in the government and government restructured hospitals and the private sector. The secondary source was the membership records of the Diabetes Society of Singapore.

Results: Using the capture-recapture method, ascertainment was assessed to be 92.2% complete. The age standardised incidence rate was 2.46 per 100,000 children 0 – 12 years old, for the period 1992 – 1994 (95% confidence interval : 2.16 – 2.75). The data seemed to indicate a rising incidence of IDDM in this population, being 1.4/100,000 in 1992, 2.4/100,000 in 1993 and 3.8/100,000 in 1994. The male : female ratio is 1:1.85. There was seasonal variation with fewer cases from July to October and more from November to May. Five percent of patients had a first degree relative with IDDM. Malays appeared to have a lower incidence (1.23/100,000) compared to the Chinese (2.25/100,000) and the Indians (5.78/100,000).

Conclusions: The incidence of IDDM in Singapore children is similar to that reported for Hong Kong and Japan, but higher than that for Shanghai. The female preponderance is similar to that seen in other Asian population. The data suggests a rising incidence of IDDM in Singapore and differences in incidence between the Malays, Chinese and Indians, but further observations are needed.

Keywords: IDDM, incidence, children, Singapore

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INTRODUCTION

Singapore is a small 622 km^2 island, 1° 17' North of the Equator with a population of 3.1 million people. The population is 77.7% Chinese, 14.1% Malay, 7.1% Indian, and about 1.1% of the population comprises a mixture of other ethnic groups including Caucasians. The incidence and prevalence of insulin-dependent diabetes mellitus in Singapore has always been thought to be low, but accurate incidence figures were hitherto unavailable for Singapore and much of Southeast Asia. There is currently no central registry for IDDM in Singapore, but we have collected incidence data for the years 1992 to 1994 using standardised criteria and a capture-recapture methodology according to the WHO Diamond protocol[1].

RESEARCH DESIGN AND METHODS

Inclusion criteria

The inclusion criteria included only patients who had insulin-dependent diabetes mellitus (IDDM) currently on insulin therapy, presenting in diabetic ketoacidosis or with symptoms of polyuria, polydipsia, glycosuria and hyperglycemia (fasting blood sugar $>$ 7.8 mmol/L or random blood sugar $>$ 11.1 mmol/L), and who were $\leq$ 12 years of age at the time of diagnosis. The date of diagnosis was taken as the date of initiating therapy for IDDM. We only counted patients who were first diagnosed during the period 1 January 1992 – 31 December 1994, and who were first diagnosed to have IDDM in Singapore. Three children were excluded because they were diagnosed to have non-insulin dependent diabetes mellitus (NIDDM).

The healthcare system in Singapore is well-developed, but children under 12 years old with IDDM tend to be admitted to a limited number of paediatric units in government and government restructured hospitals. After the age of 12 years, children are admitted to adult medical units in a larger variety of public and private institutions, so the cut-off age of 12 years was chosen for logistical reasons.

Validation of case ascertainment

The primary (capture) source was a physician survey initiated in 1993, and based on hospital records from the Singapore General Hospital (SGH), the National University Hospital (NUH), Tan Tock Seng Hospital (TTSH), Alexandra Hospital (AH), as well as an on-going mail and phone survey of paediatricians and endocrinologists in the public and private sectors under the auspices of the Endocrine and Metabolic Society of Singapore, the Singapore Paediatric Society and the Paediatric Workgroup for the Standards of Care for the management of children with diabetes mellitus, National Diabetes Commission. This was followed-up over the next two years by periodic phone calls and further correspondence. Incidence data collected included name, address, date of birth, date

of first diagnosis and the birth certificate number, in order to prevent double counting. Clinical details included the mode of presentation (whether in DKA) and family history of diabetes.

The independent secondary source (recapture) was the membership database of the Diabetic Society of Singapore (DSS), which is a voluntary self-help organisation that runs a discounted diabetes supplies scheme. Children who were initially seen in the private sector and therefore possibly missed by the primary source, would still be likely to join the Diabetic Society for discounted supplies such as syringes and glucose test strips. The cases identified by the primary source were compared with those registered by the secondary source (DSS).

School Health Service (SHS) Records serve as a useful cross-check because they represent a voluntary database of parents – reported medical conditions on all schoolchildren in Singapore, and 97% of Singapore children 6 – 12 years of age attend school. However, the SHS database did not turn up those cases not covered in the primary and secondary sources.

DEMOGRAPHIC DATA

Demographic data for this study was extracted from the census of Singapore, 1990, with a census update in 1993, and current published data from the Singapore Registry of Births and Deaths for the years 1992 – 1995[2,3]. In the 1990 census, only 0.4% of residents less than 15 years old were born outside Singapore, while the ethnic composition of the population has been stable over the decade 1980 – 1990. Using the 1990 census year as an example, the calculated population cohort aged 12 years and below, based on the crude birth cohort, was 546,169, while the actual census cohort was 546,189 a difference of only 20.

The total population at risk during this period was calculated using birth cohort figures for the years 1980 to 1994, giving a population at risk (0 – 12 years) of 579,104 in 1992; 589,330 in 1993, and 598,130 in 1994, with a total 19 population at risk of 1,766,564 over 1992 – 1994.

RESULTS

Completeness of ascertainment

Over the 3-year period, ascertainment of the primary source was 83%, that of the secondary source 53%, and the ascertainment of the combined sources was 92.2%. The ascertainment of the combined sources was 100% in 1992, 78.6% in 1993, and 94% in 1994. The ascertainment of the primary and secondary sources for each year is listed in Table I.

The small number of paediatric departments and the relatively small number of paediatricians dealing with childhood IDDM made it easier to collect accurate data on an on-going basis. Thirty-four patients were reported through the primary source. Twenty-three patients were reported through the DSS database, of which 4 were not covered in the primary source records. Of these 4 cases, 2 were found in 1993 and 2 were found in 1994.

Description of data

Because of the small number of patients over the 3 years, variations in incidence between years, age groups must be interpreted with caution. Nevertheless, some interesting patterns emerged when we studied the breakdown of incidence by year, sex, age group and ethnic group.

The raw data suggests an increase in incidence over the 3 years from 1992 – 1994, being 1.4 per 100,000 in 1992; 1.7 per 100,000 in 1993, and 3.7 per 100,000 in 1994. However, using ascertained incidence figures, the corresponding incidence figures for 1992 remained unchanged at 1.4 per 100,000, but the 1993 incidence was 2.4 per 100,000 (95% confidence limit 1.4 – 3.4), and that for 1994 was 3.7 per 100,000 (95% confidence limits 3.3 – 4.3) (Table II).

Racial composition

There were 30 Chinese (75%), 4 Malays (10%), 5 Indians (12.5%) and one Eurasian (2.5%). Singapore's racial composition in this age group is 77.7% Chinese, 14.1% Malay, 7.1% Indians and

Table I – Ascertainment of primary and secondary sources for the incidence of childhood IDDM in Singapore, 1992 – 1994

Year	Cases identified	% from primary source	% from secondary source	Both sources	Ascertained number	Variance	Incidence (+/-95% C.I)	Incidence in males	Incidence on females
1992	8	100%	62.5%	100%	8	0	1.4 per 10^5 (0)	0.5 per 10^5	1.8 per 10^5
1993	10	64%	36%	78.6%	14	9	2.4 per 10^5 (1.4 – 3.4)	1.3 per 10^5	2.2 per 10^5
1994	22	85%	58%	94%	22.3	2.4	3.7 per 10^5 (3.3 – 4.3)	2.6 per 10^5	4.9 per 10^5
1992 – 94	40	83%	53%	92.2%	43.4	2.68	2.46 per 10^5 (2.16 – 2.75)	1.56 per 10^5	3.11 per 10^5

Table II – Racial distribution of IDDM cases in Singapore children, 1992 – 1994

No. of cases by race	1992	1993	1994	1992 – 94	Percentage of cases	Ethnic distribution of Singapore	Incidence
Chinese	8	7	15	30	75%	77.1%	2.25/105 Chinese
Malay	0	0	3	3	7.5%	14.1%	1.23/105 Malays
Indian	0	3	3	6	15%	7.1%	5.78/105 Indians
Others	0	0	1	1	2.5%	1.1%	5.25/105 Others

Table III – Patients identified in each age group, incidence per 100,000 children

Age group	Males	Females	M : F ratio	1992	1993	1994	1992 – 94
0 – 4 years	8	10	1 : 1.25	0.4	2.8	4.1	2.4
5 – 9 years	4	6	1 : 1.5	1.5	0	3.2	1.6
10 – 12 years	2	10	1 : 5	3.3	2.4	4.1	3.3
0 – 12 years	14	26	1 : 1.8	1 : 1.4	2.4	3.7	2.46

1.1% Other races. The data suggests that the Malays have a lower incidence of 1.23 per 100,000 compared to the Chinese at 2.25 per 100,000 and the Indians appear to have the highest incidence of 5.78 per 100,000. The results for the Malays and Indians must however be interpreted with caution because of the small numbers and wide confidence intervals involved. This is summarised in Table III.

Sex ratio

The M:F sex ratio was 1:1.86, contrasting with a population M:F ratio of 1:0.93 in this age group. There is an unmistakable female preponderance with increasing age in IDDM in the Singapore population, with an overall male to female ratio of 1:1.86, and rising from 1:1.25 in the 0 – 4 year age group, 1:1.5 in the 5 – 9 year age group and 1:5 in the 10 – 12 year age group. This gives a sex specific incidence of 1.56 per 100,000 males, and 3.11 per 100,000 females in the 0 – 12 year age group. The sex ratio is summarised in Table II.

Age of onset

There was a peak in incidence at 0 – 4-years and again at 10 – 12 years. The overall mean age of onset of the boys was 5.6 years, while that for the girls was 7.0 years. The age-specific incidence rates were 2.4 per 100,000 for the 0 – 4-year age group, 1.6 per 100,000 for the 5 – 9-year age group, and 3.3 per 100,000 for the 10 – 12-year age group. This is summarised in Table III.

Presentation

Diabetic ketoacidosis was a presenting feature in 12/31cases (39%). Polyuria and polydipsia were presenting symptoms in all other cases, but the duration of symptoms was not recorded.

Family history of diabetes

Five percent had a family history of IDDM, while 5% of patients had mothers with gestational diabetes, and 5% had a parent with NIDDM. If second degree relatives were included, a total of 22.5% had a family history of NIDDM.

Seasonal variation

Fig 1 shows that there are peaks in incidence from November to February and April to May, while fewer cases were seen in March and from July to October.

DISCUSSION

Insulin-dependent diabetes mellitus (IDDM) has previously been shown to be rare in the Chinese and Japanese and was said to have been very rare in Singapore. Wong in 1981, found a prevalence of 0.04 per 100,000 Chinese children under the age of 12 years. In 1985, there were only a total of 20 cases of IDDM on follow-up at all 4 of the government Paediatric Units in Singapore. In 1994, the School Health Service had a total of 129 cases of childhood diabetes mellitus between the ages of 6 and 18 known to them, of which 77 were girls and 52 were boys (Tan and Rajan 1994, unpublished). Lee in 1995, found only 3 NIDDM patients in a clinic population of 30 cases of diabetes in childhood, which suggests that only 10% of childhood diabetes is of Type II NIDDM.

The apparent increase in incidence of IDDM in childhood which followed the start of our study, is intriguing. The increase was most marked in the 0 – 4-year age group, going up from 0.4 to 2.8 to 4.1 per 100,000 children at risk over the period 1992 – 1994. The cause for this is still unclear.

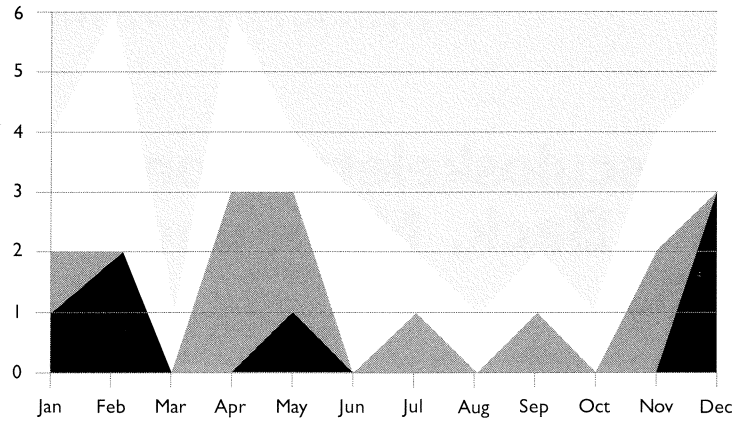

Fig 1 – New cases of childhood IDDM in Singapore by month of diagnosis, 1992 – 94

Table IV – Incidence of IDDM in some Asian countries and Singapore

Countries	Incidence	Age group	Reference
Hong Kong	1.7 per 10^5	children < 15 years	Wong 1993[4]
Japan	1.65 – 2.0 per 10^5	children < 15 years	Kitagawa 1994[7]
Korea	0.6 per 10^5	children < 15 years	Ko et al, 1994[10]
Shanghai	0.72 per 10^5	children < 15 years	Fu 1994[5]
Australia	11 – 22 per 10^5	children < 15 years	Kelly 1994 – 95
Singapore (all races)	2.46 per 10^5	children 0 – 12 years	current report
Singapore Chinese	2.25 per 10^5	children 0 – 12 years	ibid
Singapore Malays	1.23 per 10^5	children 0 – 12 years	ibid
Singapore Indians	5.78 per 10^5	children 0 – 12 years	ibid

The age specific incidence is highest for the 10 – 12-year age group, at 3.3 per 100,000. This suggests that the incidence of IDDM in the 0 – 15-year age group would be well above 2.41 per 100,000 per annum, since most studies around the world show a peak of incidence in the mid-teens.

The incidence of IDDM among the Chinese in Singapore, who are mainly of southern Chinese extraction, is similar to that of Hong Kong[4] where the population is again predominantly southern Chinese, but both Singapore and Hong Kong have a higher incidence of childhood IDDM than the Chinese of Shanghai[5]. This belies the conventional wisdom that the incidence of IDDM gets higher as we go further from the equator. Table IV compares the incidence of IDDM in Singapore with other populations in the region.

From our figures, the Indian population is at a particularly high risk with an incidence of 5.78 per 100,000 children under 12 years and this reflects their much higher risk of Type II or NIDDM in our population. While the numbers are small, they appear to agree with prevalence data from elsewhere[6,8]. Ramachandran in 1992, found a prevalence of 26 per 100,000 children under 15 years in an urban Southern Indian population[8], while Wong in Hong Kong found a prevalence of 8.3 per 100,000 children < 15 years of age in an urban Southern Chinese population[4].

Singapore boys have half the incidence of IDDM compared to Singapore girls, with an incidence of 1.56 vs 3.11 per 100,000 children 0 – 12 years. These figures are comparable to those of Hong Kong, where the respective rates are 1.1 per 100,000 males and 2.4 per 100,000 females < 15 years (Wong, 1993). A similar pattern was seen in children from Thailand, where the male : female ratio is 1:1.2 – 1.5[9]. This is in contrast to Western populations where the male : female ratio approximates 1:1.

HLA studies were not performed on this cohort of patients, but previous studies in Singapore suggest that the frequency of AW33, B17, BW58 and DR3 was increased in IDDM when the age of onset was less than 10 years, while the frequency of DR4 was significantly elevated in the 11 – 20-year age of onset group. IDDM linked only with DR3 constitutes only 10% of IDDM in whites, and it is argued that we might expect to see a ten-fold reduction in frequency in this population. This correlates with our current findings. Recently, it was reported that there was a low frequency of non-aspartate at position 57 of the HLA DQ-beta in the Chinese and Japanese populations and that this would possibly account for the low incidence of IDDM in these populations.

CONCLUSION

The incidence of IDDM in Singapore children is similar to that reported for Hong Kong and Japan, but higher than that for Shanghai. The female preponderance is similarly seen in other Asian populations. The data suggests a rising incidence of IDDM in Singapore and differences in incidence between the Malays, Chinese and Indians, but further observations are needed.

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