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An Update on the Epidemiology of Childhood Diabetes in Hong Kong

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Abstract

Objectives: To update the incidence of type 1 and type 2 diabetes in children aged <19 years from 1997 to 2007 in Hong Kong. ***Methods:*** Retrospective population-based incidence study. Primary ascertainment: reviewing medical records of diabetes patients in all public hospitals. Secondary ascertainment: impractical upon implementation of personal data privacy ordinance in Hong Kong. ***Results:*** Type 1 diabetes: Standardised age-adjusted incidence was 2.4/100,000/yr for children aged <15 years. Significant increase in incidence rate was shown (Slope=0.11/100,000/yr; R^2=0.40; p=0.036). There was a significant increase in incidence in 0-4-year age-group. Type 2 diabetes: Standardised age-adjusted incidence was 2.1/100,000/yr for 10-18-year age-group. Significant increase in incidence rate was shown (Slope=0.314/100,000/yr; R^2= 0.711; p=0.001), with a sharp rise after 2004. ***Conclusions:*** Standardised age-adjusted incidence of childhood type 1 diabetes remained low while that for type 2 diabetes was newly determined. A definite increase in incidence for both types was shown (1997-2007), with a trend towards younger age of onset.

Key words Children; Diabetes mellitus; Epidemiology; Incidence

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Introduction

Type 1 (insulin-dependent) diabetes mellitus is one of the most important chronic diseases of children worldwide especially in Northern Europe and North America.[1] In developed countries, individuals with type 1 diabetes have an 8-10 times higher risk of dying prematurely than the non-affected population.[2] In developing countries, most people with type 1 diabetes die within a few years after diagnosis.[3] Studies from Nishimura et al[4] and Matsushima et al[5] found a 10-fold variation in mortality in different countries, suggesting early diabetes mortality is related to both overall standards of health care and diabetes-specific care. The standardised mortality ratio varies from 0 to 4.7 between countries for young people with diabetes.[6] The mortality rate of diabetic ketoacidosis (DKA) was reported to be as high as 13.2% in India.[7] It appears that type 1 diabetes incidence may be rising in many areas throughout the world,[8,9] thus increasing the major health-care and economic burdens to society. There are considerable gaps in knowledge regarding the global patterns of the disease, host susceptibility, environmental risk factors, related morbidity and mortality, and health care and health economics of type 1 diabetes. The lack of information and standards for interpreting existing data impair the ability of the medical community to understand the impact of the disease. Moreover, effective public health measures cannot be developed without adequate data for their evaluation. Therefore global efforts designed to understand this disease is critically needed.

In the early 1980s, interest in the epidemiology of type 1 diabetes began to flourish as the result of the recognition that the place where a child lives is one of the most important determinants of risk of diabetes. [10] Moreover, there was indication of epidemic patterns of the disease[11] and a suggestion of north-south gradient. [9] These exciting within – and between – country comparisons pointed out the importance of cross-cultural studies and hence the need for standardisation.

Based on the rapid proliferation of standardised registries, evidence for extraordinary geographic differences in risk, and the evidence of a global increase in the incidence of this serious condition, a World Health Organizatioin program, Multinational Project for Childhood Diabetes (Diabetes Mondiale or DIAMOND) was established on 1 January 1990 to investigate and characterise global incidence, mortality, and health care. Over 10 years (1990-1999), this study collected population-based data concerning type 1 diabetes in 100 centres in 50 countries worldwide. The goals of DIAMOND are to collect standard information on incidence, risk factors, and mortality associated with type 1 diabetes; evaluate the efficiency and effectiveness of health care and the economics of diabetes; and establish national and international training programs in diabetes epidemiology.[1] It is hoped that the DIAMOND project will be instrumental for the prevention of this serious disease and its sequelae.

A well-validated register of diabetes mellitus in Hong Kong children according to the WHO DIAMOND protocol has been established from 1984 to 1996.[12] The aim of this paper is to report on the updated data for the registry from 1997 to 2007 for both type 1 and type 2 diabetes and assess the time trends in diabetes incidence in Hong Kong.

Subjects and Methods

Children newly diagnosed, satisfying standard criteria for the diagnosis of type 1 and type 2 diabetes mellitus (WHO/IDF definition of diabetes mellitus 2006),[13] were recorded retrospectively back from 1 January 1997 till 31 December 2007. All children aged under 19 years at diagnosis, and resident in Hong Kong at the time of diagnosis were eligible. The computerised medical record system (CMS) for all patients has been implemented under Hospital Authority for all public hospitals in Hong Kong since 1997. All patients with diagnostic ICD9-CM codes of 250 (diabetes mellitus), 250.0-250.9 (diabetes mellitus with other complications), 775.1 (neonatal diabetes mellitus) and V77.1 (screening for diabetes) were retrieved from CMS.

Meticulous primary ascertainment was made with participation of all the diabetologists and paediatricians working in the public hospitals in Hong Kong. Subjects were ascertained from their clinic records. Due to the easy accessibility, efficient and comprehensive medical service delivered by public hospitals in Hong Kong, most Chinese type 1 diabetes patients are referred to and followed up in public hospital clinics. So such a method of primary ascertainment should have retrieved nearly 100% of all the Chinese type 1 diabetes patients. Staff of Paediatric and Adolescent Medicine Departments in all public hospitals in Hong Kong see all patients <19 years of age. Private practitioners were not be surveyed because in our previous survey of all registered practitioners in Hong Kong in 1997, no children with type 1 diabetes was followed up in the private sector. Secondary ascertainment has been made difficult because of the implementation of the Personal Data

Privacy Ordinance in Hong Kong.

For each subject identified, basic demographic data from the clinical notes were recorded in a structured information data sheet including the child's name (initials only), sex, date of birth, hospital identification number (e.g. QMH 1, 2, 3; QEH 1, 2, 3 etc), date of diagnosis, type of diabetes (Type 1/ Type 2 / Secondary diabetes) and presenting history of diabetic ketoacidosis (Definition: heavy glycosuria and ketonuria + hyperglycaemia (BG >11 mmol/l) + pH <7.3 or bicarbonate <15 mmol/l) were noted.

Ethical approval for this study was obtained from the Research Ethics Committees of all the clusters under the Hospital Authority of Hong Kong.

Population Estimates

Census data are collected every 10 year by the Statistics Department of the Government of Hong Kong SAR.[14] The most recent census was completed in April 2001. The total population at the end of 2001 was 6,730,300. The average resident population under the age of 15 years and 19 years was 1,097,226 (16%) and 1,527,838 (23%) respectively during the study period. The Statistics Department also provided yearly intercensal estimated population data by age and sex for all districts in Hong Kong. There were no major changes in population structure from 1997 to 2007. There was an increase of about 7% in the population from 1997 (6,489,300) to 2007 (6,925,900). The annual growth rate over the decade averaged 0.6% compared with 1.4% for 1984-1997. The proportion of the population aged under 15 years fell from 18.1% in 1997 to 13.3% in 2007.

Statistical Analysis

The actual number of cases was used to calculate incidence rates and to compare between girls and boys. The age-standardised incidence rate is a weighted average of the age-specific incidence rates per 100,000 persons, where the weights are the proportions of persons in the corresponding age groups of the WHO standard population. The WHO World Standard Population was constructed based on the average world population structure for the period 2000-2025 as assessed every two years by the United Nations Population Division (UNPD) for each country by age and sex. Estimates from the UNPD 1998 assessment (being the latest one at the time the WHO Standard Population was chosen) based on population censuses and other demographic sources, adjusted for enumeration errors were used. The use of an average world population as well as a time series of observations removes the effects of historical events such as wars and famine on population age composition. WHO Standard Population is defined to reflect the average age structure of the world's population over the next generation, from the year 2000 to 2025.[15] The 2001 census population was used as reference standard in Hong Kong. Ninety-five percent confidence intervals were not given as the full Hong Kong population was involved in the study. The effects of age and sex on incidence rates were tested by X^2 statistics. P-value <0.05 was considered statistically significant. The projected incidence rate was estimated by simple linear regression. Data were analysed using SAS software.

Results

For the survey period from 1997 to 2007, we identified 553 Chinese children and adolescents with diabetes by reviewing records in all the public hospitals in Hong Kong. There were 335 type 1 and 198 type 2 diabetes patients. Patients with secondary causes of diabetes were excluded from analysis.

Type 1 Diabetes

For the 335 type 1 diabetes cases, 145 were males and 190 females with a male to female ratio of 0.76. Among these 355 patients, 204 or about 60% presented with diabetic ketoacidosis (DKA). The standardised age-adjusted incidence for males and females <19 years of age was 1.7/100,000/yr and 2.3/100,000/yr respectively. No significant difference was noted in diabetes incidence between boys and girls. The data for both sexes were therefore combined in the analysis. The standardised age-adjusted incidence for Hong Kong was 2.4 /100,000/yr for children <15 years of age and 2.0 /100,000/yr for those <19 years of age. Table 1 showed the incidence rates for the four age-groups. Table 2 showed the incidence rates by year from 1997 to 2007. 95% confidence intervals of the respective incidences were not calculated because we had covered the whole of the childhood population in Hong Kong. For children <15 years, Figure 1 showed a significant increase in the annual incidence rate of type 1 diabetes between 1997 and 2007 (Slope 0.11/100,000/yr; R^2=0.40; p=0.036). However, the increase was not so steep compared with the slope between 1984 and 1996 (Slope 0.14/100,000/yr; R^2=0.73;

p= 0.0002). The annual increase in incidence rate of type 1 diabetes from 1984 to 2007 was shown in Figure 2 (Slope 0.106/100,000/yr; R^2=0.78; p <0.001). On projection, an increase of about 1.0 new case/yr for the childhood population (<15 years old) is expected in Hong Kong. Concerning the age of onset of diabetes, the highest incidence in both sexes was in the 10-14 years age-group but there was a significant increase in the 0-4 years age-group (p<0.001). We identified 4 patients with age of onset before 1 year of age during the study period.

Type 2 Diabetes

For the 198 type 2 diabetes cases, 87 were males and 111 females with a male to female ratio of 0.78. Among these patients, only 3 presented with DKA. Three patients were 9 years old at presentation while all others were over 10 years. The highest incidence was found in the 10-14 years age-group. The standardised age-adjusted incidence for males and females <19 years of age was 1.1/100,000/yr and 1.5/100,000/yr respectively. The yearly age-adjusted incidence for Hong Kong was 0.9/100,000 for children <15

Table 1 Age-specific type 1 diabetes incidence rates for Hong Kong Chinese/100,000 person/year (1997-2007)

Age-groups	Cases (n)	Age-specific population*	Incidence#
0-4 years	65	261,800	2.2
5-9 years	110	391,700	2.4
10-14 years	118	429,900	2.4
15-18 years	42	348,400	1.0
Total 0-14 years	293	1,083,400	2.4
Total 0-18 years	335	1,431,800	2.0

* According to Hong Kong Resident Population as at End-2001

Incidence rate was age-adjusted to the world's population of WHO World Standard (2000-2025)

Table 2 Comparison of age-specific incidence rates of type 1 diabetes for Hong Kong Chinese/100,000 person/year (1984-1996 vs 1997-2007)

Age-groups	1984-1996	1997-2007	Statistical significance
0-4 years	0.9	2.2	P<0.001
5-9 years	1.5	2.4	P=0.518
10-14 years	1.7	2.4	P=0.663
Total 0-14 years	1.4	2.4	P<0.001

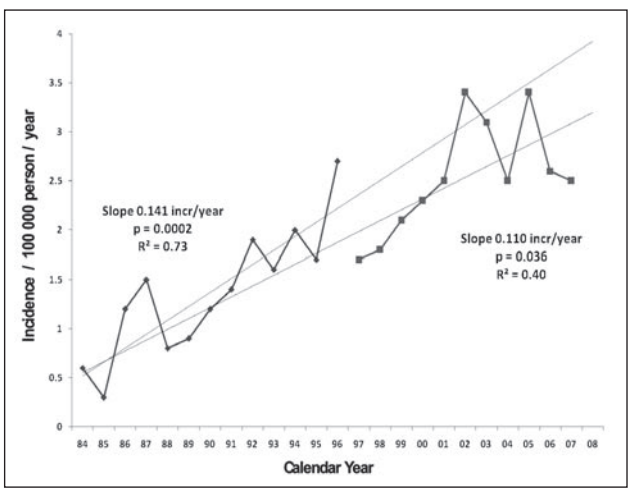

Figure 1 Time trends in incidence of type 1 diabetes for 0-14 year-old in Hong Kong from 1984 to 1996 and 1997 to 2007.

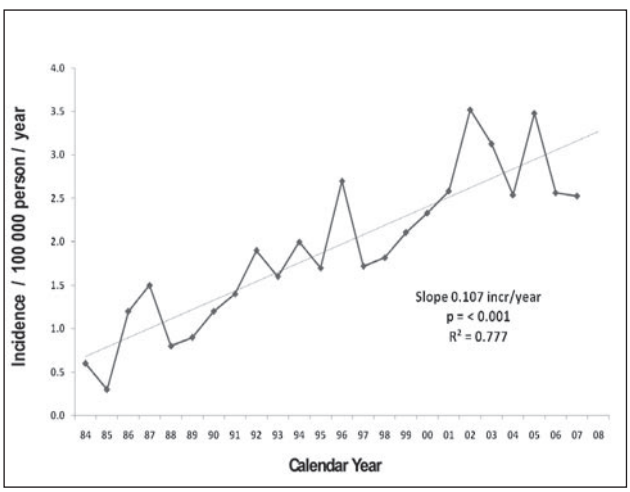

Figure 2 Time trends in incidence of type 1 diabetes for 0-14 year-old in Hong Kong from 1984 to 2007.

years and 1.2/100,000 for those <19 years of age. The standardised age-adjusted incidence for 10-18 years of age was 2.1/100,000. The incidence rates for the different age-group were shown in Table 4. The incidence rates by year from 1997 to 2007 were shown in Table 5. Figure 3 showed a significant increase in the annual incidence rate of type 2 diabetes between 1997 and 2007 by simple linear regression (Slope 0.314/100,000/yr; R^2=0.711; p=0.001). On projection, an increase of about 4.0 new cases/yr for the paediatric population (<19 years old) is expected in Hong Kong. However, we noted a significant non-linear component to the time trend (p<0.001) with a sharp rise after 2004. This probably coincided with the launching of the surveillance and screening for type 2 diabetes mellitus among obesity students by the Student Health Service in Hong Kong in 2005. Obese students (BMI >97th percentile for age) especially those with a family history of type 2 diabetes, acanthosis nigricans and polycystic ovarian syndrome were referred to paediatric specialist out-patient clinics in public hospitals for early assessment including an oral glucose tolerance test if indicated.

Discussion

A steady increase in the incidence of type 1 diabetes has been reported worldwide. The incidence of this disease varies considerably among countries and different ethnic groups. According to the registry of the WHO DIAMOND Project of children <15 years of age from 1990 to 1994 in 100 centres of 50 countries worldwide, the incidence differed by >350-fold, with the lowest rate of 0.1/100,000 in China and Venezuela and the highest rate of 36.8 and 36.5 /100,000 in Sardina and Finland respectively.[1] Even in Europe – the high-risk continent – the incidence of type 1 diabetes differs between countries by more than 10-fold.[16] A steep increase in incidence was also noted worldwide in the centres participating in the WHO DIAMOND Project – i.e. the average increase was 2.4% during 1990-1999, but 3.4% during the last part of the 1990s[8] – although this difference might have been partly explained by improved case-identification in some regions during the last years of the 10-year monitoring period. Although the peak incidence in type 1 diabetes was mostly noted at 10-14 years of age,

Table 3 Type 1 diabetes incidence rates for Hong Kong Chinese/100,000 person/year by year (1997-2007)

Year	Cases	Population <15 years of age*	Incidence
1997	20	1,162,700	1.7201
1998	21	1,154,600	1.8188
1999	24	1,137,400	2.1101
2000	26	1,114,800	2.3323
2001	28	1,083,400	2.5845
2002	37	1,051,200	3.5198
2003	32	1,023,300	3.1271
2004	25	984,300	2.5399
2005	33	948,500	3.4792
2006	24	935,800	2.5647
2007	23	909,600	2.5286

*Population estimation based on 2001 census

Table 4 Age-specific type 2 diabetes incidence rates for Hong Kong Chinese/100,000 person/year

Age-groups	Cases (n)	Age-specific population*	Incidence#
0-4 years	0	261,800	0
5-9 years	3	391,700	0.1
10-14 years	114	429,900	2.3
15-18 years	81	348,400	2.0
Total 0-14 years	117	1,083,400	0.9
Total 0-18 years	198	1,431,800	1.2

* According to Hong Kong Resident Population as at End-2001

Incidence rate was age-adjusted to the world's population of WHO World Standard (2000-2025)

Table 5 Type 2 diabetes incidence rates for Hong Kong Chinese/100,000 person-year by year

Year	Cases	Population <19 years of age*	Incidence
1997	3	1,537,100	0.1952
1998	4	1,530,800	0.2613
1999	6	1,505,500	0.3985
2000	8	1,477,800	0.5413
2001	12	1,431,800	0.8381
2002	14	1,392,300	1.0055
2003	13	1,368,700	0.9498
2004	17	1,329,000	1.2792
2005	52	1,300,700	3.9978
2006	36	1,290,800	2.7890
2007	33	1,260,300	2.6184

*Population estimation based on 2001 census

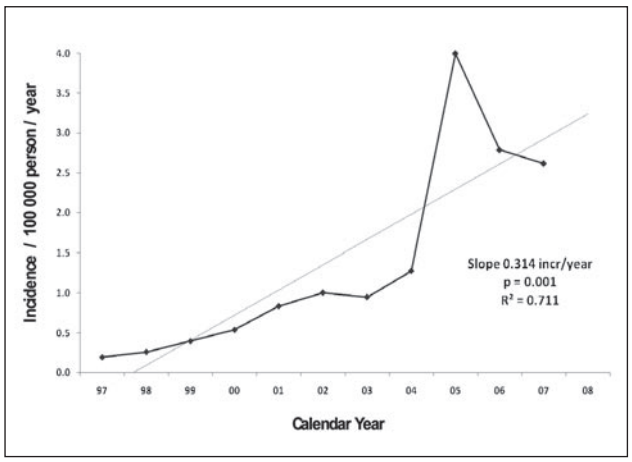

Figure 3 Time trends in incidence of type 2 diabetes for 0-18 year-old in Hong Kong from 1997 to 2007.

several countries have reported a trend towards earlier age of onset.[17] We previously reported steady increase in incidence of type 1 diabetes from 1984 to 1996 in Hong Kong.[12] In the present study, we again showed a continual increase in the annual incidence of type 1 diabetes between 1997 and 2007. Fortunately the incidence has remained low and the trend seems to be maintained at a slightly slower rate when compared with the previous study. The increase has been most pronounced in children under 4 years of age ($p<0.001$). This has also been reported in other countries like Finland and Germany.[17,18] The onset of type 1 diabetes is attributed to both genetic risk factors and external triggers or the absence of some protective factors in the child's environment. The increase in incidence indicates changes in the environment that are more harmful to people who are genetically susceptible and/or increase in the number of high-risk genes. For any degree of genetic susceptibility, age at presentation may decrease in a permissive environment. A recent study in Australia has reported the rising incidence and decreasing age at diagnosis of type 1 diabetes by the impact of environment on children with lower-risk HLA Class II genes (DR3,3 and DR4,4 and DR4, X and DR3, X genotypes but not DR3,4).[19] High birth weight and early weight gain in infancy have also been implicated as risk factors for the development of type1 diabetes.[20,21] Children with type 1 diabetes have an increased linear growth rate several years before the diagnosis[22] but this is not uniformly reported in all studies. Increased body mass is postulated to overload the β-cells because the increased insulin demand accelerates the autoimmune attack and apoptosis, known as the accelerator hypothesis.[23,24] The accelerator hypothesis was published in 2001, and proposes that type 1 and type 2 diabetes are the same disorder of insulin resistance set against different genetic backgrounds. The different genes modulate (variably accelerate) the tempo of beta cell loss and thereby determine the age at onset and incidence of the disease. It postulates the age at onset should be inversely related to BMI, a surrogate for insulin resistance and obesity.[25] Over weight in children has increased worldwide during the past two decades, and most strikingly during the past decade. Overweight and obesity have also increased among Hong Kong children especially in past 20 years. The proportion of overweight or obese children aged between 6 and 12 years raised from 16.4% in 1997-1998 to 21.3% in 2007-2008.[26,27] It is also worrying that a significant increase in the incidence of type 2 diabetes has been shown in this study especially after 2004 in Hong

Kong. Studies in other Asian countries like Japan and Taiwan have also demonstrated an increased incidence of type 2 diabetes. Incidence in Tokyo was 0.75/100,000/yr and 6.27/100,000/yr for primary and junior high school children between 1974 and 2004 with an overall incidence estimated to be 2.55/100,000/yr,[28] while that in Taiwan was 6.5/100,000/yr for children 6-18 years of age.[29] An increased prevalence of type 2 diabetes was also shown in Pima Indians (22.3 and 50.9 per 1000 for children ages 10-14 and 15-19 years, respectively in 1992-1994),[30] and Canadians (1.0 and 2.3 per 1000 for children ages 5-14 years and 15-19 years in 1998.[30] Epidemiological surveillance of type 2 diabetes is hampered by several factors, the existence of many subclinical cases (estimated to be as high as 30-50% of total cases in a population), and incomplete data collection as some patients may be followed up in private practice. Taking reference from Japan and Taiwan with very similar population characteristics, our data is probably an underestimate. The incidence rates for diabetes from Japan and Taiwan come from national screening of the childhood population for diabetes. Between 17-40% of children and adolescents with type 2 diabetes from these two countries are not obese.[28,29] In Hong Kong, we have just started high risk screening in 2005, for those who are obese (BMI >97%), have a family history of type 2 diabetes, or signs of insulin resistance. Perhaps with time, we can see if the incidence rates of type 2 diabetes mellitus are comparable to that of Japan and Taiwan and assess if high risk screening can be as effective as population screening or we may have missed a lot of non-obese type 2 diabetic patients.

If the secular increase in body mass index in children contributes to the increasing incidence and earlier onset of type 1 and type 2 diabetes, encouragement of breast feeding and measures to combat obesity from early childhood including healthy eating and exercise can hopefully decrease the incidence and delay the onset of both type 1 and type 2 diabetes in Hong Kong and worldwide.

In our analysis of newly diagnosed diabetic patients, girls are at a slightly higher risk for both type 1 and type 2 diabetes though statistically not significant (p=0.954). Other studies have also shown girls are 1.7 times more likely to develop diabetes.[31,32] A sex bias is characteristic of autoimmune diseases, with females over-represented, but unlike most immune-mediated diseases, substantial male predominance occurs in type 1 diabetes. Several mechanisms for these differences have been investigated, such as the effects of sex hormones on the immune system, but the reasons for this sex difference are not yet known.[32]

Conclusion

A diabetes registry has been updated from 1997 to 2007 in Hong Kong. The standardised age-adjusted incidence of type 1 diabetes remains low at 2.4/100,000 person/yr in children <15 years of age. The standardised age-adjusted incidence of type 2 diabetes for 10-18 years of age is 2.1/100,000. A definite increase in incidence for both types is shown from 1997 to 2007 especially for type 2 diabetes. There is a significant trend towards a younger age of onset.

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