Brief Communication

Type 1 diabetes in India: Overall insights

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ABSTRACT

Type 1 diabetes mellitus (T1DM) is also on increase like type 2 diabetes, even though not in the same proportion, but still with a trend of 3–5% increase/year. India has three new cases of T1DM/100,000 children of 0–14 years. Three sets of prevalence data shows 17.93 cases/100,000 children in Karnataka, 3.2 cases/100,000 children in Chennai, and 10.2 cases/100,000 children in Karnal (Haryana). T1DM may be autoimmune or idiopathic in nature and is present in 9% cases of insulin deficiency. T1DM is primarily caused by genetic factors, environmental factors, and disorder of the immune regulatory mechanism. A combination of all these three factors causes autoimmune disease, which may ultimately result in the destruction of pancreatic beta cells leading to hyperglycemia, ketoacidosis and potentially death, if not treated with insulin. Prediabetes is the phase before the onset of T1DM, which provides a window of opportunity for early intervention. All available interventions including steroids, immunosuppressants, and cyclosporins can be possibly applied during the prediabetes phase. The treatment goals for T1DM are simple and include maintaining near normal blood glucose levels and avoiding long-term complications, which is a constant juggle between insulin and maintaining an appropriate lifestyle. The Indian Council of Medical Research funded Registry of People with diabetes in India with young age at onset (YDR) was started in the year 2006 with 10 collaborating centres across India. This registry is focusing on to provide an overview of diabetes in the young.

Key words: Autoimmune, type 1 diabetes mellitus, type 1 diabetes mellitus in India

Introduction

Diabetes mellitus (DM) may be caused by insulin deficiency, insulin resistance, or by a combination of both. Insulin deficiency can be caused by pancreatectomy, pancreatitis, alcoholic chronic pancreatitis, hemochromatosis, cystic fibrosis, mitochondrial DNA mutations, or by drugs/toxins. Insulin deficiency may lead to type 1 diabetes mellitus (T1DM) which may be autoimmune or idiopathic in nature and is present in 9% cases of insulin deficiency. Insulin resistance may also be caused by leprechaunism, autoimmune diseases, lipoatrophy, or endocrinopathies including glucagonoma, pheochromocytoma, acromegaly, Cushing's syndrome, and thyroid disease. The combination of both (insulin deficiency and insulin resistance) may lead to gestational diabetes or to T2DM. T2DM may be caused by genetic and environmental factors (diet and exercise) and is present in 85% patients with insulin deficiency and insulin resistance. T1DM is primarily caused by genetic factors, environmental factors, and disorder of the immune regulatory mechanism. A combination of all these three factors causes autoimmune disease.

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Type 1 diabetes mellitus, in contradiction to T2DM, has an acute presentation. Prediabetes is the phase before the onset of T1DM. This period provides a window of opportunity for early intervention. All available interventions including steroids, immunosuppressants, and cyclosporins can be possibly applied during the prediabetes phase. Genetic predisposition exposes the beta cell mass to putative environmental factors leading to insulitis, beta cell injury and a decline of beta cell mass. This phase subsequently leads to the prediabetes stage which is mediated by cellular T-cell immunity including the humoral autoantibodies (islet cell antibodies, insulin autoantibodies, anti-glutamic acid decarboxylase$_{65}$, IA$_2$Ab etc.), and glucose intolerance. T1DM is caused by the destruction of pancreatic beta

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cells, and thus insulin is no longer produced in these cells, leading to hyperglycemia, ketoacidosis and potentially death if not treated with insulin. Dr. Eugene Opie was the first person to have described the concept of insulitis in 1901. The treatment goals for T1DM are simple and include maintaining near normal blood glucose levels and avoiding long-term complications. Diabetes management is a constant juggle between insulin and maintaining an appropriate lifestyle. Environmental risk factors for T1DM include seasonality at diagnosis at migration to other countries. The risk factors of T1DM recognised in the case-control studies include infant/childhood diet, viruses (exposures as early as in utero), hormones, stress, hygiene, and Vitamin D deficiency.

Type 1 diabetes mellitus is also on the increase like T2DM, even though not in the same proportion, but still with a 3–5% increase/year. T1DM is on a constant rise in Finland, Sweden, Colarado, India, and Germany. There has been an increase from an incidence of almost 10/100,000 children to around 60/100,000 children in Finland in the last 50 years. Around 78,000 children under 15 years are estimated to develop T1DM annually worldwide. Of the existing 490,000 children living with this disorder, 24% are in the European region and 23% in the South-East Asian region.[1]

India accounts for most of the children with T1DM in South-East Asia. According to the 6th edition of the International Diabetes Federation diabetes atlas, India has 3 new cases of T1DM/100,000 children of 0–14 years.[1] The prevalence of diabetes in India is variable, and three sets of data show 17.93 cases/100,000 children in Karnataka, 3.2 cases/100,000 children in Chennai, and 10.2 cases/100,000 children in Karnal (Haryana).[2-4] The bottom line remains that T1DM is quite prevalent and common.

A number of trials worldwide are being presently conducted on T1DM. In addition to intervention trials, there are three ongoing studies, in the US, on the natural history of T1DM. These include Diabetes Autoimmunity in the Young Study in Colorado,[5] Prospective Assessment in New-born of Diabetes Autoimmunity in Florida,[6] and the Diabetes Evaluation in Washington.[7] All these are based on newborn genetic screening in the general population, and, therefore, concerns have been raised about proper informed consent. Similar concerns have been raised for the Diabetes Prediction and Prevention study in Finland, which is also screening the general population. Parents of babies who carry high-risk DQB1 alleles receive a letter informing them that their infant is at "high" or "moderate" risk of developing the disease. The likelihood that these children will develop T1DM before they are 35 years of age is only about 6%. Moreover, approximately half of the children who will develop T1DM come from the "low" risk group, which is not eligible to participate in these studies.

The Indian Council of Medical Research (ICMR) funded Registry of People with diabetes in India with young age at onset youth dependency ratio was started in the year 2006 with 8 collaborating centres across India which subsequently increased to 10 centres. This registry is by the Government of India and called the ICMR registry. This registry is not just focusing at T1DM; but giving an overview of diabetes in the young. The registry has collected data on age of onset of diabetes, presentation, treatment patterns, insulin regimens prescribed, complications (neuropathy, retinopathy, nephropathy), infection, and modes of mortality. Results of the registry will soon be published. From various epidemiological studies, it has been found that T1DM is encountered majorly in the under-privileged children. The Changing Diabetes in Children program has its reason of existence because of this affliction of people from low socioeconomic strata, along with the higher socioeconomic strata, but the former is very important for this program.

There is also evidence that T1DM is, in part, a genetic disorder. Identical twins (i.e., monozygous twins) are more likely to both have T1DM than nonidentical twins (i.e., dizygous twins). But concordance rates in identical twins are <50%, supporting the hypothesis that environmental factors are also important in the development of T1DM. The T1DM risk is increased 15-fold for 1st degree relatives, and the risk is ~ 6% till 30 years of age. The risk increases in the presence of susceptibility genes. DQB1 is the best single genetic marker for T1DM, and it is the gene most often used to identify individuals with a high risk of developing disease.

However, risk estimates based on DQB1 alone are less precise than those based on the combination of alleles at both the DQA1 and DQB1 loci. These combinations are called haplotypes, and reflect the specific alleles on each of the two chromosomes. Not all haplotypes (i.e., chromosomes) with DQB1 *0201 or *0302 have high-risk DQA1 alleles. Thus, DQB1 and DQA1 typing provide more accurate risk estimates than those based on DQB1 alone. However, it is also more expensive. For that reason, most screening is based only on DQB1. The two DQA1-DQB1 haplotypes that are most strongly associated with T1DM are DQA1 *0501-DQB1 *0201 and DQA1 *0301-DQB1 *0302. That is, chromosomes with DQB1 *0201 and DQA1 *0501 confer a higher risk for T1DM than chromosomes with DQB1 *0201

with some other DQA1 allele (not * 0501). Similarly, chromosomes with DQB1 *0302 and DQA1*0301 confer a higher risk for T1DM than chromosomes with DQB1 *0302 and some other DQA1 allele (not * 0301). The relative increase in T1DM risk by the number of high-risk haplotypes varies with a difference in ethnicity. The relative risk in African-Americans with two high-risk DQA1-DQB1 haplotypes is 45% while it is 16% in Caucasians and only 11% in Asians. The absolute risk (or actual likelihood) of developing T1DM in Caucasians and African Americans with two high-risk haplotypes is about 3% before 30 years of age, depending on the population. The risk for Asians with two high-risk haplotypes is much lower (<1%). Therefore, even if a person carries high-risk haplotypes, their chances of developing T1DM are quite low irrespective of their ethnicity. In families where there is already one person with T1DM, the risk to unaffected relatives is much higher than that for the general population. For example, in Caucasian families, siblings of an individual with T1DM are about 15 times more likely to develop the disease then a person from the general population (i.e., without a family history of the disease). Since siblings share half their genes with each other, researchers often look at whether the human leukocyte antigen **(**HLA) haplotypes carried by an unaffected sibling are the same as those carried by the affected individual. Unaffected siblings can share two, one or no HLA haplotypes with their affected brother or sister. As can be seen, the T1DM risk for a sibling who has the same two HLA haplotypes as their T1DM sibling is quite high (about 25%). If they share one or no HLA haplotypes with their affected sibling, their risk is much lower, about 8% and 1%, respectively. The fact that the risk for individuals who have no shared HLA haplotype is still increased compared to that for the general population suggests that genes other than those in the HLA region must also increase susceptibility for the disease.

Future diabetes studies should evaluate the targets for young children, the various diabetes regimens, risk of hypoglycemia and techniques to avoid it, developmental issues and education. T1DM is the actual diabetes mellitus and is the virgin diabetes while other diabetes types are from mixed etiology. In a recent South-East Asian meeting, it was concluded that insulin is a birthright for children, and it is the duty of the government, organisation, and citizen to make it available for all T1DM patients.

References

1. Aguiree F, Brown A, Cho NH, Dahlquist G, Dodd S, Dunning T, *et al*. IDF Diabetes Atlas. 6th ed. Brussels, Belgium: International Diabetes Federation; 2013.
2. Ramachandran A, Snehalatha C, Krishnaswamy CV. Incidence of IDDM in children in urban population in southern India. Madras IDDM Registry Group Madras, South India. Diabetes Res Clin Pract 1996;34:79-82.
3. Kalra S, Kalra B, Sharma A. Prevalence of type 1 diabetes mellitus in Karnal district, Haryana state, India. Diabetol Metab Syndr 2010;2:14.
4. Kumar P, Krishna P, Reddy SC, Gurappa M, Aravind SR, Munichoodappa C. Incidence of type 1 diabetes mellitus and associated complications among children and young adults: Results from Karnataka Diabetes Registry 1995-2008. J Indian Med Assoc 2008;106:708-11.
5. Barker JM, Barriga KJ, Yu L, Miao D, Erlich HA, Norris JM, *et al*. Prediction of autoantibody positivity and progression to type 1 diabetes: Diabetes Autoimmunity Study in the Young (DAISY). J Clin Endocrinol Metab 2004;89:3896-902.
6. Carmichael SK, Johnson SB, Baughcum A, North K, Hopkins D, Dukes MG, *et al*. Prospective assessment in newborns of diabetes autoimmunity (PANDA): Maternal understanding of infant diabetes risk. Genet Med 2003;5:77-83.
7. The Diabetes Evaluation in Washington Study (DEW-IT) Predicting Childhood Type 1 Diabetes. Available from: http://www.lsdfa.org/documents/pdfs/meetings/Hagopian%20 LSDF%20Board%20 Dec%202010.pdf. [Last accessed on 2014 Oct 1].

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