

INTRODUCTION

Childhood diabetes (IDDM) is generally accepted to concentrate on insulin-dependent diabetes first occurring in subjects younger than 15 years of age, but it must be remarked that this type of diabetes can and indeed does appear in older patients, both adolescents and adults. In the latter this often seems to be a late-onset, slow developing form of insulin-needing diabetes which could at times be mistaken for secondary failure to oral hypoglycaemic agents. This condition was greatly underestimated in Malta for a long time, having been overshadowed by the much more common form of diabetes – NIDDM, whose prevalence here has been reported to be the highest in Europe. However, recent findings clearly show that this type of diabetes is not at all rare in our population; in fact its incidence ranks among the higher in the Mediterranean area.

PATHOPHYSIOLOGY

A brief overview of the pathophysiology of this condition reveals that IDDM is basically an auto-immune disorder appearing in the genetically predisposed and precipitated by unknown factors/s (environmental, ? viruses, etc). This causes an insulinitis which in the presence of other triggering factors leads to the destruction of the beta pancreatic cells and eventually to an insulin-deficiency, ketosisprone state. It is also known that although the clinical onset is rather abrupt occurring within days or weeks, the pathological process is much longer having developed slowly over months or years. After a variable period from diagnosis the condition then often passes through a remission (honeymoon) period where the needs of insulin become minimal for a while, before finally proceeding to total and permanent insulin dependence.

DIAGNOSIS AND MANAGEMENT

The diagnosis of this condition is unequivocal most of the times – the typical history, and characteristic symptoms and signs making it clear to

reach. This consists in an acute onset, in subjects below 20 years and desirable weight, of polyuria, polydipsia, weight loss, fatigue and weakness accompanied by heavy glycosuria, frequent ketonuria and marked hyperglycaemia. Specialized testing (although rarely needed for diagnostic purposes) show evidence of reduced C-peptide levels in the fasting state and in response to stimulation.

The management of IDDM is built around intensive insulin therapy, good hydration, meal planning (balancing nutrients with exercise and insulin) as well as education and psychological support for both patient and relatives. Monitoring of child development, blood glucose, glycated Hb, and other parameters as indicated, and the screening for complications and/or concomitant diseases are also essential during the regular follow-ups.

EPIDEMIOLOGY

The prevalence of this disease in the mid 80s in Maltese children younger than 15 years was 81/100,000, being higher in girls than in boys (94 vs 69). The mean

incidence per 100,000 during the period 1980-96 was of 14 (girls 15, boys 13), translating in an average number of 11 new cases per year. These are generally made up of 2 cases in the 0-4 age group, 4 cases in the 5-9 age group and 5 cases in the 10-14 age group. There seem to have been no statistically significant fluctuations over this period (with the exception of 1993 when 21 new cases were detected); yet the yearly incidence appears to have possibly increased slightly in the last few years from a mean of 10.8 in the period 1980-89 to an average of 12.7 during the interval 1990-96. The last few years also suggest a possible trend towards an earlier onset of the disease and an evening of the male/female ratio.

COMPARATIVE INCIDENCE RATES

The incidence rates of IDDM in Malta result to be just about higher than those of most other countries along the Mediterranean littoral, with the exception of Sardinia which has been reported to have a level approaching that of Nordic countries where IDDM is the highest in the world. However

unlike many of the Southern European countries this condition does not appear to be more prevalent in boys than in girls.

CHARACTERISTICS

Like elsewhere, the onset of IDDM in the Maltese shows a seasonal variation with the majority of cases being diagnosed in the cooler months of the year (November to February), and the lowest during the warmer summer months. Intriguingly a similar pattern was observed in the months of birth of the subjects. Boys tended to develop IDDM circa 2 years later than girls (14 vs 12 years). The commonest age group in which the disease appeared is 10-14 years, followed by the 5-9 for females and 20-24 for males.

In the Maltese the mean interval between the onset of symptoms and the start of insulin increased with increasing age at onset of the disease, varying between averages of 1 week in the 0-4 year olds and 3 weeks in the 10-14 year olds. The inverse was noted to occur with the mean amount of insulin per kg body weight needed for control – this dropped from a mean of 0.9 units in the 0-4 year olds to a mean of 0.6 units in the 10-14 year olds.

INFLUENCING FACTORS

The prevalence of IDDM in Malta was found to be influenced by a number of factors which include a 3rd or later birth rank, a maternal age at birth of the subject of more than 35 years, and lack or less than 3 months of breast feeding. Interestingly the latter habit not only seemed to protect against IDDM but also appeared to delay the onset of the disease.

The role of viral infections in IDDM in Malta is unclear, these were reported in circa 20% of cases, preceding the onset of the disease by an average of 6 weeks. Genetics also seem to be of potential relevance but more detailed study is clearly needed.

HEREDITY

The aspect of heredity was investigated from the presence or otherwise of a positive family history of diabetes in close relatives of the IDDM subjects. As expected IDDM was commoner in parents of IDDM children than in those of non diabetic offspring (4.0% vs 0.5%). Interestingly the same was noted for NIDDM, this form of diabetes being also more frequent in parents of IDDM children than in those of non diabetic ones (13.5% vs 4.5%). This could suggest that NIDDM might be associated with childhood diabetes.

IDDM was commoner in sibs of affected children than in those of non diabetic ones, the mean prevalence in the former being 8.6% (brothers 8.4%, sisters 8.8%). IDDM girls had more affected sibs than IDDM boys (11% vs 6%). Again it was noted that the risk of IDDM was enhanced by parental NIDDM too-the prevalence of IDDM in sibs of IDDM was higher if the parents had NIDDM than if they were not diabetic (16% vs 10%).

COMPLICATIONS

The complications of this form of diabetes are both of acute and chronic nature. An outline of these shows that the former include uncontrolled hyper-glycaemia which could lead to a serious condition called diabetic ketoacidosis, and hypogly-caemia resulting from improperly balanced

treatment. The chronic complications consist of both the disease specific microvascular ones involving the eyes, kidneys and nerves and the non specific macrovascular ones. Their presence and severity are influenced by the sex and age of the subject, the age at onset of IDDM, and possibly also by genetic factors, but mainly by the duration of the disease and the degree of glycaemic control. IDDM patients eventually also develop atherosclerotic cardio-vascular disease which, like microangiopathy, is associated with risk factors (including smoking, hyperlipidaemia, hypertension etc).

Unfortunately reliable figures of the rates of complications in Maltese IDDM patients are still not available, but should not be very different from elsewhere. It has been noted that circa 5-10% of IDDM cases already have some evidence of incipient complications after 10 years of diabetes, the prevalence of pathology increasing dramatically thereafter, reaching mean level of 20-30% by 15 years of IDDM and 60-80% after 20 years of disease. An European study reported that after 18 years of IDDM levels of microvascular complications averaged 31% renal, 46% ophthalmic and 19% neuropathic. It also found a mean of 12% cardiovascular disease, 15% hypertension, and 6% peripheral angiopathy.

Blood glucose control also plays an important role in the prevalence of disease. Data from Malta showed that in cases of severe retinopathy half the patients had had poor control and only 18% were deemed to have had acceptable glycaemic levels.

The complications and concomitants of diabetes lead to a significantly higher risk of death. This increased mortality in IDDM compared to non diabetic subjects is mainly due to renal, hypertensive and ischaemic heart disease.

CONTROL

As already stated, glycaemic control influences the occurrence of complications. Good control can not only prevent or delay complications but has recently been shown to be able to regress them too if strict and persistent enough. To achieve this requires dedicated team work and close monitoring. Tight control however also carries a significant risk of hypoglycaemia and hence particular attention is needed in its management. The maintenance of satisfactory control and avoidance of complications necessitates the removal of risk factors (like smoking, infection, etc.) and appropriate therapy of any co-existing pathology (including auto-immune related conditions, thyroid disorders, coeliac disease, asthma, high blood pressure, nephropathy, dyslipidaemia, etc.).

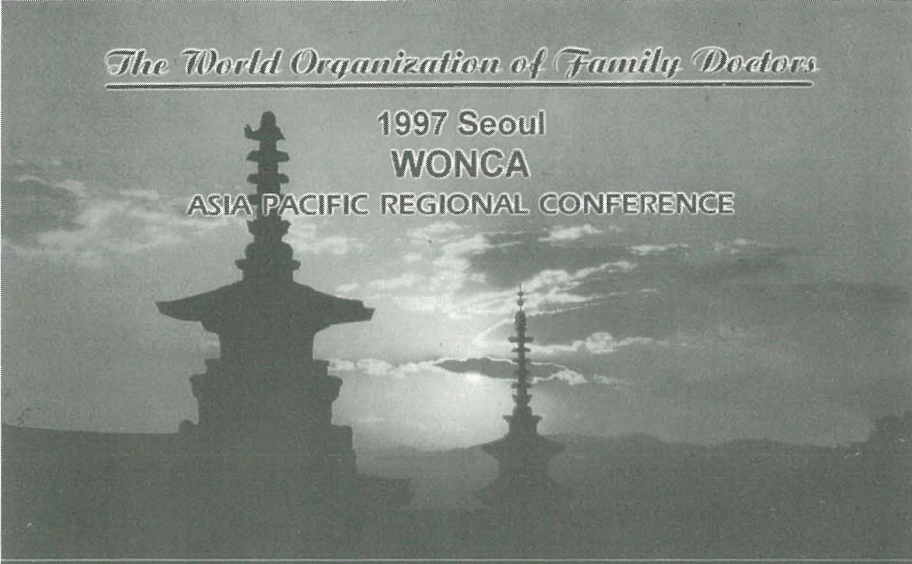
On the other hand it must be recalled that the commoner causes of poor control include, amongst others, insufficient compliance, lack of education and/or motivation, conditions of 'stress', unrecognized occurrence of the rebound (Somogi) or dawn phenomena and others (eg. insulin resistance states). Also associated with the degree of glycaemic stabilization is the utilization of health services by IDDM patients. Detailed information on this in Malta is not at hand but it is estimated that the proportion of subjects that regularly keep on attending the diabetes clinics drop from

an initial 90% to circa 60% after 5 years and to some 30% by 10 years. Moreover also the frequency of visits decreases in time; indications suggest that of those patients that keep coming for follow-up after a number of years of IDDM only about 27% attend for the scheduled 5 to 6 visits per year, 33% make 3 to 4 visits a year, whilst circa 40% merely come once to twice yearly.

THE FUTURE

The future for IDDM patients augurs well. Intensive research is being conducted towards various aspects of the disease. In particular studies are being done to improve treatment by

developing new insulin analogues and forms (eg. spray), and providing better monitoring and more sensitive screening tests. Great efforts are being made to try to cure the disease by islet cell transplantation and/or possibly prevent it. The latter involves intervening on the susceptible who are now becoming possible to identify by means of special markers (including humoral auto-antibodies against islet cell, insulin, GAD, IA2 and phogrin). Newer approaches in this field have moved from immuno-suppression towards immuno-modulation by means of BCG vaccination, low dose insulin, exclusion of cow's milk from early nutrition, etc.




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