Diabetes Mellitus

Nighat Yasmin* M.B.,B.S., M.C.P.S., (Path), M.Phil. (Haem),
Khyber Medical College,
Peshawar, Pakistan

Documentary evidence of a disease recognized as diabetes has been known since antiquity. An Egyptian Papyrus of 1500 B.C. contains a description of the symptoms. In the second century A.D. Hretaees of Cappadocia called the disorder diabetes, a Greek word meaning "to flow through a syphon". This graphic description implied that there was wasting of the whole body into a copious flux of urine. The recognition that urine was sweet can be found in Hindu manuscripts of the sixth century, although it was only in the eighteenth century that the sweet substance was identified as glucose, and the word mellitus (honeyed) was added[1].

Diabetes mellitus is not regarded as a disease, but is a syndrome characterized by a rise in blood glucose concentration above normal values, which if high enough will cause glucose to be excreted in the urine. The rise in glucose is due to an absolute or relative deficiency in insulin and to an inappropriate secretion of glucagon. The syndrome of diabetes mellitus may be caused by many different pathological processes[2], e.g.

1. Hereditary Factors: Seem to be important particularly in maturity onset diabetes[1,2,3,4,5,6].

In juvenile diabetes the histo-compatibility antigens HLA-B8, HLA-BW/15 and HLA B.W/8 occur more often than in control groups. It is possible that the possession of these antigens render them more susceptible to islet cell damage by auto-immune processes, perhaps triggered by virus infections.

2. Auto Immunity: Islet cell antibodies may be found in patients with auto immune disease affecting several other endocrine glands (e.g. adrenal and thyroid).

3. Viral Infections: Particularly Coxsackie B4 and mumps virus have been implicated as a cause of juvenile onset diabetes.

---

* Professor of Pathology, Khyber Medical College.

Anti bodies to B4 virus are more often found in young diabetics than in controls and there appears to be a seasonal variation in the development of diabetes being approximately twice as common in the winter as in the summer months which would fit with a viral aetiology.

4. Pancreatic Disorders causing destruction of islet cell tissue may lead to diabetes. They include chronic pancreatitis, carcinoma of the pancreas, haemochromatosis causing iron deposits in the pancreas and after pancreatectomy.

5. Endocrine Disorders including acromegaly, cushings syndrome, occasionally with thyrotoxicosis and phaeochromocytoma.

6. Miscellaneous conditions e.g. pregnancy, thiazide diuretics, steroid therepy and oral contraceptives[2].

Diabetes mellitus is viewed as a 'geneticist's nightmare' but rapid developments are now occurring, including recognition of HLA associations[1,2,3,4] and identification of insulin gene on the short arm of chromosome[11]. So far variations related to this gene cannot be clearly related to clinical diabetes.

Many of the problems in estimating genetic risks in diabetes arise from the obvious heterogeneity of the disorder. Diabetes mellitus can be divided into the following types:-

1. Insulin dependent (juvenile) diabetes:

a) Associated with persistent islet cell antibodies and with auto antibodies to other endocrine glands especially adrenal. Associated with HLA antigens Bg and DW3[1,2,3,4,7].

b) Not associated with other endocrine disorders and probably with little recurrence risk. Associated with HLA antigens B15 and D.W4 possibly virally induced.

2. Non-Insulin dependent diabetes:

a) Maturity onset. Common, high concordance rate in monozygotic twins.

b) Juvenile type. Rare, follows autosomal dominant pattern.

3. Diabetes associated with other primary genetic disorders (various mechanisms).

Apart from group 3 and the rare juvenile form (2b) showing dominant inheritance, no theoretical prediction of risks is possible and emperic risk estimates are widely divergent. There being an extreme variarion in risk it is difficult to know what figures to give to the patients. The best thing in practice is to first warn the families of the inadequacy of our knowledge; secondly to stress that there are different types of diabetes, some with a small and others with a larger genetic component; and thirdly to give risks only for overt clinical diabetes, ignoring the estimates for abnormal glucose tolerance tests. For insulin dependent juvenile type diabetes, a risk of diabetes in the first 20 years of life of 3 percent is given, a similar risk is given for a further child with diabetes being born to healthy parents with one diabetic child. A risk for children of conjugal diabetics of around 20% for clinical diabetes in the first 20 years of life is given, and around 50 percent of diabetes developing at some stage of life.

For non-insulin dependent maturity type diabetes, the ultimate risks are likely to be higher, around 10 percent for first degree relatives, but this is of less significance since the majority of patients will be mildly affected relatively late in life.

The question whether diabetics should marry each other and have children is a bit difficult to answer, because a World Health Organisation Commission dogmatically advised that they should not, on eugenic grounds. It is quite clear that the risk of diabetes in the children of such couples is considerably increased, and possibly the severity also; therefore, there may be good grounds for such couples to have limited families or avoiding child bearing[8].

The eugenic grounds for doing so are considered far from such; however, a final argument regarding the eugenic grounds is that with declining food sources man may need the 'thrifty geno type' of the diabetics in the future.

The risk of developing diabetes is not the only factor to be considered in giving genetic counselling to diabetic families. The offsprings of a

diabetic mother face special hazards, though with better diabetic control during pregnancy they appear to be declining.

The perinatal mortality has been shown to correlate with the severity of maternal diabetes. In a large study 20% perinatal mortality is given which may rise to 40% in the most severe groups[8].

There is also an increase in the incidence of congenital malformations in the offsprings of the diabetic mother, with three fold excess over the general population. A 6.4 percent incidence compared with a 2.1 percent in a control population is reported[6].

The malformation rate is reported to be higher in the offsprings of diabetic mothers having vascular complications compared to those without.

There is no detectable increase in malformations when the mother has preclinical or gestational diabetes.

A few rare specific malformations seem to occur particularly in the offspring of diabetic mothers including sacral agenesis, proximal femoral deficiency and related caudal regression syndrome.

The recurrence risk of these is small in relation to the other malformations, which do not follow any specific pattern.

References

1. James, M, Carbler, C. (1987): The complications of diabetes. Historical introduction In diabetic complications. Published by Churchil Livingstone: 1-15.

2. Ramsay, I. (1980): Disorders of Carbohydrate Metabolism. In a Synopsis of Endocrinology and Metabolism. Published by John Wright and Son's Limited Bristol: 150-157.

3. Seymour, R. Levin, (1983): Diabetes Mellitus. In Endocrinology. Edited by Harold E. Carlson. Published by John Wiley & Sons New York: 233-263.

4. Jeanne, R, Bonar, (1980): Definition and Classification of Diabetes Mellitus (2nd Ed). Published by Medical Examination Publicating Co. Inc.

5. Williams, R.H. (1982): The endocrine Pancreas & diabetes mellitus. In Text Book of Endocrinology. Published by W.B. Saunders Company Ltd. Philadelphia: 750-843.

6. Behrman R.E. and Vaughan, V.C. (1987): Diabetes Mellitus. In Nelson Text Book of Paediatrics Published by W.B. Saunders Company Philadelphia: 1248-62.

7. Vognl, F. and Motulsky, A.G. (1982): Diabetes Mellitus. In Human Genetics. Published by Springer Verlag Berlin: 170,171,185,468.

8. Harper, P.S. (1984): Diabetes Mellitus. In practical Genetics Conselling (2nd Ed). Published by Wright Bristol: 258-260.