

Proceedings of the Endocrinology, Metabolism and Diabetes Conference (EMD), 1993

M.M.S. Ahuja*

(Review of diabetes-related topics)

A faculty of ten eminent Indian physicians from USA and fifty from different parts of India held EMD scientific sessions for three days, Dec. 27-29, 1993 at Oberoi Towers, Bombay. More than one third of the programme was devoted to different aspects of update in diabetes. This included:

Epidemiology.

Aetiological Perspectives.

Diagnosis, effect of lithium and calcaemic status on Glucose tolerance tests (GTT).

Clinical; with special reference to malnutrition related diabetes.

Complications: metabolic and vascular and their treatment aspects.

This write up is a brief resume of the proceedings of EMD- 1993.

EPIDEMIOLOGY

IDDM- A study has been conducted in Coimbatore by Munirathnam Chetty to ascertain number of children with diabetes attending different city hospitals and the general practitioner's clinics in the town over 3 years. The city has a total population of 11.5 lacs, and is of Dravidian ethnicity, number of children 4,54,230 and diabetes was diagnosed in 0.15 per 1000 (1 per 6000). Figure from Madras was quoted as 0.25 per 1000 (1 per 4000) Maximum number is in the age group 14-19 years. There is no sex predilection and it has no relation to parental history.

Ramachandran from Madras, provided data on recent prevalence study of NIDDM in urban and rural Madras. Prevalence rate in Madras (urban) is 8.2 per cent, rural 7.8 per cent [Impaired glucose tolerance (IGT) urban 8.7%, rural 7.8%, urban body mass index (BMI) 23.8, rural 18.0]. Plasma insulin values were twice or more in urban population as compared to the rural population. A greater genetic inheritance of NIDDM in South Indian population is reported in this study.

With increasing urbanisation, increased conversion of IGT to diabetes is predicted by the investigators. HLA

* From Diabetes Foundation (India), Delhi.

studies in IDDM have shown increased risk ratio in DR₃ (DQ₂ Asp-Ve) in the Indian population (Suresh Mehtalia, Bombay), while NIDDM retains polygenic inheritance characteristics.

Presence of islet cell antibodies shows bimodality; first peak in age 1-5 years and second one at 15-20 years. First group is conventional IDDM; the latter group is often associated with other organ specific auto-immunity (Kochupillai, New Delhi).

DIAGNOSIS

A critical review of presently employed diagnostic criteria for diabetes was presented by Munichoodappa from Bangalore.

Factors discussed were: age-related alterations: (in male post-glucose 1-2 hr. venous blood glucose values is 6-13 mg/dl higher per decade); Sex related alterations: women have 10 mg/dl values higher than men at all ages; diurnal variations: higher value in the afternoon. Again discrepancy in diagnosis of IGT employing NDDG and WHO criteria was pointed out. Sullivan and Mahan criteria for diagnosis of gestational diabetes mellitus (GDM) did not seem sacrosanct, values are at-most predictive of risk of development of glucose intolerance and not maternal-foetal outcome.

CLINICAL SPECIAL TYPES, NIDDM PATHOGENESIS

With reference to specific types of diabetes being observed in our country, two types as described in WHO classification: (Fibrocalcific and Protein Deficient-Pan-creatic Diabetes) were elaborated upon by Yajnik from Pune and Samal from Cuttack.

Yajnik has studied the exocrine function in fibrocalcific pancreatic diabetes (FCPD) cases and has observed the following: C-peptide at diagnosis is comparable to IDDM cases. Glucagon shows a paradoxical rise as observed in IDDM. Immuno-reactive trypsin is low; in more than 50% of patients it is low to undetectable. He studied hepatic ketogenesis by infusion of medium chain triglycerides and intralipid. While non-essential fatty acids and β -OH-butyrate were high in IDDM, these were low in FCPD cases. With intralipid though glucagon values increased, yet β -OH-butyrate did not show greater rise.

In Cuttack, young diabetics, studied did not have any evidence of calcific pancreatitis; as ultra-sound studies have not revealed any shrinkage of pancreas on follow up for 7-10 years. C peptide values are low, though more than that observed in IDDM group, growth hormone values are higher and paradoxically rise with glucose instead of being suppressed.

Hazara from Agra attempted to characterize the lean NIDDM. This group constituted 11-25% of all NIDDM in our country. The hyperglycaemia is more than that observed in conventional obese NIDDM and a hyperactive futile cycle of carbohydrate metabolism in the liver is suggested to account for the biochemical parameters. There is negative relation between fasting blood glucose, lactate, free fatty acids and triglycerides.

M. K. Sinha from Greenville, NC reported on cellular culture system for study of proliferation of adipocytes in lean and obese individuals. Cellular protein, 27 KD molecular size and insulin like growth factor binding protein are markedly decreased in obese compared to lean subjects.

Sinha had also examined abdominal subcutaneous and omental adipose tissue and found no significant difference for insulin binding, insulin receptor kinase activity or total cellular insulin sensitive glucose transporters (GLUT 4). Sinha postulated that omental fat is more insulin resistant with regard to glucose transport compared to abdominal subcutaneous fat.

COMPLICATIONS: METABOLIC

C. B. Sridhar from Bangalore presented his experience of diabetic ketoacidosis in 107 patients over a period of 3 years. He observed that the number of patients decreased over this period. He observed a decreased bicarbonate reserve with high anion gap (31.05 ± 7.97) compared to diabetics without ketosis (20.50 ± 14.26) and raised osmolality 297.1 ± 16.6 compared to diabetic without ketosis 292.59 ± 14.26 .

Low Na was present in 20.5% and low K was observed in 9.1% IM hourly insulin injection matched IV bolus or infusion of insulin in producing a steady fall of blood glucose i.e. 60 mg per hour. Mortality was related to the degree of acidosis and in this series (after hospital admission) occurred in 32.7% of patients.

VASCULAR (Large vessel and small vessel disease)

Results of study on the Diabetes Control and Complication Trial (DCCT) were presented by Om. P. Ganda from Boston, USA. The study design

included evaluation of both the primary prevention and secondary prevention of complications in 1441 IDDM with mean follow-up of 6.5 years on intensive therapy versus conventional therapy. Intensive therapy reduced clinically significant retinopathy by 34-76%, severe non-proliferative diabetic retinopathy, non-proliferative diabetic retinopathy, proliferative diabetic retinopathy or laser therapy by 47-51%, micro-albuminuria (40-300 mg/24 hrs) by 30% clinical grade albuminuria (>300 mg/24 hrs) by 54% and clinically significant neuropathy by 60%. The results were consistent in subgroup analysis by age, gender, duration of diabetes and baseline HbA_{1c}. There were no difference in neuro-behavioural or cognitive functions.

The major adverse outcome was a 3 fold increase in the incidence of severe hypoglycaemia in the intensive therapy group.

There was no difference in the mortality rates between the two treatment groups. There was an increased incidence of weight gain in patients in the intensive therapy group.

In discussion, queries were raised regarding characteristics of IDDM that would benefit most, scope for application of intensive therapy for NIDDM and possible benefits for long term extended study and the cost benefit ratio of intensive therapy.

Ashok Kumar Das, Pondicherry brought into focus non-coronary cardiac dysfunction in diabetics that accounts for cardiomyopathy seen in diabetics. It seems to be due to metabolic alterations along with vascular alterations in the small vessels in the intramural coronary arteries.

Simple sensitive and non-invasive tests as systolic time interval, diastolic function test or echocardiography can detect this entity even in the preclinical phase.

Lily John from Bangalore suggested that besides metabolic status, molecular gene probes in future may become applicable to decipher vascular complications in the diabetics.

Ahuja from New Delhi reviewed vascular complications i.e. large and small vessel disease amongst the 4673 NIDDM cases studied in a collaborative ICMR project from 1986-89. A comparison with WHO MNSVD and UKPDS brought out no major differences in large vessel disease except peripheral vessel disease (low amongst Indians). The incidence of background retinopathy was comparable in two groups. In India, ESRD

accounted for 45% of mortality in diabetics less than 30 years of age.

A higher incidence of coronary artery disease and related mortality in Asian Indian was described and possible related factors: high insulin values, triglycerides and hypertension, discussed.

Interesting data was presented by J. Shah from Tucson, Arizona, USA on the endocrine effects of lithium. This included: inhibition of action of anti-diuretic hormone, thyroid hypofunction, hypercalcaemia and unmasking of hyperparathyroidism, stimulation of corticosterone release and inhibition of gastrin release.

Detailed effect on glucose tolerance has been studied; glucose disappearance rate is delayed and insulin release lowered in acute experiments in rats. These effects are reversible.

Effect of induced hypo and hypercalcaemia and glucose tolerance and immuno-reactive insulin release

was also studied by J. Shah. Results showed that hypocalcaemia causes a defect in glucose and tolbutamide induced insulin release and also impairs the glucose disposal rate. However, acutely induced hypercalcaemia has no effect on these parameters.

TREATMENT

Insulin analogues and newer insulin were discussed by Anil Kapur, Bombay. Two objectives have been sought, one to have insulin preparation with rapid absorption and second to have insulin with effect for long duration to maintain basal insulin levels beyond 24 hrs. Such possibilities are being sought by restructuring of the amino-acid sequence of insulin. Several analogues are in various stages of development though some issues are still unsettled.

Mention was made of sprinkler needles or magnesium-insulin combinations. Probably in future answer to some of the existing problems of having insulins with instant and markedly prolonged bioavailability will be addressed successfully.