Malnutrition Related Diabetes Mellitus

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Introduction

Malnutrition related diabetes mellitus (MRDM) has already been accepted as an entirely new classification by WHO group[1]. This is different from two main types of diabetes mellitus such as Insulin dependant diabetes mellitus (IDDM) and Non-Insulin dependant diabetes mellitus (NIDDM). MRDM are of two main subtypes[2].

(a) Fibro calculus pancreatic diabetes (FCPD)

(b) Protein deficiency diabetes mellitus (PDDM)

Available report of study by scientists on MRDM in consideration of its different metabolic character, nature and duration fo disesse, laboratory data (oral glucose tolerance test, fasting blood glucose, total protein, albumin globulin ratio, urine acetone), body compositions (i.e. % Fat, total body water and Lean body mass) and insulin requirement may bring out a new idea of further classifications of MRDM and help to acquire more informations regarding its aetiology and pathogenesis [3].

MRDM which has clinical evidences of exocrine pancreatic malfunction, fibrosis and stone in the pancreatic duct is known as FCPD (Fibro calculus pancreatic diabetes mellitus) and in absence of such evidences MRDM is known as PDDM (Protein deficiencyt diabetes mellitus). Both the groups have distinct clinical findings.

Epidemiology

In Bangladesh, of all 894 diabetics studied 49.6% were under weight, and ketosis in them were rare [6]. In Sri Lanka 68% and in India 52% were underweight[7]. A recent study of IDDM patients under age 30 in BIRDEM has shown that most of them were underweight and undernourished[6] 30 to 35% of young diabetics with age of onset of the disease less than 30 years were presented with FCPD and reported in many underdeveloped countries like Bangladesh, Brazil, Ghana, India, Indonesia, Jamaica, Madagaskar, Nigeria, Sri Lanka, Thailand, Uganda, Zaire and Zambia[7]. Protein Deficiency Diabetes Mellitus (PDDM) occurs commonly between age group 15-25 years and onset is before age 30 years. An incidence of 45-60% of all diabetics in developing countries under age 30 was recorded to have suffered from PDDM[7]. In Nigeria 50% of diabetics under age 20 had tropical pancreatic diabetes. 14% of all diabetics and 75% of those under 25 years had pancreatic calculi shown in another study [8].

The occurence of MRDM is almost 0% of all diabetics in Ethiopia [9] and about 80% in Indinesia [10]. In some parts of India it is about 22% of all diabetics[11] and 6.7% in Jamaica [12].

Aetiological Factors

An association between cassava (rich in cyanogenic glycoside) consumption and prevalence of FCPD has been observed by epidemiological studies. The cassava is grown in both sides of equator and taken essentially by about 400 million people. Excess of cassava intake along with low protein diet which is dificient in sulphur containing aminoacids start initiation of

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accumulation of cyantide in the body; this is probably the toxicological effect necessary for pathogenesis of FCPD[7]. Pancreatic lithiasis was reported first in India [17]. The toxins produced in the body cause impaired secretion of watery bicarbonate rich alkaline pancreatic juice and so viscid acidic material accumulate in the pathway with further impediment of flow of juice and stone is formed. With continuous progress of the disease both periductular and interlobular fibrosis occurs. With further advancement both acinar and islet contents are completely replaced by fibro fatty tissue.

Cassava Consumption in Bangladesh

The data on cassava consumption in Bangladesh are not available but definitely less consumed than in Indonesia and Kerala, India. In Indonesia poorest 30% obtain about 40% of their calories from cassava while richest 30% obtain only 14% of their calories from cassava In Bangladesh though cassava consumption is less yet there is MRDM. Other food items like cabbage, yam, sorghum and millet consumed periodically may provide the toxins necessary to initiate FCPD. To work out physiological and toxicological behaviour of these and other food items may open a new era of information. The main cyanogenic glycoside in the cassava root is linamar which liberates HCN on hydrolysis. The cyanide thus liberated is detoxified by several pathways in the body which in presence of malnutrition and an ineffective agent may begin the process of FCPD. So several factors either singly or together along with protein energy malnutrition may lead to FCPD syndrome.

Diagnosis of MRDM

MRDM may be diagnosed by taking clinical history, physical examination and by laboratory test. Table I shows diagnostic critera of MRDM. Table II and III summarises diagnostic criteria of PDDM and FCPD.

Table 1. *Diagnostic Criteria for MRDM* [19]

Clinical Profile	Points Score
1. Age of onset under 30 years	1
2. Leanness with BMI less than 19	2
3. Frequent history of malnutrition in childhood	1
4. Stigmata of present or past malnutriton and deficiency states	2
5. Moderate or severe hyperglycaemia	1
6. Lack of pronness to Ketosis in the absence of stressful situation	3
7. Insulin administration required to achieve optimal metabolic control but no dependance on insulin for prevention of Ketosis	2
8. Pancreatic Calcification	3
9. Between 7-9 is suggestive Aggregate score 10 points is considered diagnostic and score	

Body mass index = BMI

Table 2. *Classification and Laboratory Diagnosis of FCPD* [19]

1.	Age of diabetes onset frequently under 30 years.
2.	Family history of diabetes in less than 10% of cases
3.	Male Female ratio 3-4:1
4.	History of frequent upper abdominal pain, sometimes from childhood
5.	Stigmata of previous and present malnutrition (BMI less than)
6.	Moderate to severe hyperglycaemia
7.	Ketosis variable but generally absent
8.	Steotorrhoea and evidence of exocrine pancreatic disfunction common
9.	Pancreatic calcification present in greater than 90% of cases using conventional and newer imaging technique

Table 3. *Clinical Characteristic of PDDM* [19]

1.	Age of onset of diabetes under 30 years.
2.	Constitues 30 -60% of youth onset of diabetes
3.	Family history of diabetes seen in less than 10% cases
4.	Extreme leanness with BMI generally between 14-18
5.	Moderate to severe hyperglycaemia
6.	Ketosis generally absent but occurs during stressful situation
7.	Insulin resistance usually partial but occurs frequently
8.	History of malnutriton in infancy and early childhood extremely common
9.	Clinical signs of previous and present protein malnutrition and other deficiency state common.

Criteria for diagnosis of MRDM suggested by Ahuza[29] are as follows:

(a) A blood glucose greater than 200 mg/dl (11.1 mmol) at any time.

(b) Onset of diabetes before age 30

(c) Body mass index of less than 19 kg/m^2 recently modified by 19 kg/m^2

(d) Absent of Ketosis on withdrawl of insulin

(e) Poor socio-economic status or history of childhood malnutrition.

(f) Insulin requirement of more than [60] units/day or more than 1.5 units/ kg body wt. (usually more than 2 units/kg body wt.)

In FCPD there is also recurrent abdominal pain for early age and presence of pancreatic calculi on plain X-ray abdomen[29]. Special Investgations for FCPD:

1. Radiological presence of pancreatic calcifi-cation strongly supports the diagnosis. It is only detected in 75% of such cases [7].
2. In the absence of positive radiological findings ultrasonography shows ductular obstruction and dilatation.
3. Endoscopic retrograde cholangio pancreato-graphy (ERCP) shows also ductular obstruction and dilatation.

Insulin Requirement and Cause

Very high does of insulin is rquired to control MRDM. In induced protein energy malnutrition both exocrine and endocrine functions were found to be disturbed [23, 24, 25]. Methionine deficiency in rat resulted in loss of pancreatic enzyme [26]. Peripheral insulin resistance is mostly due to decreased intracellular enzyme content or activity, loss of cellular mass, raised concentration of insulin antagoninst such as growth hormone, cartisol, non-esterified fatty acid and catecholamine [27,28].

Ketosis Resistivity

When carbohydrate is not utilised for energy almost all the energy of the body come from fat and ketosis may occurs. Thus during excess fat metabolism ketone bodies in excess are accumulated in the body and the process is enhanced by excess secretion of corticotrophin, glucocorticoids and decrease secretion of pancreas[17]. After a dose of intravenous glucose a significant decrease in Insulin output was marked along with less glucose disposal in MRDM [18]. After oral glucose, mesurement of Isulin and C peptide in MRDM was found decreased but in IDDM was virtually absent irrespective of age, sex, weight and duration of the disease between MRDM and IDDM. The fact gives us a point to understand ketosis resistivity in such cases [19].

5-15 micro unit of insulin per ml is enough to initiate the mechanism of lipolysis and muscle proteolysis but not sufficient to inhibit gluconeogenesis or to stimulate muscle glucose uptake. Post-prandial insulin concentration of 50-100 micro unit of insulin per ml are required to stimulate muscle glucose uptake and to inhibit gluconeogenesis but hepatic glucose output is stopped at a concentration of 55 micro-unit of insulin per ml. It can be concluded that partial beta cell function in PDDM maintain peripheral insulin concentration enough to inhibit lipolysis but not enough to control hyperglycaemia. So there is no ketosis.

Residual insulin secretion in tropical diabetes may help to explain the lack of ketosis in MRDM. In tropical pancreatic diabetes (FCPD) the pancreas become firm, shrunken and iregularly fibrosed with multiple calcium carbonate and calcium phosphate stone in major ducts 31,32,33. When pancreatic structure along with alpha cells are also lost. Lack of resultant glucosen may be a factor to resistance to ketosis.

The ketosis resistance of the tropical diabetes also may be due to lack of creatinine in MRDM which is essential to transport fatty acids into mitrochondria in the process of fat metabolism [17, 20].

Fat free mass (FFM), fat mass (FM) and total body water (TBW) are the body compartments which generally give us informations on nutritional status on human 21. Changes in body composition associated with moderate degree of nutritional compromise were related mainly to body cell mass (-15%) where body fat was normal. With severe undernutrition both fat depot (-29%) and body cell mass (-29%) was reduced. Muscle cell mass was more affected (-41%). These data indicate that in severe malnutrition both fat depot and body cell mass in significantly depleted [22].

Recent studies in the protein deprived rat have shown reduction in the number of adipocyte per unit weight of adipose tissue and a significant reduction in lypolytic response was found when these adipocytes were incubated in presence of lipolytic hormone [15]

A study to measure the body fat % in MRDM patients to find out further cluese to ketosis resistivity of such syndrome is needed. It may be hypothesised that necessary fat is not available to initaite the process of ketosis in FCPD or PDDM.

Discussion

Malnutrition related diabetes mellitus is a load to the already loaded health service of the developing world. The understanding of case, natural history may be opened up avenues to control the condition in future.

Knowledge needed are being acccumulated, further listing of the hypothesis are required to find out the effective and uniform guideline to control, treatment and prevent the MRDM and thereby adding years to poverty striken people of the world.

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