

Case Report Series: Malnutrition Related Diabetes Mellitus (MRDM)

Reginald Nnamdi Oputa

Department of Internal Medicine, Federal University Teaching Hospital,
Owerri. Imo State. Nigeria; & Imo State University, Nigeria. Professor of
Medicine/Consultant Physician/Endocrinologist/Fulbright Scholar.
MBBS, MSc, FWACP, FEMSON.

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BACKGROUND

I was a senior resident doctor at the University College Hospital (UCH), Ibadan, Nigeria between October, 1987 and October, 1990. My Part 11 research dissertation was titled, "CASE BOOK IN ENDOCRINOLOGY." I presented this work to the West African College of Physicians (WACP) as part of the requirement for the award of academic fellowship in Internal Medicine and Endocrinology. My book contained twenty cases that I managed during the period, of which twelve of the cases were diabetes mellitus. Three of these twelve diabetic cases were malnutrition related diabetes mellitus (MRDM). MRDM was common then, but in the past three decades are very rare or virtually none existent. I have not seen any case in the past thirty years. And my colleagues share similar experience.

The World Health Organization (WHO), 1985 classification of diabetes mellitus had MRDM as a distinct clinical entity.¹ The WHO 1999 classification of diabetes mellitus, removed MRDM as a distinct clinical type of diabetes mellitus because of lack of any clear aetiopathogenic mechanism.² The WHO 2019 classification of diabetes mellitus subsumed MRDM in the other specific types, under diseases of the exocrine pancreas.^{3, 4} Under this subheading it is called fibrocalculous pancreatopathy. Other causes of diabetes mellitus in this subheading are: trauma, tumour, cystic fibrosis, haemochromatosis, pancreatitis and pancreatectomy. The suggested pathogenic mechanisms for MRDM include: Malnutrition, with or without chronic cassava consumption; the use of indigenous spirits and herbal medicines; tropical pancreatitis syndrome; and hereditary factors.⁴

CASE-REPORTS

Case 1

Miss EP was a 24 year old female student that presented with the history of recurrent colicky abdomen pain since the age of six years. The onset of diabetic symptoms was in the recent past three months. Her bowel habit was normal and there was no change in her stool. There was no family history of diabetes mellitus. Her Body Mass Index (BMI) was 18.8 kg/m² on examination (Height of 1.53 m and weight of 44 kg). Her Random Blood Sugar (RBS) was 384 mg/dl. Her kidney function test showed mild metabolic acidosis (plasma HCO₃ of 16 mmol/l). The plain abdominal X-ray showed multiple pancreatic calcification. She was managed on outpatient basis with Lente insulin. Trial of oral hypoglycemic medication failed. Control of her blood sugar

was achieved with 52 units of Lente insulin daily, in addition to diet management and other lifestyle advice. She gained two kg weight in one month. She was followed up in our clinic subsequently and she did well.

Case 2

Mr. AM was a 24 year old self employed technician that presented on 02/01/1989 on referral from the emergency department with four months history of colicky epigastric pain, and three week history of polyuria, polydipsia, weakness and weight loss. The abdominal pain was aggravated by peppery meals and was not relieved by antacids. The pain did not radiate to any other part of the body. He was single and neither drank alcohol nor smoked cigarette. There was no history of use of non-steroidal anti-inflammatory analgesic and no family history of peptic ulcer disease or diabetes mellitus. He had herniorrhaphy surgery in 1985. On examination his BMI was 19 kg/m² (Height of 1.77m and Weight of 59.3 kg). He was dehydrated and had tachycardia (Pulse 112/min). Urinalysis showed glycosuria, trace proteinuria and no acetone. The RBS was 364 mg/dl. The plain abdominal X-ray confirmed pancreatic calcification.

During his second day on admission he vomited 1.5 litres of gastric fluid about two hour after breakfast. On examination he was drowsy, dehydrated and afebrile (Temp. 36 °C). The pulse showed a tachycardia of 130/min. His Blood Pressure (BP) was 100/70 mmHg. He had a deep and regular respiration (acidotic respiration) and tachypnea (Respiratory rate 28/min). He was in hyperglycaemic pre-coma state. The urinalysis showed glycosuria (2%), but no acetone and no protein. The RBS was 536 mg/dl. The kidney function showed depressed bicarbonate (13 mmol/l), elevated Urea (120 mg/dl), elevated Creatinine (6.3 mg/dl), and normal Sodium (135 mg/dl), Potassium (4.1 mmol/l), and Chloride (98 mmol/l). He was managed with our standard protocol for hyperglycaemic emergencies. He spent four weeks on hospital admission. Trial on oral hypoglycemic drug, Glibenclamide was successfully on 10 mg twice daily. His follow-up treatment remained impressive.

Case 3

Mr. MO was a 50 year old carpenter and a known diabetic for two years. He was receiving 60 units of Lente insulin daily. He presented on 10/06/1988 with a two week history of cough, polyuria, polydipsia, weight loss and recurrent episodes of diarrhoea. The cough was productive of scanty whitish sputum that was not related to posture. There was no associated fever, chest pain, haemoptysis, dyspnea or palpitation. The stool was watery, but not bulky, pale or foul smelling, and did not contain blood, mucus nor undigested food particles or meat fibre. His appetite was normal and there was no vomiting or abdominal pain. There was associated history of blurring of vision, but no numbness or paraesthesia. He was treated five years ago in 1983 for pulmonary tuberculosis at Jericho Chest Clinic for six months with intramuscular injections for two months and oral tablets for six months. He recovered then and was well on follow-up.

His family and social history were not contributory. He was very ill looking, afebrile (Temp. 36.8 °C), pale, anicteric, emaciated (weighed 57 kg) and mildly dehydrated. He had grade 3 digital clubbing. Chest examination showed bilateral apical flattening, central trachea and signs of consolidation at the right upper zone. His pulse (84/min) and blood pressure (110/70 mmHg) were normal. Abdominal examination was normal. He had bilateral immature cataract of both eyes. The central nervous system was normal. His RBS was 292 mg/dl. CXR showed patchy

consolidative changes with multiple cavities in the right upper lobe. The abdominal X-ray showed pancreatic calcification. He was treated for pulmonary tuberculosis again with intramuscular injection of Streptomycin, 1 g three times weekly and tab thiazinah 450 mg, daily. His blood sugar was controlled with Lente insulin 60 units daily. In one month he was asymptomatic and gained 3 kg in weight (60 kg). Repeat CXR after ten weeks showed significant clearing of the patchy consolidation in the right upper lobe. He remained asymptomatic twelve months on treatment: he gained 8 kg in weight (65 kg). He was referred to the Chest Physician and given follow-up plan in our clinic.

DISCUSSION

The first reported association between malnutrition and diabetes mellitus was in 1955, by Hugh-Jones in Jamaica.⁵ He called it J-type diabetes. However, he made no mention of a possible pancreatic disorder. In 1959, Zuidema in Indonesia described the syndrome of pancreatic insufficiency occurring in young people in the tropics, which was characterized by abdominal pain, diabetes mellitus – mostly insulin dependent, malabsorption and pancreatic calcification.⁶ This syndrome was subsequently described in Uganda,^{7,8} Nigeria,⁹⁻¹⁵ Zaire,¹⁶ Malawi,¹⁷ Singapore,¹⁷ and India.¹⁸ All the countries lie within 15° of the equator, north or south. Davies noted similar clinical and pancreatic histological changes in pancreatic diabetes and kwashiorkor.¹⁹ Similar findings as described by Davies were found in other studies.^{7,15,16,20,21} However, pancreatic calcification is not a feature of kwashiorkor.

Genetic factors and infections were thought to play significant roles in the aetiopathogenesis of MRDM as described in tropical pancreatitis syndrome by Nwokolo and Oli.¹⁴ Endemic cassava consumption without adequate protein in the diet was also put forward as a cause of MRDM.²² The bark of the cassava root contains Linamarin, a major cyanogenic glycoside which on hydrolysis yields hydrocyanic acid (HCN). HCN when absorbed into the blood is inactivated by conjugation with Sulfhydryl (-SH) radicals derived from Sulphur containing amino acids (Methionine, Cysteine and Cystine). In protein deficiency HCN accumulate in the tissues and cause toxic damage to the islet cells. Therefore, if the bark of the cassava root is not properly removed during preparation for use, the toxic substance Linamarin will be retained.

However, MRDM is not endemic in all cassava consuming areas i.e. Latin America. It may be because that cassava preparation is efficient in this area. MRDM also occur in areas where cassava is an unimportant component of the diet i.e. Madras, India.²² This may be because other factors play more significant role in the aetiology of MRDM: hereditary and infections¹⁴ and indigenous spirits^{23,24} and herbal medicines.²⁵⁻²⁹ The reduction in the incidence and prevalence of MRDM is likely due to multiple factors: better means of preparing cassava, better diet with adequate protein, increase in knowledge, better lifestyle values and technological advancement. The Clinical Practice Guidelines for the management of Diabetes in Nigeria, 3rd Edition, 2023 did not present any topic on MRDM.³⁰ Thirty specialists and academics contributed to the 22 Chapters in the book. The book is enriching and a very useful tool for all those involved in the care and management of diabetes, patients inclusive.

The Diabetes Association of Nigeria (DAN) in collaboration with the following partners: International Diabetes Federation (IDF), Federal Ministry of Health (FMoH) Nigeria, Novo Nordisk, Eli Lilly, MEGA and Roche have contributed immensely to the advocacy and provision of support for the management of diabetes mellitus in Nigeria.³⁰ This effort is well appreciated

and has yielded many positive results. My Case-Book in Endocrinology dated October, 1990 is available at the University College Hospital (UCH), Ibadan, Nigeria Library.³¹ The advent of climate change, global increase in the prevalence of diabetes mellitus, insecurity, conflicts and poverty may lead to adverse health conditions and resurgence of previously eradicated diseases. Therefore, physicians should be aware and report incident findings, MRDM inclusive.^{4,30}

References

1. Diabetes Mellitus. Report of World Health Organization (WHO) Study Group. Technical Report Series 727. Geneva; World Health Organization. 1985
2. World Health Organization: Definition, Diagnosis, and Classification of Diabetes Mellitus and its Complications. Part 1. Diagnosis and Classification of Diabetes Mellitus. Geneva: World Health Organization 1999
3. World Health Organization. Classification of Diabetes Mellitus. WHO 2019
4. Oputa RN. Classification of Diabetes Mellitus: Why the Flux – a review. *East H Med J* 2020; 1: 84-89
5. Hugh-Jones P. Diabetes in Jamaica. *Lancet* 1955; 2: 891-897
6. Zuidema PJ. Cirrhosis and disseminated calcification of the pancreas in patients with malnutrition. *Trop Geogr Med* 1959; 11: 70-74
7. Banwell JP. Endocrine pancreatic disease and malabsorption in Tropical Africa. *Gut* 1967; 8: 388-401
8. Sharper AG. Chronic pancreatic disease and malnutrition. *Lancet* 1960; 2: 1223-1224
9. Adetuyibi A. A study of 130 consecutive cases of diabetes mellitus seen at the Diabetic Clinic of the University College Hospital, Ibadan. *Niger Med J* 1977; 7(3): 247-250
10. Adetuyibi A. Diabetes in the Nigerian African: A review of long-term complications. *Trop Geogr Med* 1976; 28: 155-158
11. Osuntokun BO, Akinkugbe FM, Francis TI, Reddy S, Osuntokun O, Taylor GOL. Diabetes Mellitus in Nigeria: A study of 832 patients. *West Afr Med J* 1971; 20: 295-312
12. Kinnear TWG. The pattern of Diabetes in a Nigerian Teaching Hospital. *E Afr Med J* 1963; 40(5): 288-294
13. Bella AF. Calcific pancreatic diabetes mellitus in Ibadan. *Central Afr J Med* 1985; 31: 180-182
14. Nwokolo C, Oli JM. Pathogenesis of juvenile tropical pancreatitis syndrome. *Lancet* 1980; 1: 456-459
15. Olurin EO, Olurin O. Pancreatic calcification: a report of 45 cases. *Br Med J* 1969; 2: 534-539
16. Sonnet J, Prisboise P, Bastin JP. Chronic pancreatitis with calcification in Congolese Bantus. *Trop Geogr Med* 1965; 18: 97-113
17. Pitchamoni CG. Pancreas in primary malnutrition disorder. *Am J Clin Nutr* 1973; 26: 374-379
18. Greevarghese PJ, Pillai VK, Joseph MP, Pitchamoni CG. The diagnosis of pancreatogenous diabetes mellitus. *Ass Phys India* 1962; 10: 173-175
19. Davies JWP. The essential pathology of Kwashiorkor. *Lancet* 1948; 1: 317-320
20. Kajubi SK, Sharper AG, Owor R. In: *Medicine in a tropical environment*. (Ed: Sharer SK, Kibukamusoke JW, Hutt MSR) London. BMA 1972. pp 380-394
21. Walker LS. Diabetes in the tropics. In: *Gastroenterology* (Ed: Truelove SC, Goodman MJ) London. Blackwell 1975. Vol 3, pp 108-121
22. Bajaj JS. Malnutrition-related Fibrocalculous Pancreatic Diabetes. In: *Proceedings, 12th IDF Congress, Madrid*. Serrano-Rio M, Lefebvre PJ. (eds) Excerpta Medica, Amsterdam 1986. pp 1055-1072

23. McLarty OG. Diabetes in Africa. In: Krall AP, Alberti KGMM, Serrano-Rio M. eds. World book of diabetes in practice. Amsterdam: Elsevier 1988; 2: 218-228
24. Jackson WPU, Vimk AI. In: Epidemiology of diabetes and its vascular complications. Keen H, Pickup JC, Talwalkar CV eds. International Diabetes Federation 1976. pp 39-43
25. Nnochiri EA. A case of juvenile diabetes mellitus complicated by treatment with herbs. *West Afr Med J* 1961; 10: 58-61
26. Cole TO, Adadevoh BK. Herbs and diabetes mellitus. *Niger Med J* 1974; 4(1): 51-55
27. Dodu SR. Diabetes in the tropics. *Br Med J* 1967; 2: 747-752
28. Akanji AO. The causes of diabetes mellitus in Africans. *Niger Med Pract* 1989; 17(3): 31-34
29. Oli JM, Nwokolo C. Diabetes after infectious hepatitis: a follow-up study. *Br Med J* 1979; 1: 926-931
30. Clinical Practice Guidelines for the management of diabetes in Nigeria. A publication of the Diabetes Association of Nigeria (DAN). Editors: Mohammed Alkali, Ejiofor Ugwu, Sule Bathnna. 2023
31. Oputa RN. Case-Book in Endocrinology: West African College of Physicians (WACP) Dissertation. October 1990.