Diabetes Mellitus in the First 2 Years of Life

Thesis

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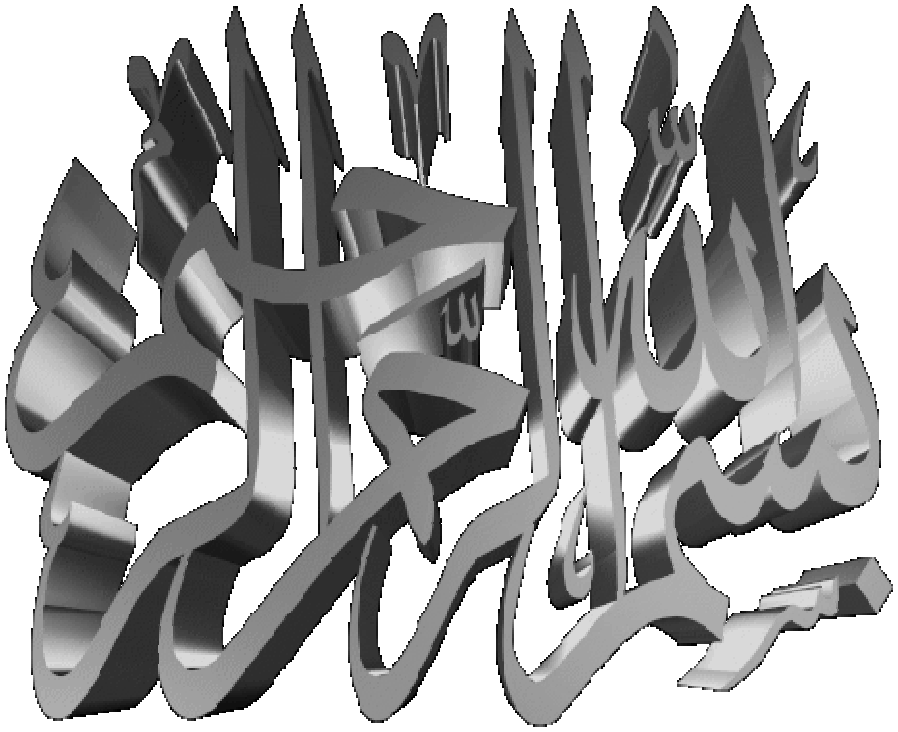

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ABSTRACT

The onset of type 1 diabetes before the first year of age is a rare condition and is probably due to an interaction between genetic and environmental factors. Infantile onset diabetes needs to be distinguished from "Neonatal diabetes" which can be either permanent or transient. The aim of the current study is to describe the clinical characteristics and laboratory findings and the different triggering factors in patients who developed permanent diabetes mellitus during the first two years of their life. There was a slight female predominance with male to female ratio 1:1.2, their average age of onset was 13.65 months. The highest percent (92%) were presenting with polyurea / polydepsia, (66%) were presenting with weight loss,(50%) were presenting with DKA. Thirty eight (76%) of studied patients had cow milk before the age of 1 year, 28(56%) were exclusively breast fed till the age of 6 months and 29(58%) of the patients have +ve family history of diabetes. In conclusion, we focused on an important age group of diabetic patients with early onset of the disease and the importance of avoiding exposure to the different predisposing factors which may precipitate early onset of diabetes.

Key words: Infantile onset diabetes- Neonatal diabetes- predisposing factors –cow milk.

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List of Abbreviations

ABCC8	ATP binding cassette, subfamily C, member 8
ADA	American Diabetes Assoiation
Alb/Creat Ratio	albumin/ creatinine ratio
AST	Aspartate aminotransferase.
B.F	Breast feeding
BG	Blood glucose
CDA	Canadian Diabetes Association
CM	Cow milk
CSII	Continuous Subcutaneous Insulin Infusion
CTLA-4	cytotoxic T lymphocyte-associated 4
DEMPU	Diabetes Endocrine and Metabolism Paediatric Unit
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
EUR	European
FPG	Fasting plasma glucose
GAD65	glutamic acid decarboxylase
GCK	glucokinase
GDM	Gestational diabetes mellitus
GE	Gastroentritis
GLP1	glucagon-like peptide 1
HB	hemoglobin.
HbA_{1c}	Haemoglobin A1c
HBW	High bith weight
HLA	human leukocyte associated antigen
IDDM	Insulin dependent diabetes mellitus
IFN-g	interferon-gamma
IL-2	interleukin-2
INS	Insulin gene.
IPEXsyndrome	immune dysregulation, polyendocrinopathy with

	neonatal DM, enteropathy and X-linked thrombocytopenia
IPF1	insulin promoter factor-1
IPF-1	Insulin promoter factor-1.
ISPAD	International society for pediatric and adolescents diabetes
IUGR	Intra urtine growth restriction
IZS	Insulin Zinc Suspension
KCNJ11	The potassium channel, inwardly rectifying subfamily J, member 11
LBW	Low birth weight
MDI	Multiple Daily Injections
MODY	Maturity-onset diabetes of the young
NDM	Neonatal diabetes mellitus
NPH	Neutral protamine hagedorn
OGTT	Oral glucose tolerance test.
PDMI	Permanent Diabetes Mellitus in Infancy
PDX-1	pancreas duodenum homeobox 1
PNDM	Permanent neonatal diabetes mellitus
POLY U	Polyurea
S.creat	serum creatinine.
SDS	standard deviation score
SEA	South-East Asian
SMBG	Self monitoring of blood glucose
SUR1	sulfonylurea receptor 1
T h1 cells	T helper 1 cells
T NDM	Transient neonatal diabetes mellitus
T1D	Type1 diabetes
T1DM	Type1 diabetes mellitus
T2DM	Type2diabetes mellitus
T4	Thyroxin hormone

TNF-b	tumour necrosis factor-b
TSH	thyroid stimulating hormone
URTI	Upper respiratory tract infections
WP	Western Pacific
WT loss	Weight loss

INTRODUCTION

Diabetes mellitus is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs, especially the eye, kidney, nerves and blood vessels ***(ADA, 2008).***

Type 1 diabetes is a serious disease that approximately affect 4.9 million people (in all age groups), amounting to 0.09% of the world's population. The number of people with diabetes is expected to increase alarmingly in the coming decades. In 1985 an estimated 30 million people worldwide had diabetes & in 2000 little over a decade later, the figure had risen to over 150 millions. This figure is expected to rise to almost 350 million by 2025 ***(Stern et al., 2005).***

The onset of type 1 diabetes before the first year of age is a rare condition and is probably due to an interaction between genetic and environmental factors , which together may explain such an early event ***(Tannus et al., 2007).***

Environmental triggers in infancy and early childhood may accelerate the onset of diabetes**.** For example, enteroviral infection documented by polymerase chain reaction was detected in twins developing type 1 diabetes in infancy, before detection of islet-cell antibodies.***(Hathout, 2003).***

In recent years, several viruses have been implicated in the pathogenesis of type 1 diabetes. Children with a congenital rubella infection commonly acquire type 1diabetes and children who develop diabetes have experienced more enterovirus infections than control subjects before the appearance of autoantibodies and in fetal life. Single

reports have also connected mumps and cytomegalovirus infections with type 1 diabetes. (***Blomqvist et al., 2002).***

According to a Swedish study, children who are exclusively breastfed for a long period of time may be at lower risk of developing type 1 diabetes than those who are not. The researchers also found that postponing new foods and cow's milk seemed to be protective against the development of type 1 diabetes. ***(Brekke et al., 2005).***

Another theory is that breastfed children tend to grow more slowly and steadily while formula-fed babies often have growth spurts. That is because mother's milk contains fewer calories than formula. ***(Sadauskaite et al., 2004).***

Breast milk protects against enteric infections; enteric infections in turn could increase immunity to dietary antigens by increasing intestinal permeability. It is also possible that an alteration in gut mucosal immune function in genetically susceptible individuals underlies any effect of dietary or viral proteins on the development of islet autoimmunity in early life. ***(Couper, 2001).***

Cow's milk feeding is an environmental trigger of immunity to insulin in infancy that may explain the epidemiological link between the risk of type 1 diabetes and early exposure to cow's milk formulas. This immune response to insulin may later be diverted into autoaggressive immunity against beta-cells in some individuals, as indicated by our findings in children with diabetes-associated autoantibodies.***(Vaarala et al, 1999).***

Infantile onset diabetes needs to be distinguished from "Neonatal diabetes" which is a rare entity. In the majority of such cases, however, the diabetes disappears within few weeks to few months and this

condition is termed as "Transient Diabetes Mellitus of New Born" or "Transient Neonatal Diabetes Mellitus". Very few of these cases continue to have permanent diabetes whereas onset of diabetes after one month of age i.e. infantile onset diabetes is likely to be permanent and therefore termed as Permanent Diabetes Mellitus of Infancy ***(Kumar, 2002).***

NDM is a monogenic form of diabetes that occurs in the first 6 months of life. It is a rare condition occurring in only one in 100,000 to 500,000 live births. Infants with NDM do not produce enough insulin, leading to an increase in blood glucose. NDM can be mistaken for the much more common type 1 diabetes, but type 1 diabetes usually occurs later than the first 6 months of life. In about half of those with NDM, the condition is lifelong and is called permanent neonatal diabetes mellitus (PNDM). In the rest of those with NDM, the condition is transient and disappears during infancy but can reappear later in life; this type of NDM is called transient neonatal diabetes mellitus (TNDM). Specific genes that can cause NDM have been identified ***(Sperling et al., 2007).***

AIM OF WROK

The aim of the current retrospective/prospective study is to describe the clinical characteristics and laboratory findings and the different triggering factors in patients who developed permanent diabetes mellitus during the first two years of their life.