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DIABETES IN CHILDHOOD, ADOLESCENTS AND YOUNG ADULTS-THE ROLE OF OBESITY

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ABSTRACT
The incidence of type 1 diabetes (T1D) in young children (age <6 years) is rising. Diabetes management guidelines offered by the American Diabetes Association and health care teams understandably place a high burden of responsibility on caregivers to check young children's blood glucose levels, administer insulin, and monitor diet and physical activity with the ultimate goal of maintaining tight glycemic control. Unfortunately, this tight control is needed during a vulnerable developmental period when behavior is unpredictable, T1D can be physiologically difficult to control, parenting stress can be elevated, and caregivers are strained by normal child caretaking routines. Despite the potentially different management needs, specific education and clinical services for managing diabetes in young children are rarely offered, and behavioral research with this young child age group has been limited in scope and quantity. Research findings pertinent to young children with T1D are reviewed, and potential clinical implications, as well as areas for future research, are discussed.

KEYWORDS: young children, type 1 diabetes, parenting.

INTRODUCTION
Diabetes mellitus in childhood, adolescents and young adults, like in adults can be as result of absolute insulin deficiency (type 1DM)or relative insulin deficiency (Type 2 DM).

Absolute Insulin Deficiency could be due to
*****Autoimmune destruction of insulin secreting β-cells(Type 1A)and other congenital (genetic defects in the formation or function of the endocrine pancreas).
*Acquired(relapsing pancreatitis and pancreatectomy) conditions.
*Total absence of insulin receptors, a rare events, where in there is absolute deficiency of insulin action.

Relative Insulin Deficiency occurs with
*Genetic or acquired defects in insulin synthesis or secretion that are inadequate to Overcome the resistance caused by fewer functioning insulin receptors.
*Resistance to insulin action induced by stress, drugs and most commonly obesity Till the end of 20th century, T1 DM was more common compared to T2 DM in the paediatric age group ,adolescents and youg adults. Since then however, frequency of T2 Diabetics has markedly increased.

However, coinciding with the increasing prevalence of obesity among children, the incidence of Type 2 Diabetes in children and adolescents has markedly increased, To the extent that it now accounts for as many as one third of all new cases of diabetes diagnosed in adolescents. This trend is particularly pronounced among Asians.

An increased prevalence of Type 2 Diabetes has also been recognized in countries Other than the united States, including Japan, where the incidence of Type 2 Diabetes in school children after 1981 was found to be strongly related to an increasing prevalence of obesity.[1]

Prevalence is higher among girls than boys,just as theprevalece I higher among adult females than it is in adult males.[1]

Studies among the Indian, British, Chinese, Taiwanese, Libyan, Bangladeshi, Australian, and Maori populations also have shown increasing incidence of youth-onset Type 2 Diabetes.[2,3,4,5,6]

Risk Factors
The Major Risk Factors For Type 2 Diabetes in young persong are[7]

*Obesity and inactivity- important contributors to insulin resistance.
*Asian, Native American, black, Hispanic, or Pacific Islander descent.
*Family history of Type 2 Diabetes in first-and second –degree relatives.
*Age of 12-16 years, the mean age range of onset of Type 2 Diabetes in youths-co-incides with the relative insulin resistance that occurs during pubertal development.
*Low birth weight and high birth weight.[8]
*Maternal gestational diabetes or Type 2 Diabetes.[9,10]
*Not breastfed during infancy.[11]
*Anti psychotic use;3-fold increased risk.Risk increased with higher doses and remained elevated for up to 1 year after medications were discontinued.[12,13]

Link between Obesity and Diabetes
Three main hypotheses have been developed in recent years to bridge the gap between epidemiology and payho-biochemistry.

1.Inflammation Hypothesis
Asserts that obesity represents a state of chronic inflammation. Inflammatory molecules produced by infiltrating macrophages in adipose tissue exert pathological changes in insulin-sensitive tissues and β-cells.

2.Lipid overflow hypothesis
Predicts that obesity result in increased ectopic lipid stores due to the limited capacity of adipose tissue to properly store fat in obese subjects. Potentially harmful lipid components and metabolites may exert cytotoxic effects on peripheral cells.[14,15,16]

3.Adipokine Hypothesis cells function
White adipose cells function as paracrine function .Expanding fat stores can cause dysfunctional secretion of such endocrine factors, thereby resulting in metabolic impairment of insulin target tissues and eventually failure of insulin producing β-cells.

Although inflammation is thought to be a major factor in the development of insulin resistance and diabetes, inflammatory processes do not account exclusively for the development of insulin resistance since there are studies showing subjects with T2DM with out any alterations in inflammatory markers.

The development of Type 2 Diabetes is caused by a combination of insulin resistance andimpaired pancreatic B-cell secretion. With progression from euglycemia to T2DM, B-cells progressively fail to compensate for the increase insulin demand in peripheral tissues.

The pathogenesis is thereby characterized by different stages,leading from compensatory insulin resistance to decompensated hyperglycemia.

In manifest Type 2 Diabetes, B-cells are exposed to both high doses of glucose(glucotoxicity)and lipids(lipotoxicity), respectively. Lipotoxicity, manifests as incorporation oflarge amounts of triglycerides in pancreatic islets, leading to β-cell death.

The UK Prospective Diabetes Study found that beta cell function was 50%of normal at the time of diagnosis of Type 2 Diabetes in adults.[19] A case study of the progressionof diabetes in an adolescent female found an aimost 15% decline in beta cell functionper year over the 6-year duration of diabetes,with no substantial changes in insulinsensitivity.[20]

Typical Characteristics of Type 2 Diabetes are
*Slow and insidious in onset.
*Being overweight and obese-strong association
*Signs of insulin resistance such as Acanthosis Nigricans, skin tags etc.
*Strong family history of T2DM,metabolic syndrome or cardiovascular disease.

Screening and Diagnosis
Testing for Type 2 Diabetes should be considered when a patient is overweight and hasany 2 of the following.[19]
*Family history of Type 2 Diabetes in first-degree or second-degree relative.
*Asian.
*Signs of insulin resistance or conditions associated with insulin resistance (e.g., Acanthosis Nigricans, hypertension dyslipidaemia & PCOS).

Recommendations for Screening are as follows
*Initial screening may begin at age 10 years or at onset of puberty if puberty occursat a young age.
*Screening should be performed every 2 years.
*A fasting plasma glucose test is the preferred screening study;if clinical suspicion is high but fasting blood glucose is normal(<100 mg/dL), an oral glucose tolerance test should be considered.

Glucose Values may be interpreted as follows
*A random plasma glucose concentration of 200 mg/dL or greater in association with polyuria, polydipsia, or unexplained weight loss is diagnostic of diabetes.[20]
*In an asymptomatic patient,a fasting plasma glucose value of 126 mg/dL or greateror a 2-hour plasma glucose value of 200 mg/dL or greater during an oral glucosetolerance test is also diagnostic of diabetes.[20]

Treatment
The goal of therapy is to achieve and maintain euglycemia and near-normal hemoglobin A_{1c}(HbA_{1c})levels(<7%).More specifically,glycemic and nonglycemic goals may includethe following;
*Fasting glycemia of less than 126 mg/Dl
*Resolution of polyuria,nocturia,and polydipsia.
*Healthy body weight.
*Maintenance of cardio-protective levels of lipids and blood pressure(LDL level< 100 mg/dL, triglyceride< 150

mg/dL, HDL level >35 mg/dL;blood pressure< 95th percentile for age, sex, and height).
*Participation of the whole family as a unit.

Treatments for Paediatric Type 2 Diabetes include the following
*Diabetes education and lifestyle changes (diet, exercise,weight control)
*Pharmacologic therapy with metformin,insulin,a sulfonylurea,or another hypogly- cemic agent
*Lipid-lowering agents and blood pressure medications to achieve cardio-protection,if necessary

Additional Monitoring should be performed as follows
*Microalbuminuria and fasting lipid profile(annually)
*Dilated eye examination(annually)
*Blood pressure evaluation and careful neurologic examination(at each clinic visit)

Testing for Albuminuria can be done by means of 1 of the following 3methods
*Measurement of the albumin-creatinine ratio in a random spot collection
*A 24-hour collection for albumin and creatinine determinations,which allows simul-taneous measurement of creatinine clearance
*Timed(e.g.,4-hour or overnight)collection Fasting lipid profiles should be obtained after stable glycemia is achieved and every 2years thereafter if normal.Optimal values for children with Type 2 Diabetes are as follows.
*Triglycerides<150 mg/dL
*Low-density lipoprotein(LDL)<100 mg/dL
*High-density lipoprotein(HDL)>35 mg/dL

SUMMARY AND CONCLUSION
Diabetes mellitus (DM) is a chronic metabolic disorder caused by an absolute or relative deficiency of insulin. Absence, destruction, or loss of beta cells of the islets of Langerhans causes an absolute deficiency of insulin, leading to type 1 diabetes (insulin-dependent diabetes mellitus [IDDM]). Most children with diabetes have IDDM and a lifetime dependence on exogenous insulin (Gale et al., 1999).

Diabetic nephropathy is a clinical syndrome characterized by persistent albuminuria (>300 mg/d or >200 mcg/min) that is confirmed on at least 2 occasions 3-6 months apart, a relentless decline in the glomerular filtration rate (GFR), and elevated arterial blood pressure. Diabetic nephropathy is the leading cause of chronic renal failure . Diabetes is reponsible for 30- 40% of all end-stage renal disease (ESRD). Microalbuminuria is defined as albumin excretion of >20 mcg/min or >30mg/dl . This phase indicates incipient diabetic nephropathy and calls for aggressive management, at which stage the disease may be potentially reversible (Eknoyan et al., 2003). Monocyte chemoattractant protein-1 (MCP-1) is a member of the chemokine family and specifically attracts monocytes. There is an increasing evidence that the CC chemokine monocyte chemoattractant protein-1 (MCP-1) plays a major role Summary, Conclusion & Recommendations 29 in the pathogenesis of progression of renal failure. Locally produced MCP-1 seems to be particularly involved in the initiation and progression of tubulointerstitial damage (Tesch et al., 1999).

Previous studies focused on the role of MCP-1 in renal inflammation and its induction of inflammatory signals. Recent data suggest that MCP-1 is more than just a chemoattractant. Rather, MCP-1 can directly elicit an inflammatory response by inducing cytokine and adhesion molecule expression in the kidney. This is an important new mechanism in the pathogenesis of tubulointerstitial inflammation (Sergerer et al., 2000).

Antioxidants such as beta-carotene and vitamin C are scavengers of free radicals—unstable and potentially damaging molecules generated by normal chemical reactions in the body. Vitamin E reduces oxidative stress, thus improving membrane physical characteristics and related activities in glucose transport.In short, Vitamin E (800 to 1200 I.U.) improves insulin action and prevents a host of long-term complications of diabetes including nephropathy (Perkins et al., 2003).

In the present study, we investigate role of MCP-1 in development of early nephropathy in IDDM children & adolescent patients was investigated. In addition, the effect after 8 weeks of high dose of vitamin E (600mg b.i.d) on early stages of diabetic nephropathy was studed.

This study was carried out Summary, Conclusion & Recommendations 29 on 30 diabetic patients subdivided into 2 groups : IDDN patients with early nephropathy (with microalbuminurea) & IDDM patients without nephropathy where MCP-1(pg/dl), glycated Hb(% of Hb) &microalbuminurea(mg/dl) before & after vitamin E treatment were measured.

In the present study, it was found that
1- There was a significant elevated serum MCP-1 in patients with microalbuminurea and poor glycemic control when compared to normoalbminuric diabetic patients and healthy control.
2- HbA1c was significantly higher in microalbuminuric diabetic patients than normoalbuminuric diabetic patients.
3- Plasma MCP-1 was positively correlated with HbA1c.
4- Both MCP-1 and albuminurea decreased significantly after vit. E treatment, despite no change in HbA1c i.e. no change in glycemic control.

In conclusion, the present study supports the hypothesis that upregulation of MCP-1 gene expression by persistent hyperglycemia in type 1 diabetic patients results in the recruitment of monocytes into the kidney, possibly contributing to the development of diabetic nephropathy. Moreover, these results suggest that the

causative role of poor glycemic control in diabetic nephropathy is mediated by increased oxidative stress . These findings are potentially important from a fundamental stand point because they indicate a pathogenetic role for MCP-1 in the evolution of diabetic microvascular complications. From a practical perspective, these results raise the possibility that vitamin E may provide a novel form of therapy for prevention of microvascular complications in type 1 diabetic patients, in whom an acceptable glycemic control is difficult to achieve despite appropriate insulin treatment.

RECOMMENDATIONS

*Because of the potential for rapid clinical deterioration expected in untreated children with type 1 diabetes, unnecessary delays in the diagnosis must be avoided and a definitive diagnosis should be made promptly.

* As the incidence of type 2 diabetes in children and adolescents increases, it becomes increasingly important to differentiate newly diagnosed type 1 from type 2 diabetes as the method of treatment will differ in both.

*average capillary blood glucose (BG) levels based on both pre- and postprandial measurements & also are directly correlated to the risk of complications.

*long-term complications of diabetes mellitus can be reduced by tight glycemic control, intensive treatment regimens.

*Plasma MCP-1 was significantly increased in type 1 diabetic patients with early nephropathy and it would be used as an indicator for early detection of diabetic nephropathy.

*vitamin E may provide a novel form of therapy for prevention of microvascular complications in type 1 diabetic patients.

REFERENCES

1. Urakam! T, Kubota S, Nitadori Y, Harada K, Owada M, Kitagawa T. Annual incidence and clinical characteristicsof Type 2 Diabetes in children as detected by urine glucose screening in the Tokyo metropolitan area. Diabetes Care, 2005 Aug; 28(6): 1876-81.
2. Ehtisham S, Hiattersley AT, Dunger DB, Barrett TG, First UK survey of paediatric Type 2 Diabetes and MODY. ArchDis Child, 2004 Jun; 89(6): 526-9.
3. Kadiki OA Reddy MR. Marzouk AA. Incidence of insulin-dependent diabetes(IDDM)and non-insulin-dependent diabetes(NIDDM)(0-34 years at onset)in Benghazi, Libya. Diabetes Res Clin Pract, 7996 May. 32(3): 765-73.
4. Chan JC. Cheung CK, Swaminathan R, Nicholls MG, Cockram CS. Obesity, albuminuria and hypertensionamong Hong Kong Chinese with non-insulin-dependent diabetes mellitus(NIDDM). Postgrad Med J., 1993 Mar; 59(809): 204-10.
5. Ramachandran A Snehalatha C, Satyavani K Sivasankari S. Vijay V. Type 2 Diabetes in Asian-Indian urbanchildren. Diabetes Care, 2003; Apr. 26(4): 1022-5.
6. Saveed MA, Hussain MZ, Banu A, Rumi MA, Azad Khan AK. Prevalence of diabetes in a suburban populationof Bangladesh. Diabetes Res Clin Pract, 1997 Jan; 34(3): 149-55.
7. Rosenbloom AL, Joe JR, Young RS, Winter WE. Emerging epidemic of Type 2 Diabetes in youth. Diabetes Care, 1999 Feb. 22(2): 345-54.
8. Wei JN Sung FC, Li CY, et al. Low birth weight and high birth weight infants are both at an increased risk tohave Type 2 Diabetes among schoolchildren in Taiwan. Diabetes Care, 2003 Feb; 26(2): 343-8.
9. Siiverman BL, Metzger BE, Cho NH, Loeb CA. Impaired glucose tolerance in adolescent offspring of diabeticmothers. Relationship to fetal hyperinsulinism. Diabetes Care, May 1995; 18(5): 611-7.
10. Young TK, Martens PJ, Taback SP. et al. Type 2 Diabetes mellitus in children: prenatal and early infancy riskfactors among native canadians. Arch Pediatr Adolesc Med, 2002 Jul; 156(7): 657-5.
11. Mayer-Davis EJ. Dabelea D, Lamichhane AP. D'Agostino RB Jr, Liese AD, Thomas J. Breast-feeding and Type 2Diabetes in the youth of three ethnic groups:the SEARCH for diabetes in youth case-control study. Diabetes Care, 2008 Mar; 31(3): 470-5.
12. Brauser D. More Proof Antipsychotics Bcost Kids'Diabetes Risk. Medscape Medical News. Available at http:/lwww.medscape.com/ viewarticle/809942 Accessed, August 27, 2013.
13. 8obo WV, Cooper WO, Stein CM, Olfson M, Graham D. Daugherty J, et al. Antipsychotics and the Risk of Type2 Diabetes Mellitus in Children and Youth. JAMA Psychiatry, 2013 Aug 21.
14. Weir GC, Bonner-Weir S. Five stages of evolving beta-cell dysfunction during progression to diabetes. Diabetes. Dec 2004; 53(3): S16-21.
15. Joost HG. Pathogenesis, Risk Assessment and Prevention of Type 2 Diabetes mellitus. Obesity Facts, JUN 2008; 1(3): 128-137.
16. Unger RH. Minireview.: weapons of lean body mass destruction:the role of ectopic lipids in the metabolicsyndrome Endocrinology, Dec 2003; 144(12): 5159-5165.
17. Matthews DR. Cull CA, Stratton IM, Holman RR, Turner RC. UKPDS 26:Sulphonylurea failure in non-insulin-dependent diabetic patients over six years. UK Prospective Diabetes Study(UKPDS) Group. Diabet Med, 1998 Apr; 15(4): 297-303.
18. Gungor N, Arslanian S. Progressive beta cell failure in Type 2 Diabetes mellitus of youth. J Pediatr, 2004 May; 144(5): 656-9.
19. Guideline Diagnosis and classification of diabetes mellitus. Diabetes Care, 2004 Jan; 27(1): S5-S10.
20. American Diabetes Association Type 2 Diabetes in children and adolescents. Diabetes Care, 2000 Mar; 23(3): 381-9.
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