A brief study on Diabetes Mellitus: Pathophysiology and diagnosis

ABSTRACT

Background : This article is a review of published articles as well as existing diagnostic and therapeutic techniques that are relevant to adolescent with obesity and diabetes mellitus.
Obesity, in addition to DIABETES MELLITUS, is a key risk factor for the occurrence of future chronic and noncommunicable diseases.
Obese and overweight teenagers are more prone to acquire Adult Onset Diabetes, which was formerly found to be rare in occurrence among the younger population. However, a global trend of Adult Onset Diabetes was noted in the late 1990s and early 2000s. Not only in the United States and the United Kingdom, but also in other developing and developed countries, this is particularly true. In some locations, Adult Onset Diabetes is nearly as common as Insulin Dependent Diabetes. In a number of population groups, there has been a major surge in the prevalence and severity of obesity in teenagers.
Objective and Methodology: To read and review the existing literature on the prevalence of Diabetes Mellitus and obesity in adolescence. About 15 articles and literature were studied using the PubMed and Google Scholar search engine in order to produce a detailed review article on the topic of interest so chosen.
Result & Conclusion: After reviewing the articles, we can agree that TYPE-2 DIABETES MELLITUS is linked easily to young adults who are obese, that is having Body Mass Index more than 30 or more than 30. TYPE-2 DIABETES MELLITUS causes destruction of receptors for insulin which results in increased level of glucose causing various diseases. Obesity in young adults is a key factor in the occurence of Adult Onset Diabetes which makes them at risk of developing serious diseases in 3rd or 4th decade of life.

Keywords: Obesity, Adolescents, Hyperinsulinemia, Adult Onset Diabetes, Hyperglycaemia

INTRODUCTION

Earlier, Adult Onset Diabetes was not considered very common occurrence in paediatric age group or young adults. However, increased cases of Adult Onset Diabetes has been observed all over the world, since the late 1990s to early 2000s. This is particularly the case not only in the countries like US, UK but also been reported in other countries, both developing and developed. [1][2] In some countries, the prevalence of Adult Onset Diabetes can be as common as Insulin Dependent Diabetes. A striking increase has been observed in generality of Adult Onset Diabetes amongst overweight young adult population.[1][3]

Obesity in both industrialised and emerging countries; in children and adults, is the commonest type of malnutrition to be seen globally. It is the sixth most important worldwide mortality risk factor.

[3] Obesity can be considered a big factor responsible for this increasing trend of Adult Onset Diabetes in young adults. This attributes to the fact, that the universality of obese population is not increasing but the affect it has on children and adolescents is causing problems. Obesity is the leading cause for 5% of all the global morbidities.[4] Dietary factor being the major cause for the prevalence of obesity in young adults.

Obesity predisposes an individual to many co-morbidities, not only Type 2 DM but also to chronic heart diseases, hyper-insulinemia, hypertension, polycystic ovarian syndrome, hyper-androgenemia and many others. [4]

Diabetes Mellitus type 2 is a dangerous condition as long standing case of Diabetes Mellitus can result to chronic consequences such as accelerated cardiovascular disease, chronic renal disease, retinopathy, limb amputations due to the development of gangrene following an injury to the limb, neuropathic changes and many more. All of these problems present with increasing risk ofmorbidity and mortality in people with this disease.[1]

We as a society are going to see a number of young adults with complications if the rate at which Type 2 DM keeps on increasing amongst the adolescent population of the country. The affect we will have of DIABETES MELLITUS and its complications will change the life of our coming generation if the situation is not handled carefully.[1]

The key factor for the disease mentioned is obesity. Majority youngsters with Adult Onset Diabetes are obese with BMI higher than 30 or severely overweight at the time of clinical symptoms, with presence of reducing sugar in urine but no ketone bodies, MILD POLYURIA and POLYDISPIA, and almost no loss of weight[5]. Young adolescents who are in the early phases of puberty are currently coming up diagnosed as TYPE-2 DIABETES MELLITUS[1][5].

PATHOPHYSIOLOGY

Adult Onset Diabetes , also known as type-2 diabetes mellitus, a disorder which arises from insulin resistance and relative insulin insufficiency in absence of destroyed beta cells. The illness has a substantial hereditary (possibly multigenic) component, important being GENETIC MAKEUP highlighted with disparities in relation to Adult Onset Diabetes in different races is taken into account .[1][5] Significant progress has been made in our understanding of the familial basis of the disease related , these new findings in the prevalence of the disease discussed are too rapid due to increasing gene frequency and a changed gene pool, highlighting the role of environmental influences.[1]
Insulin secreted by beta-cells of pancreas and action of INSULIN must be in equilibrium for glucose homeostasis to occur. Insulin resistance to glucose absorption driven by insulin is a problem. well-known feature of patients with Adult Onset Diabetes and impairment of the metabolism of glucose. The progression from good glucose tolerance to IMPAIRED GLUCOSE TOLERANCE (IGT) is linked to an increase in the resistance to insulin.[1]
Impaired glucose endurance is a stage linked with an increased risk of being diagnosed with the disease discussed and cardiovascular disease. Insufficiency of insulin is not enough to cause the onset of the disease discussed; insufficient beta-cell insulin production is also required.[1][6]

In children and young adults with diminished endurance of insulin, however, In coming few years, there will be a significant rate of quick and unprompted conversion from diminishing glucose endurance to normal glucose tolerance.[7] Changes in insulin resistance around the end of adolescence have been blamed for this normalisation.[1]

Insulin secretory failure and reduced insulin action are common in TYPE-2 DIABETIC INDIVIDUALS. Hyperglycemia is being demonstrated to worsen insulin resistance and its secretion irregularities, hastening the transition from glucose resistance into DIABETES.[1][8]

Adolescence plays very significant influence in occurrence of the disease mentioned [8] as in adolescence, there is a spike in tolerance of insulin, culminating in increased level of glucose in blood.[1]

Insulin responses, both basal and stimulated, decrease during puberty. Insulin-mediated glucose disposal is 30 percent poorer in teenagers between Tanner stages II and IV compared to prepubertal children and adolescents, according to hyperinsulinemic-euglycemic clamp studies. Insulin resistance during puberty is hypothetically found to be linked with increased GROWTH HORMONE release during puberty.[1][9]

Adult onset diabetes is marked by obesity[10]. A large proportion of children with the disease mentioned and discussed are obese or have excessively increased body mass index at the time of being diagnosed, with a high BMI, sugars in urine but no ketone bodies, absence or minimal POLYURIA and POLYDISPIA, and essentially none loss of weight. Adult Onset Diabetes is currently identified in young adolescent girls and boys above the age of 10 who are still in the early phases of puberty.[10,11]

DIAGNOSTIC CRITERIA FOR ADULT ONSET DIABETES IN YOUNG ADULTS

Even in the absence of beta-cell autoantibodies is what defines Type 2 DM. Positive beta-cell antibodies in insulin independent adolescents and young adults may indicate the presence of a latent self-destructing diabetes mellitus comparable to that seen in adults (LADA: LATENT AUTOIMMUNE DIABETES MELLITUS of Adults). According to a global survey, beta-cell autoantibodies occur in 10% to 20% of adult diabetics who do not use insulin. [1][11] Insulin resistance is similar in Latent Autoimmune Diabetes Mellitus of Adult patients to type 2 diabetes patients, but their -cell capacity is drastically diminished.[1]

Clinical features of DIABETES MELLITUS, such as POLYDISPIA, increased urine output, and loss of weight without any explanation, are combined with a casual glucose concentration of 200 MG/DL (11.1 mmol/L) in venous plasma, fasting glucose, of 126 mg/dL (7.0 mmol/L) in venous or capillary plasma, or two-hours glucose during oGTT of 200 MG/DL (11.1 mmol/L) in The American Diabetes Association (ADA) has changed its criteria to allow for the use of haemoglobin A1c (HbA1c) levels of less than 6.5 percent in the diagnosis of disease mentioned. [1]FASTING GLUCOSE, HBA1C, GTT tests must be performed on a different day in the case of asymptomatic manifestation.[1][12]

Majority of people suffering from this disease can be effectively classified based on their symptoms and presentation and course. Other tests, such as preparandial GLUCOSE or c-peptide determinations and, on rare occasions, cell autoantibodies measures, may be required in the event of an uncommon scenario that necessitates a specific classification .A set of tests is required to reach a high degree of sensitivity, which considerably raises the cost of categorization.[1]

In patients with Adult Onset Diabetes, C-peptide levels were higher than in patients with insulin dependent diabetes or MODY diabetes. Individuals with immune-mediated insulin dependent diabetes have autoantibodies against INSULIN, GAD-II, or the TYROSINE PHOSPHATASES antibodies (IA)-2 and IA-2b at the time of diagnosis. HLA typing is not an effective diagnosis marker for insulin dependent diabetes, which has a great HUMAN LEUKOCYTE ANTIGEN connection.[13]

The diagnosis of Adult Onset Diabetes in its mildest form is achieved during a normal medical check-up in an asymptomatic child by detecting hyperglycemia or glycosuria[1][14]. Urinanalysis is used to diagnose one-third of patients during standard physical examinations[1,14]. Increased urine output, polydipsia, and loss of weight are all symptoms of this condition in its most severe form. Ketonuria affects up to 33% of people in some racial groups at diagnosis, while ketoacidosis affects 5% to 25% of people at presentation[14].

EPIDEMIOLOGY

The major part of juvenile persons diagnosed with Adult Onset Diabetes were from certain racial minor groups such as Black-Americans, Hispanics, south asian Islanders, and American-Indians, with Pima Indians having the greatest prevalence (22.3/1000 in 10- to 14-year-old population). In addition, most of the subjects found to be overweight. Overweight adolescents aged 12 years had a generality of Adult Onset Diabetes ranging from 0.4 percent to 1%, according to screening studies[1]. When compared to TYPE-1 DIABETES, the overall occurrence of Adult Onset Diabetes in the entire paediatric age surveyed remained low. Even though there is universal agreement that Adult Onset Diabetes in young considered to be becoming a severe medical problem[1][14], this has led some researchers to dispute the assertions of a "EPIDEMIC" of paediatric Adult Onset Diabetes [1].

COMPLICATIONS IN YOUNG ADULTS WITH TYPES 2 DIABETES MELLITUS

Heart related complications have been found to be common in Adult Onset Diabetes adolescents than insulin dependent diabetes adolescents. According to a TODAY study, 14 % of adolescents suffering from Adult Onset Diabetes had high level of Blood Pressure, 80% had reduced HDL levels, and 10% have high levels of TRIGLYCERIDES.[14]

Contrasted to Adults with DIABETES, paediatric age group and young adults with the disease mentioned and discussed have a higher risk of complications. As a result, Adult Onset Diabetes diagnosed at a juvenile period of life is linked to a substantially increased chances of developing into heart related disease than Adult Onset Diabetes diagnosed at of 30-45 years.[14] junior persons with TYPE-2 DIABETES tend to have an greater chance of acquiring DIABETES-RELATED problems early in life than those with TYPE-1 DIABETES. This increased possibility found to be linked to the incidence of hypertension and dyslipidemia rather than overall glycemic control or disease duration.[15]

Microvascular diabetic diseases like retinopathy and microalbuminuria can be diagnosed at an early age and are the hallmark of hyperglycaemia.[1]

DISCUSSION

Several research have been conducted in recent years, and discovered that increased weight increases the risk of Adult Onset Diabetes by over 40%. The rate at which obesity has become more common among teenagers, as well as the obesity-related co-morbidities, is concerning.

Despite the fact that current research suggests that Diabetes Mellitus is mostly a hereditary disease, its link to obesity must not be neglected. [1][15]

In youngsters, puberty appears to have a significant impact on the development of the disease mentioned and discussed. During the period of adolescence, INSULIN RESISTANCE increases, eventually leading to increased levels of glucose in blood. Both basal and stimulated insulin responses decrease during adolescence. INSULIN-MEDIATED GLUCOSE clearance is thirty percent worse in teenagers between TANNER STAGES II and IV seen in contrast to primary children and youngsters, according to hyperinsulinemic-euglycemic clamp studies. Insulin

resistance during puberty is hypothesised to be caused by increased GROWTH HORMONE production throughout puberty. [1][15]
INSULIN RESISTANCE and inadequate -cell INSULIN production found to be causes of diabetes mellitus. INSULIN secretory failure and decreased insulin action are frequent in patients with the disease mentioned and discussed. Hyperglycemia has been shown to exacerbate intolerance of insulin and aberrant INSULIN production, hastening the establishment of diabetes mellitus due to decreased glucose tolerance.[15]

RATIONALE

There is a physiological increase in insulin levels throughout puberty that is triggered by fat, resulting in hyperinsulinemia, which invariably leads to intolerance of insulin, which leads to, adolescent non-insulin dependent diabetes. Insulin receptors become immune to insulin due to devepment of insulin resistance. Beta cells secrete more insulin at the pre-clinical stage of the disease, resulting in hyperinsulinemia.[16-20]
Obesity has a negative impact on glucose metabolism starting in childhood. Obese children are hyperinsulinemic, with insulin-stimulated glucose levels 40 percent lower than non-obese children. Most people with diabetes mellitus can be classified based on their clinical presentation and progress. If an uncommon scenario justifies a specific classification, additional tests, such as preparandial insulin or C-peptide readings, and, in rare cases, cell autoantibody measures, may be required. A succession of tests is required to reach a high level of sensitivity, which considerably raises the cost of classification. Adversity is more likely in children and young adults with the disease mentioned and discussed .[21-23]
As a result, TYPE-2 DIABETES diagnosed at a even more young age age is linked to a higher risk of long-term heart related disease than Adult onset diabetes detected later in life. Adolescents persons with non insulin dependent diabetes are considerably more likely than those with insulin dependent diabetes to have DIABETES-related problems early in life. This increased risk appears to be linked to the onset of hypertension and dyslipidemia rather than overall glycemic control or the length of time that the condition has been present.

CONCLUSION

Many factors influence the clinical symptoms of Diabetes Mellitus. Obesity is a significant contributor to the presence and severity of this illness, although it is neither sufficient nor necessary for Diabetes Mellitus to develop.
Adult Onset Diabetes is still uncommon in youth and puberty, but current research suggests that its incidence is increasing over the world, possibly as a result of rising childhood and teenage obesity rates. This is particularly true in the United States, but it has also been observed in Asia and Europe. If they show clinical symptoms of intolerance to insulin(blackening of neck and axilla, DYSLIPIDEMIA, increased blood pressure, POLYCYSTIC OVARIAN SYNDROME), family history of Adult Onset Diabetes , or come from specific race-related groups, obese children and adolescents over the age of 10 should be evaluated for Adult Onset Diabetes (Asian, American Indian, African-Americans, Hispanics). Preventing and treating the disease mentioned and discussed should be a major focus for public health intervention programmes. Prevention and the development of preventative strategies should be prioritised much earlier in our society.
Beginning in childhood, obesity has a deleterious impact on glucose metabolism. Overweight early adolescents are HYPERINSULINEMIC and have a 40% reduced GLUCOSE METABOLISM activated by insulin than non-obese children. In addition, visceral abdominal fat has a stronger negative relationship with insulin sensitivity than subcutaneous fat.
In conclusion, and probably more required, increasing public awareness of the epidemic's mounting health and economic consequences is vital. If not taken into consideration and adequate measures in controlling the incidence of the disease so highlighted, in near time there can be a steep rise in the

adolescent type 2 Diabetes rate, making the future population of the country susceptible to various other co-morbidities associated with it. Physicians should inform the public about the paediatric obesity pandemic and its severe consequences, which include the disease mentioned and discussed. Appropriate steps should be taken for the timely diagnosis of this disease, thus mentioned and discussed, in order to prevent any further future risks of the disease.

REFERENCES:

1. Reinehr T. TYPE-2 DIABETES MELLITUS in children and adolescents. World J Diabetes. 2013 Dec 15;4(6):270-81. doi: 10.4239/wjd.v4.i6.270. PMID: 24379917; PMCID: PMC3874486.
2. Arslanian S. Type 2 diabetes in children: clinical aspects and risk factors. Hormone Research in Paediatrics. 2002;57(Suppl. 1):19-28.
3. Han JC, Lawlor DA, Kimm SY. Childhood obesity. The lancet. 2010 May 15;375(9727):1737-48.
4. Park,K. (2020) Park's Textbook of Preventive and Social Medicine, 26th Edi. Jabalpur, India: M/s Banarasidas Bhanot Publisher.
5. Florez JC. The genetics of type 2 diabetes: a realistic appraisal in 2008. The Journal of Clinical Endocrinology & Metabolism. 2008 Dec 1;93(12):4633-42.
6. Mire-Sluis AR, Das RG, Lernmark A. American diabetes association-http://www. diabetes. org. Diabetes/metabolism research and reviews. 1999 Jan 1;15(1):78-9.
7. Kleber M, Desousa G, Papcke S, Wabitsch M, Reinehr T. Impaired glucose tolerance in obese white children and adolescents: three to five year follow-up in untreated patients. Experimental and clinical endocrinology & diabetes. 2011 Mar;119(03):172-6.
8. Arslanian SA. TYPE-2 DIABETES MELLITUS in children: pathophysiology and risk factors. Journal of pediatric endocrinology & metabolism: JPEM. 2000 Jan 1;13:1385-94.
9. Pinhas-Hamiel O, Lerner-Geva L, Copperman NM, Jacobson MS. Lipid and Insulin Levels in Obese Children: Changes with Age and Puberty. Obesity, 15, 2825-2831.
10. Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, Yeckel CW, Allen K, Lopes M, Savoye M, Morrison J, Sherwin RS. Obesity and the metabolic syndrome in children and adolescents. New England journal of medicine. 2004 Jun 3;350(23):2362-74.
11. Pozzilli P, Di Mario U. Autoimmune diabetes not requiring insulin at diagnosis (latent autoimmune diabetes of the adult): definition, characterization, and potential prevention. Diabetes care. 2001 Aug 1;24(8):1460-7.
12. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes care. 2013 Jan;36(Suppl 1):S67.
13. Copeland KC, Zeitler P, Geffner M, Guandalini C, Higgins J, Hirst K, Kaufman FR, Linder B, Marcovina S, McGuigan P, Pyle L. Characteristics of adolescents and youth with recent-onset type 2 diabetes: the TODAY cohort at baseline. The Journal of Clinical Endocrinology & Metabolism. 2011 Jan 1;96(1):159-67.
14. Hillier TA, Pedula KL. Complications in young adults with early-onset type 2 diabetes: losing the relative protection of youth. Diabetes care. 2003 Nov 1;26(11):2999-3005.
15. Eppens MC, Craig ME, Cusumano J, Hing S, Chan AK, Howard NJ, Silink M, Donaghue KC. Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes. Diabetes care. 2006 Jun 1;29(6):1300-6.
16. Jameel, Patel Zeeshan, Sham Lohiya, Amol Dongre, Sachin Damke, and Bhavana B. Lakhkar. "Concurrent Diabetic Ketoacidosis and Pancreatitis in Paediatric Acute

Lymphoblastic Leukemia Receiving L-Asparaginase." BMC PEDIATRICS 20, no. 1 (May 18, 2020). https://doi.org/10.1186/s12887-020-02136-3.
17. Kaple, Meghali Narayan, Chandrashekhar C. Mahakalkar, Anita Kale, and Swati Shambharkar. "Correlation of Metal Ions in Diabetic Patients." JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH 14, no. 5 (May 2020): BC14–16. https://doi.org/10.7860/JCDR/2020/43798.13730.
18. Thakare, Pratiksha, And Ruchira Ankar. "To Assess The Knowledge Regarding Prevention Of Sign And Symptoms Of Diabetic Ketoacidosis Among Diabetes Patients In Selected Hospitals Of Wardha District." International Journal Of Modern Agriculture 9, No. 3 (2020): 125–30.
19. Thakare PS, Ankar R. To Assess the Knowledge Regarding Signs and Symptoms of Diabetic Ketoacidosis and Its Prevention among Diabetes Patients in Wardha District, Maharashtra, India. JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS. 2021 May 10;10(19):1413–6.
20. Thool AR, Dhande NK, Daigavane SV. Study of Correlation between Renal Function Test and Severity of Diabetic Retinopathy in Patients with Type 2 Diabetes Mellitus. JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS. 2021 May 17;10(20):1511–4.
21. David P, Yeola M, Ankar R. Efficacy of Nursing Skin Care Protocol on Prevention of Skin Related Problems among Newly Diagnosed Diabetic Patients. JOURNAL OF PHARMACEUTICAL RESEARCH INTERNATIONAL. 2021;33(31A):1–8.
22. Kumar CA, Mahakalkar C, Yeola (Pate) M. Assessment of Risk Factors in the Causation & Outcomes of Diabetic Foot. JOURNAL OF PHARMACEUTICAL RESEARCH INTERNATIONAL. 2021;33(37A):264–70.
23. Muley PA, Biswas DA, Taksande A. A Pilot Study Investigating the effect of Glycemic Control on Electrodiagnostic Parameters in Type II Diabetic Patients. JOURNAL OF PHARMACEUTICAL RESEARCH INTERNATIONAL. 2021;33(32B):146–53.