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Original Research Article Epidemiology and phenotype variation in young diabetes patients

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ARTICLE INFO	A B S T R A C T		
Article history: Received 10-09-2020 Accepted 23-09-2020 Available online 28-10-2020	 Introduction: More and more people are diagnosed with type 2 diabetes at a younger age nowadays. It is need of an hour to study epidemiology and phenotype variations in this group. Aims: To study phenotype among the young diabetes population. Materials and Methods: We retrospectively analysed data of all type 2 diabetes patients attending OPD from Jan 2019 to march 2019. Total 106 patients attended OPD during this period. BMI, PBF (% BODY 		
<i>Keywords:</i> Diabetes in young phenotypes in diabetes risk factore of diabetes in young carbohydrates intake non HDL and young onset diabetes.	 FAT), VFI (Visceral fat index), Hba1c, Triglyceride, LDL and NON HDL, Total Calorie intake and % daily carbohydrate intake were reviewed for all 106 patients. All 106 subjects were divided in two groups based on their age; group A age ≤ 40 years (n=33), group B age > 40 years (n=73). Group B was further divided into group B1 (age 41-60 years) (n=58) and group B2 (age ≥ 61 year) (n=15). Average of BMI, Body fat analysis and biochemical parameters were compared between these two groups. Student's T test was used to calculate the p value for all parameters. Results: We analysed data of all 106 patients and average of BMI, PBF, VFI, HbA1c, TG, LDL, NON HDL, TOTAL CALORIES, % Carbohydrate was compared between Group A and Group B. Average TG, LDL, NON HDL and % daily carbohydrate intake were higher in group A as compared to total as well as group B. out of this all parameters NON HDL and % of daily carbohydrate intake was higher in group A as compared to group B [(NON HDL (p value 0.0412); % carbohydrate intake (p value 0.064)]. In sub analysis the difference was more significant in group B2 (NON HDL) p value 0.0118; % of carbohydrate intake (p value 0.0275). Conclusion: NON HDL level and % of daily carbohydrate intake are significantly associated with a young Type 2 diabetes population (≤ 40 years) as compared to the adult population particularly type 2 diabetes population with age ≥ 60 years. NON HDL cholesterol and % of daily carbohydrate intake can be more easy targets to reduce prevalence of type 2 diabetes in the younger population. However, it may require further research in mass population. © 2020 Published by Innovative Publication. This is an open access article under the CC BY-NC license (https://creativecommons.org/licenses/by-nc/4.0/) 		

1. Introduction

Type- 2 diabetes was considered as a disease of the middle or old aged group so far. Though this age group holds a higher risk of diabetes than younger adults, more and more people are diagnosed with type 2 diabetes at a younger age. Type2 diabetes has already been reported in children across the whole world. Among youth with diabetes, the proportion of type 2 diabetes among non-Hispanic whites is 5.5%, while the proportion of type 2 diabetes among non-Hispanic blacks is 37.6%. For American Indian/Alaskan Natives, the proportion of type 2 diabetes is 80.0%. The proportion of type-2 diabetes in Asian or Pacific Islander and Hispanic youth is 34.2 and 35.2%, respectively. Additionally, among youth < 20 years of age, prevalence increases with age. There were an estimated 20,262 youth with type 2 diabetes in the USA in2009. Disease pathogenesis is driven by both environmental and genetic factors, with elevated hepatic glucose production, impaired insulin secretion, and insulin resistance acting as key drivers in the development of disease. Altered glucose-insulin homeostasis is typically

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associated with obesity and most, although not all, of those with type 2 diabetes are obese at disease onset. While disease onset is primarily in adults, the increase in prevalence of obesity among youth has resulted in an increasing incidence of onset of type 2 diabetes in youth.¹ In India, cereals account for half of the plate. Apart from this, children have more inclination on western diet patterns and Junk food. Asian population is already genetically prone to develop Type- 2 DM. On the top of this, a higher proportion of carbohydrate intake enhances this risk in early age.

1.1. Purpose of review

Early onset of diabetes also brings microvascular and macrovascular complications in young age, which will lead to higher morbidity and mortality at the height of their productive age. It also impacts the health care system throughout the world. Early onset of type 2 diabetes is an important factor which impacts the future burden of the disease. For this reason, we analysed the data of our OPD patients to see the association of various epidemiological and phenotypic parameters in young onset of type 2 diabetes

1.2. Inclusion criteria

- 1. People with type-2 diabetes and Pre-diabetes.
- 1.3. Exclusion criteria
 - 1. Patients with type-1 diabetes,
 - 2. Gestational diabetes,
 - 3. Cirrhosis of liver,
 - 4. Chronic kidney disease.

(As Type -1 has different Pathophysiology. Phenotype study for GDM, cirrhosis of liver and chronic kidney disease was difficult.)

2. Materials and Methods

We retrospectively analysed data of all type 2 diabetes patients attending OPD from Jan 2019 to march 2019 from our electronic medical record system (HealthPlix). The patients with recorded anthropometric data and biochemical parameters along with 24 hour diet recall were included for the analysis. Anthropometric measurements [BMI, PBF (% BODY FAT), VFI (Visceral fat index)] were measured by bioelectrical impedance method (IN BODY 270). Biochemical parameters were recorded such as HbA1c (HPLC method BIO RAD D10) and lipid profile (AGAPPE MISPAace). For diet analysis, 24 hours dietrecall was taken and IFCT (Indian food composition tables by K.venkaiah et al.) was referred for the calculation of nutritive value. Total Calorie intake and percentage of daily carbohydrate intake were calculated and recorded. There were a total 106 patients fulfilling the inclusion criteria. All 106 subjects were divided in two groups based on

their age: group A age \leq 40 years (n=33), group B age > 40 years (n=73). Group B was further divided into group B1 (age 41-60 years) (n=58) and group B2 (age \geq 61 year) (n=15). Average of BMI, Body fat analysis and biochemical parameters were compared between these two groups. Student's T test was used to calculate the p value for all parameters.

3. Results

We analysed data of all 106 patients and average of BMI, PBF, VFI, HbA1c, TG, LDL, NON HDL, TOTAL CALORIES and percentage of carbohydrate was compared between Group A and Group B. Average TG, LDL, NON HDL and percentage of daily carbohydrate intake were higher in group A as compared to total as well as group B. out of this all parameters NON HDL and % of daily carbohydrate intake was higher in group A as compared to group B [(NON HDL (p value 0.0412); % carbohydrate intake (p value 0.064)]. In sub analysis the difference was more significant against group B2 (NON HDL p value 0.0118; percentage of carbohydrate intake p value 0.0275).

4. Discussion

Type 2 diabetes is the major contributor of morbidity and mortality in society. The grip of diabetes is stronger in Asian Indian. In the current scenario, the situation is becoming worse even in the young population, at very early age young populations are diagnosed with type 2 diabetes and quality of life compromised owing to early introduction of macrovascular and microvascular complications. To halt this progression and delay the onset of the disease in the next generation, it is necessary to see all attributed parameters very closely.

4.1. Relationship between carbohydrate intake and diabetes in youth

In our study, we found that the percentage of carbohydrate intake is significantly associated with diabetes in the young population. There is a lot of literature supporting carbohydrate intake in diabetes of youth. A cohort study by Rennan Feng et al., involving 4,154 north chinese participants over 4.2 years found that high carbohydrate intake and carbohydrate intake from starchy foods both were strongly associated with the pathogenesis of hyperlipidemia and metabolic syndrome. In their study, they kept the carbohydrate cut off value 220 gm in a day. Rice, roots vegetables, refined wheat and their products were included for carbohydrate sources from starchy food. During the 4.2year follow-up visceral adiposity index (VAI) (P = 0.05) and TG (P = 0.04) increased and HDL-C decreased (P= 0.01) in all four quartiles of Carb-S. There were no changes in other anthropometric (BMI, WC, SBP, or DBP) or biochemical (fasting blood glucose [FBG], 2-hour post-

	Total	Group A	Group B	Group B1	Group B2
BMI	28.06	28	28.16	27.90	27.98
PBF	28.67	29	28.60	28.36	29.53
VFI	12.65	12	12.91	12.34	15.15
HBA1C	8.91	09	8.83	8.86	8.70
TG	231.77	248	224.59	231.03	199.70
LDL	98.29	106	95	99.15	79.59
NON HDL	138.54	152	132.55	136.89	115.79
T. CALORIE	1253.66	1282	1240.74	1205.78	1375.89
% CHO	54.08	56	53.17	53.79	50.75

Table 1: Average parameters of all groups.

	Group A Vs all (p value)	Group A Vs B (p Value)	Group A Vs B1 (p value)	Group A Vs B2 (p value)
BMI	0.8460	0.7848	0.9599	0.5156
PBF	0.9430	0.9196	0.8413	0.8197
VFI	0.4960	0.3655	0.7768	0.1479
HBA1C	0.7103	0.6034	0.6631	0.5637
TG	0.5177	0.3939	0.5754	0.1250
LDL	0.3405	0.1971	0.4487	0.0165
NON HDL	0.1173	0.0412	0.1405	0.0118
T. CALORIE	0.7039	0.5935	0.3478	0.3104
% CHO	0.1774	0.0640	0.1588	0.0275

load blood glucose [2h-PG], fasting insulin [F-insulin], 2-hour post-load insulin [P-insulin], or insulin resistance [HOMA-IR], TC).² The mechanism of onset of Diabetes and High carbohydrate intake is well explained by twin cycle hypothesis.Higher percentage of carbohydrate intake promotes the denovo lipogenesis pathway that handles carbohydrates which cannot be stored as glycogen and promotes fat accumulation around the liver. For the storage of glycogen & fat accumulation, insulin is required. In insulin resistance (as per genes, degree of obesity & lifestyle), a higher amount of insulin is produced, which makes this fat accumulation more extensive. Consequently, hepatic glucose production does not respond to insulin due to accumulation of fat around the liver. Over many years, a small increase in fasting plasma glucose leads to increased basal insulin secretion to maintain euglycemia. The consequent hyperinsulinemia further increases the conversion of excess calories into liver fat. A vicious cycle of hyperinsulinemia and blunted suppression of hepatic glucose production is thereby established. Fatty liver leads to increased export of VLDLs triglyceride into the circulation (and thus excess ectopic fat in the blood), which increases fat delivery to all tissues, including the pancreatic islets. This process is further stimulated by increased plasma glucose concentrations. Excess fatty acid availability in the pancreatic islets would be expected to impair the acute insulin secretion in response to ingested food, and at a certain level of fatty acid exposure, postprandial hyperglycemia supervenes. The hyperglycaemia further

increases insulin secretion rates, with consequent increase of hepatic lipogenesis, spinning the liver cycle faster and driving on the pancreas cycle. Eventually the fatty acid Figure 1. Twin Cycle hypothesis and glucose inhibitory effects on the islets reach a trigger level, leading to β -cell failure and a fairly sudden onset of clinical diabetes.

4.2. LIPID profile and diabetes in young

Metabolic syndrome is the primary road before the turn on diabetes road. In our study, NON HDL was significantly associated with a young diabetes population. while other parameters were not associated significantly. In current OPD data, p value for all groups (group A, group B, group B1, and group B2) were significant (GROUP A Vs all (p value 0.1173), GROUP A Vs B (p Value 0.0412) GROUP A Vs B2 (p value0.0118). Hence, NON-HDL should be considered to mitigate CV risk from the initial stage. It should be a target parameter for therapeutic treatment along with LDL and Triglyceride. It may require further mass population study.

In a cross sectional study involving 2293 (842 men & 1451 women) Bangladeshi participants with diabetes & prediabetes, Bishwajit Bhowmik et al. revealed that high total cholesterol, high TG & low HDL were significantly associated with the degree of glucose intolerance. Another Tehran lipid and glucose study by Pegah Khaloo et al. involving 5474 people without diabetes on median follow up over 8.9 years revealed significant associations of 3-year changes in all lipid parameters (TC, Ln-TG, HDL-C,

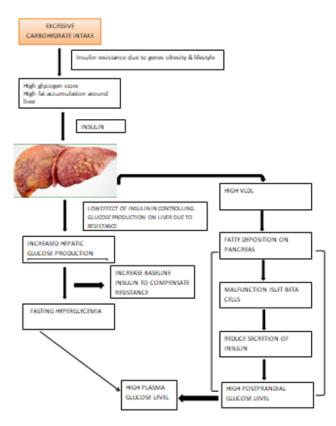


Fig. 1: Twin Cycle hypothesis

LDL-C, non-HDL-C, Ln-TG/HDL-C and TC/HDL-C) with incident T2DM. 3

Insulin resistance has a crucial role in pathogenesis of dyslipidemia even before the onset of hyperglycemia. The free fatty acid flows more from adipose tissues and muscle uptake of free fatty acid is impaired due to impaired insulin mediated pathway. Subsequently, free fatty acids deposit in the form of Triglyceride around the muscle, liver, heart and pancreas. Insulin resistance also enhances hepatic Lipase activity, which is responsible for hydrolysis of phospholipids from LDL & HDL. Consequently, LDL particles become more small and dense as well as HDL $_{b2}$ particles also decrease in plasma.

In diabetes or pre-diabetes, hypertriglyceridemia accompanied by low HDL make it atherogenic dyslipidemia. LDL can be normal or elevated from baseline, but their composition is altered. The cholesterolester content of LDL decreases, whereas the TG content of LDL increases by the activity of CETP. However, the increased TG content within the LDL is hydrolysed by hepatic lipase, which leads to the formation of small, dense LDL particles. Small dense LDL has comparatively low affinity to LDL receptors which slows down its metabolism with a five day residence time. This leads to Greater transportation of LDL to subendothelial space, increased binding with arterial wall proteoglycan, more oxidative changes. In this way, small dense LDL particles may cause more damage to arterial walls associated with diabetes dyslipidemia.⁴

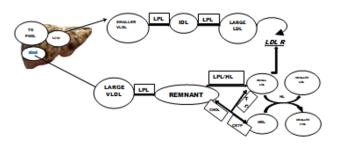


Fig. 2: The relation of altered metabolism of triglyceride-rich lipoproteins to the development of an atherogenic lipoprotein phenotype. (CETP, cholesterol ester transfer protein; Chol, cholesterol; HL, hepatic lipase; LDLR,LDL receptor; LPL, lipoprotein lipase; TG, triglyceride)

HDL has a direct cardio protective effect. It is renowned for its anti-oxidative and anti- inflammatory effects. It maintains the cellular cholesterol flows. Hyperinsulinemia and hypertriglyceridemia independently associated with low level HDL. There are multiple reasons for low levels of HDL in insulin resistance and Type 2DM. one of them, Increase transfer of cholesterol ester to triglyceride rich Lipoprotein and reciprocal transfer of triglyceride to HDL, which leads to formation of triglyceride rich HDL that is hydrolysed by the liver resulting in low levels of HDL in the plasma. In type- 2 diabetes, there is typically reduction in HDL $_{2b}$ subspecies and increase in HDL $_{3A}$ and HDL $_{3B}$ subspecies, which are smaller and dense in size.⁴

NON-HDL and DIABETES – NON-HDL is the stronger predictor of coronary artery disease than LDL in patients with diabetes. It can be obtained in an inexpensive way or just by calculation. It is measured by deducting HDL from Total Cholesterol. It includes all atherogenic markers, Apolipoprotein B, which is the carrier of LDL, IDL, and VLDL, while LDL only can be a misleading marker due to TGRLP. In patients with diabetes, high triglyceride with high or normal LDL is quite common. So LDL may not be able to identify the risk for CVD. Moreover, NON-HDL is reliable to measure even in non- fasting state. As per NCEP guidelines, the target for LDL and NON-HDL should be <100mg/dl and < 130 mg/dl respectively. The person with severe risk of CVD, target for LDL and NON-HDL should be focused on < 70 mg/dl and < 100 mg/dl.⁵

A population based study among Iranian adults also demonstrated a significant association between metabolic syndrome and NON-HDL. idaris et al. also demonstrated Significant discordance between LDL and NON HDL with high triglyceride or metabolic syndrome and high CV risk. Despite achieving LDL target, CV risk remains elevated.⁶ Hence, treatment for both LDL and NON-HDL is equally crucial to reduce the CV risk in patients with diabetes.

4.3. FAT distribution and phenotype

Body composition varies as per age, sex and ethnicity. Male and female have different body composition in different phases of life. In puberty, men have more muscle mass and low body fat due to the mounting level of Testosterone.

In our clinical data, BMI, PBF and VF index were directly correlated with diabetes in young people but not statistically significant. thus health hazards cannot be neglected owing to body composition. There are many studies that have revealed the role of body composition in the pathogenesis of Type-2 diabetes and dyslipidemia. Mass study needs to be done, clinical data is not sufficient to prove this point.

In a study on 3367 chinese adults (2307 male and 1060 female) yongchuan chen et al., found the predictive relationship between body composition indicators (waist-to-hip ratio, body fat percentage, and visceral fat area) and risk of type 2 diabetes mellitus.⁴

The MONICA/KORA Augsburg Cohort Study on 3055 men and 2957 women aged 35–74 year without diabetes has shown both overall and abdominal adiposity are strongly related to the development of type 2 diabetes. WC should be measured in addition to BMI to assess the risk of type2 diabetes in both sexes.⁷

Excessive adipose tissues release free fatty acids in the form of triglycerides. These fatty metabolites deposit on the muscles, liver and pancreas and impair the insulin dependent metabolic pathway, leading to hyperglycemia and dyslipidemia.

5. Conclusion

The percentage of daily CHO intake and NON HDL should be focused in primary screening on preventive basis as well as for patients with type 2 diabetes, so that future risk of complication can be halted. NON HDL cholesterol and percentage of daily carbohydrate intake can be an easier target to reduce prevalence of type 2 diabetes in the younger population. However, it may require further research in mass population.

6. Source of Funding

None.

7. Conflict of Interest

None.

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