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Estimation of Cardiovascular Risk Factors & Their Relative Impact in Diabetic Mellitus-2 Adult Patients' in Mnazi Mmoja Hospital - Zanzibar

Mohammed S. Juma[1], Chukwuma J. Okafor[2*], F. A. Dida[3], Said Ali Yusuf[4] and Salum S. Salum[2]

[1]Department of Allied Health Sciences, State University of Zanzibar, Tanzania.
[2]Department of Pathology and Biochemistry, State University of Zanzibar, Tanzania.
[3]School of Medicine, Muhimbili University of Health and Allied Sciences, Tanzania.
[4]Department of Surgery, State University of Zanzibar, Tanzania.

Authors' contributions

This work was carried out in collaboration among all authors. Authors MSJ and CJO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors FAD, SAY and SSS managed the analyses of the study including the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Diabetes is characterized by chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism. We aimed to estimate the cardiovascular risk factors and their correlation with type 2 diabetes mellitus (T2DM) in Zanzibar (Mnazi MMoja Hospital) hypothesizing that early detection and treatment of lipid abnormalities can minimize the risk for atherogenic cardiovascular disorders and cerebrovascular accident in patients with T2DM.

Methods: The study populations were those patients who presented themselves at Mnazi Mmoja hospital with T2DM, and who are within the age bracket of 18 to 45 years. Fasting blood glucose (FBG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and triglyceride (TG) levels were evaluated. Pearson's correlation studies were performed between the variables of blood glucose and serum lipid profiles and also within the lipid profile parameters.

**Corresponding author: Email: chukwuma.okafor@suza.ac.tz, chumario2k@yahoo.com;*

Results: TC, TG, LDL-C mean levels were significantly higher in diabetics compared with the control subjects p< 0.05. The HDL-C was however lower in diabetics compared with the controls. Also, the mean FBG, TC, TG, and LDL-C were significantly higher in female diabetic subjects compared to the male counterparts p< 0.05. A positive correlation was observed between FBG and TC, TG and LDL-C (r=0.643 p=0.0021; r=0.679, p=0.0001; r=0.534, p=0.0091 respectively) while HDL-C showed a negative correlation (r= -0.799, p= 0.0021). TC also showed a positive correlation with TG and LDL-C (r=0.590, p=0.0021; r= 0.628, p=0.0001) and negative correlation with HDL-C (r=-0.670, p=0.0041).

Conclusion: There is an influence of gender on cardiovascular disease risk factors with more of the females seriously at risk. Measurement of serum lipid profile should be introduced to the management plan of diabetes mellitus. There is an urgent need for the establishment of regional and national training courses for diabetic educators and also the creation of new evidence-based management plan for diabetics in Zanzibar for a better healthcare.

Keywords: Type 2 diabetes mellitus; total cholesterol; low density lipoprotein; high density lipoprotein; triglyceride.

1. INTRODUCTION

Diabetes is one of the leading causes of death in developed countries and accounts for approximately one-third of deaths in developing ones [1]. The increase is related to different socio-economic factors suchas industrialization, urbanization, economic development, and globalization [2]. Zanzibar has many contacts with West Africa and the eastern part have maintained close links with countries who had undergone ethnic absorption of immigrant Arabs during the times of Islamizing and had culturally become Arabised [3]. Regular internal migration in a different part of Zanzibar has taken place fromthe rural areas and small towns to big cities, particularly to the capital Zanzibar town [4]. In recentyears permanent external migration has also occurred. These social and economic advances were accompanied by changes to modem lifestyle characterized by higher caloric intake and less physical activity and the emergence of non-communicable diseases such as diabetes mellitus a major health problem causing high morbidity and mortality [1]. Strong evidence now shows that physical inactivity increases the risk of many adverse health conditions, including major non-communicable diseases such as coronary heart disease and type 2 diabetes, which shortens life expectancy, and because much of the world's population is inactive, this link presents a major public health issue [5]. Cardiovascular disease (CVD) is a leading cause of death among adults with T2DM. Specifically, among those with T2DM in the US, CVD accounts for 44% of mortality [6]. T2DM rates have doubled over the past 20 years and CVD risk increases two to fourfold with a diagnosis of T2DM [7]. Atherogenic dyslipidemia, a known risk factor for CVD is highly prevalent in patients with T2DM [8,9] and tightly linked to high-carbohydrate diets [10].

The condition is characterized by increased triglycerides, decreased high-density lipoprotein cholesterol concentration (HDL-C) and increased small low-density lipoprotein particle number (small LDL-P) [9]. Elevated concentrations of small LDL particularly in patients with insulin resistance and T2DM are often associated with increased total LDL particle number (LDL-P) and ApoB [11]. Previous studies of carbohydrate restriction of up to 1-year found a consistent decrease in triglycerides and an increase in HDL-C, while LDL-C slightly increased or decreased [10,12]. Inflammation, as assessed by elevated high- sensitivity C-reactive protein (hs-CRP) or white blood cell count (WBC), is an independent CVD risk factor and is involved in all stages of atherogenesis [13]. Inflammation is often observed in T2DM concurrent with atherogenic dyslipidemia and represents an additional CVD risk even in individuals with low to normal LDL-C [14]. Hypertension is an additive risk factor in this patient population. Tighter blood pressure control has been associated with a reduction in the risk of deaths related to diabetes. This included decreased CVD, stroke, and microvascular complications [15]. The pathogenesis of obesity includes the balance between calories consumed and energy expenditure followed by the maintenance of body weight [16]. It is not only about how excess body fat is acquired but also about how this excess is biologically assimilated [17]. Even though the development of obesity is multifactorial with genetic, environmental, and lifestyle causes, it is extensively associated with comorbidities such as cardiovascular diseases,

diabetes, hypertension, cancer, and sleep disorders [16]. It can be estimated from the hospital record that the number of diabetic patients is increasing in all socioeconomic classes. Type 2 diabetes mellitus accounts for almost 75% of all diabetic patients attending the Mnazi Mmoja hospital diabetic clinic in Zanzibar [18]. Non Type 1 diabetes mellitus is a common disease with severe clinical course and most patients are poorly controlled and exhibit a high prevalence of acute and chronic complications [19]. Poor metabolic control of Zanzibar diabetic patients was attributed to poor compliance and poor knowledge of diabetes coupled with the problems associated with injection and drug availability. Also, the ability of patients with diabetes to understand and manage their diseases in ordinary daily life is most important for successful therapy [20]. The World Health Organization (WHO) estimated that the number of people with diabetes worldwide in the year 2000 was 177 million, this will increase to at least 336 million by the year 2030 and with a prevalence of around 5.4%. The major concerns are that much of this increase will be in developing countries (approximately 75% of all persons) [21]. Chronic hyperglycemia is associated with the long-term consequences of diabetes that include damage and dysfunction of the cardiovascular system, eyes, kidneys, and nerves. The complications of diabetes are often divided into two groups: microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (ischaemic heart disease, stroke, peripheral vascular disease) [22]. Heart attack and stroke are the major killers in all parts of the world. About 80% of premature deaths from these causes could be avoided by controlling the main risk factors such as physical inactivity, unhealthy diet, and tobacco use, obesity, high LDL or low HDL cholesterol levels, high triglyceride levels, high blood pressure, and age [23].

International guidelines on cardiovascular disease (CVD) prevention include lifestyle counseling to improve unhealthy lifestyle habits to reduce cardiovascular risk. These guidelines emphasize that the highest clinical priority for prevention should be directed towards patients at high cardiovascular risk, such as those with type 2 diabetes mellitus (T2DM) and impaired glucose tolerance (IGT) [23,24]. Scientific evaluations of programs to improve lifestyle habits are scarce, despite the knowledge that healthy lifestyle habits are important for reducing cardiovascular risk [25]. Despite the above studies, there is still a paucity of information on diabetes in Zanzibar. Also, lipid testing rates among individuals with diabetes have been far less than ideal. The available knowledge has prompted us to conduct the current diabetes research, to contribute to the overall improvement of diabetes care in Zanzibar.

2. MATERIALS AND METHODS

2.1 Study Design and Site

This was a hospital-based cross-sectional study conducted at the diabetic clinic of the Mnazi Mmoja Hospital (MMH),. MMH is the main referral hospital in Zanzibar. The hospital is located in Stone Town, the historic center of Zanzibar City. It has an outpatient clinic, specialized clinics as well as several wards for in-patient services. Although termed as a referral hospital, basic outpatient services are also provided to the nearby communities.

2.2 Methodology

A total of one hundred and sixty-one T2DM patients made up of eighty-five (85) males and seventy-six (76) females were recruited for the work using a convenient sampling methodology. All patients who presented themselves with a history of T2DM were screened first to confirm their status. Subjects were all Tanzanians within the age bracket of 18 and 45 years randomly selected. Inclusion criteria were all T2DM patients and it was purely voluntary. We excluded Patients with Type 1 Diabetes Mellitus (T1DM), Patients with pregnancy, Patients with known malignancy, Patients who had undergone any invasive procedure or surgery in the last three months, and Patients with communicable diseases. The control samples comprised of 50 non-diabetic subjects made up of twenty-one (21) males and twenty-nine (29) females who were within the same age brackets as the patients.

2.3 Sample Collection

Ten milliliters of fasting venous blood samples were collected from each subject. The samples were divided into two parts in plain tubes and fluoride oxalate bottles. The samples were collected in the morning between 8 am and 9 am and those in the plain bottles were allowed to clot, centrifuged, separated and the serum stored at -4^{o}C until analyzed. The samples in the fluoride oxalate bottles meant for the glucose

estimation were centrifuged and the plasma separated and analyzed within 30 minutes.

2.4 Laboratory Analysis

2.4.1 Laboratory procedure

All patients with T2DM and all non-diabetic controls were screened for Lipid profiles including (TG, TC, LDL-C, HDL-C) and Plasma Glucose levels using MINDRAY BS 200 Chemistry Analyzer machine conducted at Clinical Chemistry Laboratory of the Mnazi Mmoja Hospital Zanzibar.

2.4.2 Determination of total cholesterol

Principle: Cholesterol esters are enzymatically hydrolyzed by cholesterol esterase to cholesterol and free fatty acids. Free cholesterol, including that originally present, is then oxidized by cholesterol oxidase to cholest-4-ene-3-one and hydrogen peroxide. The hydrogen peroxide combines with hydroxybenzoic acid (HBA) and 4-aminoantipyrine to form a chromophore (quinoneimine dye) which is quantitated at 500 nm.

2.4.3 Determination of triglyceride

Principle: Triglycerides are enzymatically hydrolyzed by lipase to free fatty acids and glycerol. The glycerol is phosphorylated by adenosine triphosphate (ATP) with glycerol kinase (GK) to produce glycerol-3-phosphate and adenosine diphosphate (ADP) which is then oxidized by Glycerol-3-phosphate oxidase (GPO) producing Dihydroxyacetone phosphate and hydrogen peroxide (H_2O_2). In a color reaction catalyzed by peroxidase, H_2O_2 reacts with 4-aminoantipyrine (4-AAP) and 4-chlorophenol (4-CP) to produce a red-colored dye. The absorbance of this dye is proportional to the concentration of triglyceride present in the sample.

2.4.4 Determination of High Density Lipoprotein Cholesterol (HDL-C)

Principle: The chylomicrons, VLDL, and LDL cholesterol of the serum are precipitated by phosphotungstic acid and magnesium ions. After centrifugation, the HDL-C left in the supernatant is then measured by the enzymatic cholesterol method.

2.4.5 Determination of Low Density Lipoprotein Cholesterol (LDL-C)

This was computed using the Friedewald calculation [26].

LDL = Total Chol - (Triglyceride / 5) – HDL

2.4.6 Determination of Fasting Plasma Glucose (FPG)

Principle: Glucose oxidase (GOD) catalysis the oxidation glucose to give hydrogen peroxide (H_20_2) and gluconic acid. In the presence of enzyme peroxidase (POD) the hydrogen peroxide is broken down and oxygen released reacts with 4 aminophezone (4 amino antipyrine) and phenol to give a pink colour which is proportional to the concentration of glucose present

2.4.7 Body mass index

Body mass index (BMI) was calculated using the formula weight (kg)/ height squared (m^2).

2.5 Statistical Analysis

Data were analyzed using the Statistical Package of Science and Social Science (SPSS) software version 15 and Epin info. Independent Students' 't' test was used to compare groups. Pearson's correlation coefficient determination was performed to evaluate the degree of association. Values were expressed as means ± standard deviation (SD). Probability values of less or equal to 0.05 were accepted to be significant ($P \leq 0.05$).

3. RESULTS

Table 1 shows the Essential Physical Data of Diabetic Patients and Control Subjects (Mean ± SD). There were statistically significant differences when the age, weight, and BMI of the diabetic patients were compared with the nondiabetics $p< 0.05$.

Table 2 shows the levels of Glucose and Serum Lipid Profile in Diabetic Patients and Control Subjects. There were statistically significant differences between the levels of Plasma Glucose, TG, TC, LDL-C and HDL-C in diabetic patients and the nondiabetic controls $p< 0.01$.

Table 3 shows the mean levels of Plasma Glucose, TG, TC, LDL-C, and HDL-C in female diabetics compared to the male diabetics. There were statistically significant differences between the females' Plasma Glucose, TG, TC, LDL-C compared to their male counterparts. ($p<0.05$).

4. DISCUSSION

Cardiovascular disease (CVD) is a leading cause of death among adults with T2DM. Compared

with individuals without diabetes, patients with T2DM have a considerably higher risk of cardiovascular morbidity and mortality and are disproportionately affected by cardiovascular disease. Most of this excess risk is associated with an augmented prevalence of well-known risk factors such as hypertension, dyslipidaemia, and obesity in these patients [27]. Persistent dyslipidaemia shown in our work was collaborated by some other workers [28,29]. The characteristic features of diabetic dyslipidemia are high plasma triglyceride concentration, reduced HDL-C concentration, and increased concentration of LDL-C particles. These changes are caused by increased free fatty acid flux secondary to insulin resistance and aggravated by increased inflammatory adipokines [30]. All of the processes involved in atherogenesis can be exacerbated by insulin resistance and/or metabolic syndrome. Hypertriglyceridemia is a strong predictor of coronary heart disease [31]. In diabetes, blood glucose is not utilized by tissue resulting in hyperglycemia. The fatty acids from adipose tissue are mobilized for energy purposes and excess fatty acid is accumulated in the liver, which is converted to triglyceride [32]. Our work recorded an inverse relationship between serum levels of HDL-C and TG in diabetic patients, with low serum HDL-C levels possibly representing an independent risk factor for cardiovascular disease. Small, dense, LDL-C particles are also highly atherogenic as they are more likely to form oxidized LDL and are less readily cleared [31]. Elevated TG levels are a common dyslipidemic feature accompanying type 2 diabetes and pre-diabetic states [33]. A high fasting TG level is one of five accepted criteria for defining individuals at high risk for cardiovascular disease and type 2 diabetes, arguably termed the "metabolic syndrome" [34,35]. Some evidence suggests that fasting TG levels can aid in predicting future type 2 diabetes [36]. However, this was shown mainly when triglyceride levels were combined with additional clinical parameters, such as BMI, blood pressure, and other classic risk factors for cardiovascular disease, or with "high-normal" fasting plasma glucose levels [37]. The level of circulating triglycerides is highly influenced by the fed-fasted state, insulin sensitivity, and lifestyle factors such as diet and physical activity [38,33]. These make triglyceride levels a highly sensitive lifestyle biomarker at a given time point.

Type 2 diabetes in this work seems to increase the risk of coronary heart disease (CHD) more markedly in females than in males. Although the mechanism is incompletely understood several explanations can be offered. First, adverse changes induced by type 2 diabetes in some cardiovascular risk factors, such as HDL-C, TG, LDL-C particle size, and blood pressure, are more pronounced in female gender than in males [39,40]. Our work recorded significant increases in Plasma Glucose, TC, TG, and LDL-C among our female patients compared to their male counterparts. Second, gender may alter the effect of some cardiovascular risk factors for CHD in diabetic subjects, thereby making the female patient have a stronger risk effect. Third, diabetes in the female gender may interfere more with protective mechanisms in the vascular wall and thereby lead to enhanced atherogenesis and/or thrombogenesis [41]. Fourth, It might be related to different degrees of insulin resistance between the two sexes or a direct effect of the hormonal status on one or more enzymes implicated in lipoprotein metabolism [42,43]. The fifth may be the increased testosterone levels which are negatively associated with TC, LDL-C, and TG levels [44]. Other workers found out that as the testosterone/estradiol ratio decreased, LDL-C decreased while HDL-C levels increased [45].

The pattern of correlation between the glucose levels and lipid profiles showed that hyperglycemia is closely associated with dyslipidaemia. This also points to the significance of control of blood glucose in diabetic patients. Also, correlation studies within the lipid groups showed interesting results. It indicates the need for control of plasma cholesterol and triglyceride levels to have lower LDL levels and elevated HDL levels. Other workers collaborated with our findings [46]. The various lipids and lipoproteins are closely correlated with each other, and control of one influences the others.

Table 1. The essential physical data of diabetic patients and control subjects (Mean ± SD)

Characteristics	Diabetic patients	Control subjects	t-statistics	p-value
Age (YR)	51.20 ± 11.203	45.72±11.169	2.975	0.012
Weight (Kg)	68.02± 13.429	60.02± 13.181	3.045	0.011
Height (Cm)	160.82 ±8.573	163.28±9.450	1.236	0.360
BMI (Kg/m^2)	26.915±4.05637	22.324±3.90677	2.766	0.041

Table 2. The levels of Glucose and Serum Lipid Profile in Diabetic Patients and Control Subjects

Measurement (mg/dL)	Diabetic patients (Mean± SD) N=161	Non-Diabetic Controls (Mean ±SD) N=50	t-statistics	pvalue
FPG	169.000±63.9692	81.00±16.247	9.617	0.0001
TG	137.915±59.0534	111.040±29.8395	3.094	0.0022
TC	176.807±36.0918	144.912±34.1804	5.526	0.0001
LDL-C	151.224±64.0362	117.714±26.2476	4.848	0.0008
HDL-C	44.80±15.7758	56.894±10.5376	5.076	0.0001

Table 3. The mean levels of Plasma Glucose, TG, TC, LDL-C, and HDL-C in female diabetics compared to the male diabetics

Measurement mg/dl	Female diabetic patients (Mean ± SD) N=85	Male diabetic patients (Mean ± SD) N=76	t-statistics	pvalue
FPG	174.280±48.00	153.720±59.2818	-2.429	0.0163
TG	141.281±59.4943	116.214±26.5127	3.010	0.0049
TC	190.118±38.4228	173.496±33.6621	2.904	0.0042
LDL-C	159.482±62.40581	132.966±65.2019	2.635	0.0092
HDL-C	43.746±15.1988	45.856±16.4182	0.847	0.3984

Table 4. Levels of correlation between Plasma Glucose and Lipid Profile indices in diabetic subjects. There were positive correlations between Plasma Glucose and TC, TG, and LDL-C and negative correlation with HDL-C (p< 0.01)

Variables	FPG (r)	p-value
TC	0.643	(0.0021)**
TG	0.679	(0.0001)**
LDL-C	0.534	0.0091)**
HDL-C	-0.799	(0.0021)**

*** Correlation is significant at p< 0.01 levels*

Table 5. Levels of correlation between Cholesterol and other Lipid Profile indices in diabetic subjects. There were positive correlations between Chol and TG, LDL and negative correlation with HDL (p< 0.01)

Variables	TC (r)	p-value
TG	0.590	(0.0021)**
LDL-C	0.628	(0.0001)**
HDL-C	-0.670	0.0041)**

*** Correlation is significant at p< 0.01 levels*

5. CONCLUSION

Dyslipidaemia is a serious cardiovascular risk factor even among young diabetics. The pattern of the risk factors is highly influenced by gender with more of the females seriously at risk of cardiovascular disease. Early measurement of blood glucose as well as serum lipid profiles should be introduced to the management plan of diabetes mellitus. There is therefore an urgent need for the establishment of regional and national training courses for diabetic educators and also the creation of a new evidence-based management plan for diabetics in Zanzibar for better healthcare.

CONSENT

Informed consent of the subjects was gotten through the aid of a well-structured questionnaire.

ETHICAL APPROVAL

Ethical approval was obtained from the Muhimbili University of Health and Allied Sciences

(MUHAS) Senate Research and Publication Committee and research permission from the Ethical Committee of the Ministry of Health Zanzibar.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Keller A. Food and diseases in zanzibar eating habits and practices in relation to the," Les Cah. d'Afrique l'Est / East African Rev. 2019;45:87–115.
2. Shao ER. Lipid profile of type 2 diabetic patients at a Tertiary Hospital in Tanzania: Cross Sectional Study, J. Endocrinol. Diabetes. 2017;4(1):1–6.
   DOI: 10.15226/2374-6890/4/1/00170
3. Ghazal AN. Islamic reform and Arab nationalism: Expanding the crescent from the Mediterranean to the Indian Ocean (1880s-1930s); 2010.
4. Kotlewski DC, Dudzińska-Jarmolińska A. Artificial islands as a manifestation of glocalisation, Kwart. Nauk o Przedsiębiorstwie, 2017.
   DOI: 10.5604/01.3001.0010.0146
5. Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT. Effect of physical inactivity on major non-communicable diseases worldwide: An analysis of burden of disease and life expectancy. Lancet. 2012;380(9838):219–229.
   DOI: 10.1016/S0140-6736(12)61031-9
6. Gregg EW, Gu Q, Cheng YJ, Narayan KMV, Cowie CC. Mortality trends in men and women with diabetes, 1971 to 2000, Ann. Intern. Med. 2007;147(3):149–155.
   DOI:10.7326/0003-4819-147-3-200708070-00167
7. Martín-Timón I, Sevillano-Collantes C, Segura-Galindo A, Del Cañizo-Gómez FJ. Type 2 diabetes and cardiovascular disease: Have all risk factors the same strength?, World J. Diabetes. 2014;5(4): 444–470.
   DOI: 10.4239/wjd.v5.i4.444
8. Fruchart JC, et al. The residual risk reduction initiative: A call to action to reduce residual vascular risk in patients with dyslipidemia., Am. J. Cardiol. 2008; 102(10) Suppl:1K-34K.
   DOI: 10.1016/S0002-9149(08)01833-X.
9. Arca M, Pigna G, Favoccia C. Mechanisms of diabetic dyslipidemia: relevance for atherogenesis., Curr. Vasc. Pharmacol. 2012;10(6):684–686.
   DOI: 10.2174/157016112803520864
10. Volek JS, Fernandez ML, Feinman RD, Phinney SD. Dietary carbohydrate restriction induces a unique metabolic state positively affecting atherogenic dyslipidemia, fatty acid partitioning, and metabolic syndrome., Prog. Lipid Res. 2008;47(5):307–318
    DOI: 10.1016/j.plipres.2008.02.003
11. Sniderman AD, St-Pierre AC, Cantin B, GR Dagenais, JP Després, B Lamarche. Concordance/discordance between plasma apolipoprotein B levels and the cholesterol indexes of atherosclerotic risk., Am. J. Cardiol. 2003;91(10):1173–1177.
    DOI: 10.1016/s0002-9149(03)00262-5
12. Volek JS, et al. Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. Lipids. 2009;44(4):297–309.
    DOI: 10.1007/s11745-008-3274-2
13. Ridker PM, Buring JE, Shih J, Matias M, Hennekens CH. Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. Circulation. 1998;98(8): 731–733.
    DOI: 10.1161/01.cir.98.8.731
14. Sampson UK, Fazio S, Linton MF. Residual cardiovascular risk despite optimal LDL cholesterol reduction with statins: the evidence, etiology, and therapeutic challenges. Curr. Atheroscler. Rep. 2012;14(1):1–10.
    DOI: 10.1007/s11883-011-0219-7
15. Turner R, et al. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38," Br. Med. J. 1998;317(7160):703–713.
    DOI: 10.1136/bmj.317.7160.703
16. Pi-Sunyer FX. Pathogenesis of obesity, Drug Benefit Trends. 2000;12(SUPPL. A):28–33.
17. Whyte MB, Velusamy S, Aylwin SJB. Disease severity and staging of obesity: A rational approach to patient selection. Curr. Atheroscler. Rep. 2014;16(11):456.
    DOI: 10.1007/s11883-014-0456-7
18. Jasem D, Majaliwa ES, Ramaiya K, Najem S, Swai ABM, Ludvigsson J. Incidence, prevalence and clinical manifestations at onset of juvenile diabetes in Tanzania, Diabetes Res. Clin. Pract. 2019;156: 107817.

DOI: 10.1016/j.diabres.2019.107817
19. Mayige M, Kagaruki G, Ramaiya K, Swai A. Non communicable diseases in Tanzania: A call for urgent action, Tanzan. J. Health Res. 2011;13(5):SUPPL.ISS:1–11.
DOI: 10.4314/thrb.v13i5.7
20. EC Vogt, et al. Assessment of diabetic polyneuropathy in Zanzibar: Comparison between traditional methods and an automated point-of-care nerve conduction device," J. Clin. Transl. Endocrinol. 2017; 10:9–14.
DOI: 10.1016/j.jcte.2017.09.001
21. Peripheral D, Neuro C. IDF Clinical Practice Recommendations on the Diabetic Foot – 2017. Brussels Belgium: International Diabetes Federation IDF ©; 2017.
22. Amutha A, Pradeepa R, Chella KS, Anjana RM, Unnikrishnan R, Mohan V. Lipid profile in childhood-and youth-onset type 2 diabetes and their association with microvascular complications, J. Assoc. Physicians India. 2017;65:42–47.
23. Metrics GH. Global, regional and national age-sex specific mortality for 264 causes of death, 1980 – 2016: A systematic analysis for the Global Burden of Disease Study 2016;390:1980–2016.
DOI: 10.1016/S0140-6736(17)32152-9
24. Ekblom-bak E, Damberg M. Improved unhealthy lifestyle habits in patients with high cardiovascular risk: Results from a structured lifestyle programme in primary care," Ups. J. Med. Sci. 2019;124(2):94–104.
DOI: 10.1080/03009734.2019.1602088
25. Centre for Disease Control, "HIPAA privacy rule and public health. Guidance from CDC and the U. S. Department of Health and Human Services," US Natl. Libr. od Med. 2003;52(Suppl 1):78001766.
26. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge., Clin. Chem. 1972;18(6): 499–502.
27. Abdul-Ghani M, DeFronzo RA, Del Prato S, Chilton R, Singh R, Ryder REJ. Cardiovascular disease and type 2 diabetes: Has the dawn of a new era arrived?," Diabetes Care. 2017;40(7):813–820.
DOI: 10.2337/dc16-2736
28. Mishra K, Mawar A, Singh S, Kare PK. Study of lipid profile in type -2 diabetes mellitus patients in Agra city Study of lipid profile in type -2 diabetes mellitus patients in Agra city "," Indian Res. J. Genet. Biotech. 2013;5(11594):245–252.
29. Kolhar U, PP. Study of Lipid Profile in Type 2 Diabetes Mellitus Patients and its Correlation with HbA1c," Int. J. Adv. Med. 2017;4(6):1513–1516.
DOI:http://dx.doi.org/10.18203/2349-3933.ijam20174639 Study
30. Chehade JM, Gladysz M, Mooradian AD. Dyslipidemia in type 2 diabetes: prevalence, pathophysiology, and management.," Drugs. 2013;73(4):327–339.
DOI: 10.1007/s40265-013-0023-5
31. Nesto RW. Beyond low-density lipoprotein: addressing the atherogenic lipid triad in type 2 diabetes mellitus and the metabolic syndrome., Am. J. Cardiovasc. Drugs. 2005;5(6):379–387.
DOI: 10.2165/00129784-200505060-00005
32. Balagopal PB, et al. Nontraditional risk factors and biomarkers for cardiovascular disease: mechanistic, research, and clinical considerations for youth: A scientific statement from the American Heart Association. Circulation. 2011;123 (23):2749–2769
DOI: 10.1161/CIR.0b013e31821c7c64
33. Ginsberg HN. Nonpharmacologic management of low levels of high-density lipoprotein cholesterol.," Am. J. Cardiol. 2000;86(12A):41L-45L.
DOI: 10.1016/s0002-9149(00)01469-7
34. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III)., JAMA. 2001;285(19): 486–2497.
DOI: 10.1001/jama.285.19.2486
35. Kahn R, Buse J, Ferrannini E, Stern M. The metabolic syndrome: Time for a critical appraisal. Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes.," Diabetologia. 2005;48(9):1684–1699.
DOI: 10.1007/s00125-005-1876-2
36. IJ Perry, Wannamethee SG, Walker MK, Thomson AG, Whincup PH, Shaper AG. Prospective study of risk factors for development of non-insulin dependent

diabetes in middle aged British men. BMJ. 1995;310(6979):560–564.
DOI: 10.1136/bmj.310.6979.560

37. Tirosh A, et al. Normal fasting plasma glucose levels and type 2 diabetes in young men.," N. Engl. J. Med. 2005;353(14):1454–1462.
DOI: 10.1056/NEJMoa050080
38. Ginsberg HN, Zhang YL, Hernandez-Ono A. Regulation of plasma triglycerides in insulin resistance and diabetes. Arch. Med. Res. 2005;36(3):232–240.
DOI: 10.1016/j.arcmed.2005.01.005
39. Siegel RD, Cupples A, Schaefer EJ, Wilson PW. Lipoproteins, apolipoproteins, and low-density lipoprotein size among diabetics in the Framingham offspring study.," Metabolism. 1996;45(10):1267–1272.
DOI: 10.1016/s0026-0495(96)90246-2
40. "Gender Difference in the Impact of Type 2 Diabetes on Coronary Heart; 2004.
41. HO Steinberg, et al. Type II diabetes abrogates sex differences in endothelial function in premenopausal women," Circulation. 2000;101(17):2040–2046.
DOI: 10.1161/01.CIR.101.17.2040
42. Schwab KO, et al. Spectrum and prevalence of atherogenic risk factors in 27,358 children, adolescents, and young adults with type 1 diabetes: cross-sectional data from the German diabetes documentation and quality management system (DPV).," Diabetes Care. 2006;29 (2):218–225.
DOI: 10.2337/diacare.29.02.06.dc05-0724
43. Guy J, et al. Lipid and lipoprotein profiles in youth with and without type 1 diabetes: The SEARCH for diabetes in youth case-control study," Diabetes Care. 2009;32(3): 416–420.
DOI: 10.2337/dc08-1775
44. Garcés C, de Oya I, Lasunción MA, López-Simón L, Cano B, de Oya M. Sex hormone-binding globulin and lipid profile in pubertal children.," Metabolism. 2010;59 (2):166–171.
DOI: 10.1016/j.metabol.2009.06.033.
45. Laskarzewski PM, Morrison JA, Gutai J, Khoury PR, Glueck CJ. Longitudinal relationships among endogenous testosterone, estradiol and Quetelet index with high and low density lipoprotein cholesterols in adolescent boys., Pediatr. Res. 1983;17(8):689–698.
DOI:10.1203/00006450-198308000-00018
46. Cavaghan MK, Ehrmann DA, Byrne MM, Polonsky KS. Treatment with the oral antidiabetic agent troglitazone improves beta cell responses to glucose in subjects with impaired glucose tolerance., J. Clin. Invest. 1997;100(3): 530–537.
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