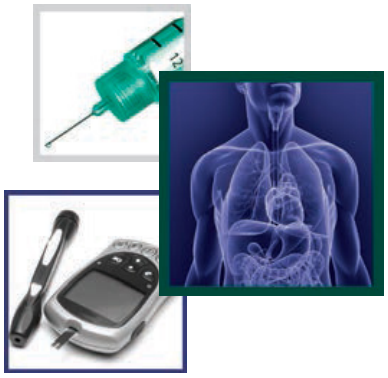
SHORT COMMUNICATION

Diabetes Management



Cardiovascular disease as one of the main complication of uncontrolled diabetes

Amira Ragab El Barky* & Tarek Mostafa Mohamed

ABSTRACT

Diabetes mellitus is a metabolic disorder, which is characterized by chronic hyperglycemia and disturbances of the metabolism of carbohydrate, fat and protein that resulted due to defects in insulin secretion, action or both of them. People with diabetes are prone to increased risk of many diseases, such as cardiac, peripheral arterial and cerebrovascular disease. There are many people with diabetes that refuse to take their medication such as insulin or synthetic drugs to reduce and control their raised blood glucose level. They depend on, when they eat much sweetness food, take their medication. So, this commentary discusses some of the complications of uncontrolled diabetes mellitus and their relation with cardiovascular disease.

Introduction

Patients suffering from diabetes are prone to increased risk factors for Cardiovascular Disease (CVD), blindness, end-stage of renal disease, and legs fingers or leg amputations [1]. People suffering from diabetes had a two to eight-fold more risk of developing heart disease as well as an increased risk factor of mortality by up to 3 times [2,3].

Diabetic people are more potential to have coronary artery disease, which is multi vessel, and to have episodes of silent myocardial ischemia. Traditional coronary heart disease hazard like hypertension, dyslipidemia, and obesity in patients with diabetes mellitus, but this clustering does not account for all of the increased risk in these patients [4].

Diabetic patient with the coronary arteries have more content of lipid-rich, inflamed atheromas, with macrophage infiltration, and subsequent thrombosis that is more vulnerable to rupture than a plaque found in patients without diabetes [5].

Diabetes mellitus enhances the accumulation of foam cells in the sub endothelial via raising the productivity of leukocyte adhesion molecules and pro-inflammatory mediators [6]. This augmented vascular inflammatory reaction might result from over expression of the receptor for advanced glycation end products. The receptors for advanced glycation end products promote matrix metalloproteinase activity that can destabilize plaques [7].

The Changes which occur in the vascular function give the poorer outcomes in diabetes mellitus. The increment of the levels of endothelin-1 enhances vasoconstriction, prompt vascular smooth muscle hypertrophy, and activates the renin-angiotensin. Simultaneously, it can decrease the prostacyclin and nitric oxide levels, enhances the platelet aggregation and adhesiveness, which leads to endothelial dysfunction [8]. In addition to the atherosclerotic and vascular effects, the hematologic system is reversely smitten. Diabetes mellitus promotes platelet adhesion via raising platelet-surface expression of glycoprotein Ib, that mediates binding to the glycoprotein IIb/IIIa receptor and to the von Willebrand factor [9]. Moreover it is raising the coagulation activity via stimulating production of pro-coagulants like those tissue factor and by reducing the levels of the anticoagulants as

Chemistry Department, Biochemistry Division, Tanta University, Tanta, Egypt
Author for correspondence: amiramaram52@yahoo.com

KEYWORDS
- diabetes
- diabetes mellitus
- plaques

protein C and anti-thrombin III [10]. Patients that suffering from diabetes mellitus have an increment of the levels of plasminogen activator inhibitor type 1 in plasma and in atheromas [11]. The increment of tissue plasminogen activator which is inhibited for type 1 could suppress fibrinolysis, elevate thrombus formation, and accelerate plaque formation [12]. So, agents directing at inhibiting platelet aggregation, as aspirin, clopidogrel, and glycoprotein IIb/IIIa blockers, are indispensable in reducing the incidence of thrombotic events [13].

The lipid profile analysis has been shown to be important in determining the development of cardiovascular diseases; it also has been shown to be linked to the indexes of death, which resulted as a result of cardiovascular diseases [14]. Elevated blood cholesterol level (Hypercholesterolemia) is considered one of the most common risk factors for coronary heart disease [15].

The increment of blood TAG levels in the calculation of LDL-C by using a Friedewald formula point to HDL-C is beneficial in determining the risk factor of atherosclerosis and CVD in patients with hypertriglyceridemia [15]. It may be also an important estimation of diseases as diabetes mellitus and obesity, in which excessive triacylglycerol levels and LDL-C is elevated and the level of HDL-C is decreased [16].

In a study by EL Barky [17] they stated that STZ-induced diabetes in female rats has gain, high blood cholesterol and TAG level after duration of four weeks of STZ-induction which attributed the increment of both cholesterol and TAG to several other symptoms, for instance, hyperlipidemia, which consider one the cause of micro vascular complication of diabetes and, the major causes of morbidity and mortality [18]. Diabetes mellitus causes a significant decrease in good cholesterol and raise both of triacylglycerol and bad cholesterol levels, which increase the risk factor for heart diseases and stroke.

The increment of the total cholesterol level is attributed to the increment in β-oxidation of long chain fatty acid and raised oxidation of ketogenic amino acids, which produced excess amount of hepatic acetyl CoA which enter in cholesterol synthesis [19,20].

Insulin hormone affects numerous sites of mammalian lipid metabolism as it can stimulate the synthesis of fatty acids in the liver and adipose tissues. Insulin deficiency in the intestine also causes a significant increase in the level of cholesterol synthesis and significantly increases the activity of lipoprotein lipase in white adipose tissue [21], moreover, it suppresses the lipid degradation by stimulation of transcription factors such as steroid regulatory element-binding protein in the liver and in adipose tissue [22].

VLDL biosynthesis are promoted by an increment in the flux of the free fatty acids in the liver and at the end, the particles are converted to LDL, the increment in the level of VLDL as an effect of decreased clearance and over-production in type 1 DM patients [23]. In contrast, after six weeks of the experiment in the study by EL Barky [17], there was a significant decrease of lipid profiles in diabetic rats. The decrease of lipid profile may be due to the diabetic rats cannot use glucose for obtains energy and instead it depends on lipids in obtaining energy. This leads to depletion of the storage of lipids in the body. Moreover, diabetic rats that injected with STZ-induced diabetes showed a significant decrease in their heart weight and a significant increase in the liver weight [24,25]. The lighter hearts of diabetic rats were responsible for the depressed ATPase content [26].

The hypertrophy of liver weight could be attributed to increased levels of serum triacylglycerol accumulation which cause enlarged liver. This explained by increased flow of fatty acids into the liver which resulted due to decreased levels of insulin and the low capacity of excretion of lipoprotein secretion from the liver resulting from a deficiency ofapolipoprotein B synthesis [27].

Conclusion

Diabetes represents a global epidemic and one of the leading causes of morbidity and mortality. Diabetic people are more potential to have coronary artery disease, which is multi vessel, and to have episodes of silent myocardial ischemia. Traditional coronary heart disease hazard like hypertension, dyslipidemia, and obesity in patients with diabetes mellitus, but this clustering does not account for all of the increased risk in these patients.

References

1. Inzucchi S, Bergenstal RM, Buse JB *et al.* Management of hyperglycemia in Type 2 diabetes: a patient-centered approach position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 35(6), 1364–1379 (2012).
2. Preis SR, Hwang SJ, Coady S *et al.* Trends in all-cause and cardiovascular disease mortality among women and men with and without diabetes in the Framingham Heart Study, 1950 to 2005. *Circulation.* 119(3), 1728–1735 (2009).
3. Martín-Timón I, Sevillano-Collantes C, Segura-Galindo A *et al.* Type 2 diabetes and cardiovascular disease: Have all risk factors the same strength? *World J. Diabetes*. 5(4), 444–470 (2014).
4. https://www.scholars.northwestern.edu/en/publications/braunwalds-heart-disease-a-textbook-of-cardiovascular-medicine-8t-2
5. Moreno PR, Murcia AM, Palacios IF *et al.* Coronary composition and macrophage infiltration in atherectomy specimens from patients with diabetes mellitus. *Circulation.* 102(18), 2180–2184 (2000).
6. Beckman JA, Creager MA, Libby P. Diabetes and atherosclerosis epidemiology, pathophysiology and management. *JAMA*. 287(19), 2570–2581 (2002).
7. Cipollone F, Iezzi A, Fazia M *et al.* The receptor RAGE as a progression factor amplifying arachidonate-dependent inflammatory and proteolytic response in human atherosclerotic plaques: role of glycemic control. *Circulation*. 108(9), 1070–1077 (2003).
8. Cosentino F, Eto M, De Paolis P *et al.* High glucose causes upregulation of cyclooxygenase-2 and alters prostanoid profile in human endothelial cells: role of protein kinase C and reactive oxygen species. *Circulation.* 107(3), 1017–1023 (2003).
9. Vinik AI, Erbas T, Park TS *et al.* Platelet dysfunction in type II diabetes. *Diabetes Care.* 24(1), 1476–1485 (2001).
10. Ceriello A, Giugliano D, Quatraro A *et al.* Evidence for a hyperglycemia-dependent decrease of antithrombin III-thrombin complex formation in humans. *Diabetologia*. 33(1), 163–167 (1990).
11. Pandolfi A, Cetrullo D, Polishuck R *et al.* Plasminogen activator inhibitor type 1 is increased in the arterial wall of type 2 diabetic subjects. *Arterioscler. Thromb. Vasc. Biol.* 21(4), 1378–1382 (2001).
12. Sobel BE, Woodcock-Mitchell J, Schneider DJ *et al.* Increased plasminogen activator inhibitor type 1 in coronary artery atherectomy specimens from type 2 diabetic compared with nondiabetic patients: a potential factor predisposing to thrombosis and its persistence. *Circulation*. 97(1), 2213–2221 (1998).
13. Colwell JA, Nesto RW. The platelet in diabetes: focus on prevention of ischemic events. *Diabetes Care*. 26(7), 2181 –2188 (2003).
14. McQueen MJ, Hawken S, Wang XY *et al.* Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case-control study. *Lancet*. 372(2), 224–233 (2008).
15. Emdadul Haque ATM**,** Yusoff FBM, Ariffin MHS *et al.* Lipid profile of the Coronary Heart Disease (CHD) patients admitted in a hospital in Malaysia. *J. Appl. Pharm. Sci.* 6(05), 137-142 (2016).
16. Shimano H, Arai H, Harada-Shiba M *et al.* Proposed guidelines for hypertriglyceridemia in Japan with non-HDL cholesterol as the second target. *J. Atheroscler. Thromb.*15(3), 116–121 (2008).
17. El Barky AR, Hussein SA, Alm–Eldeen AA *et al*. Anti–diabetic activity of *Holothuria thomasi* saponin. *Biomed. Pharmacother.* 84(2), 1472–1487 (2016).
18. Taskinen MR. Diabetic dyslipidemia. *Atherosclerosis Supplements*. 3(1), 47–51 (2002).
19. Kandeil MA, Amin KA, Hassanin KM *et al.* Serum levels of insulin and leptin in lipoic acid-treated and nontreated experimentally diabetic rats. *Bs. Vet. Med. J.* 5(1), 87–95 (2007).
20. Abdel-Azim SA, Bader AM, Barakat MA. Effect of metformin, glyburide, and/or selenium on glucose homeostasis, lipid peroxidation, glutathione levels and changes in glutathione peroxidase activity in streptozotocin-induced diabetic rats. *Egypt J. Biochem.* 20(3), 393–411 (2002).
21. Suryawanshi NP, Bhutey AK, Nagdeote AN *et al.* Study of lipid peroxide and lipid profile in diabetes mellitus. *Indian J. Clin. Biochem.* 21(1), 126–130 (2006).
22. Ferre P, Foufelle F. SREBP-1c transcription factor and lipid homeostasis: clinical perspective. *Horm Res*. 68(2), 72–82 (2007).
23. Andallu B, Vinay Kumar AV, Varadacharyulu N. Lipid abnormalities in streptozotocin-diabetes: Amelioration by *Morus indica* L. cv Suguna leaves. *Int. J. Diabetes Dev. Ctries*. 29(3), 123–128 (2009).
24. El Barky AR, Hussein SA, Alm-Eldeen AA *et al.* Saponin ameliorate diabetes in STZ-diabetic rats. *Sci. J. Sci.* 38(2), 165–170) (2017).
25. El Barky AR, Hafez YA, Mohamed TM *et al.* Can stem cells ameliorate the pancreatic damage induced by streptozotocin in rats? *Can. J. Diabetes.* 267(17), 30050–30053 (2017).
26. Scheuer J, Bhan AK. Cardiac contractile proteins. Adenosine tnphosphatase activity and physiological function. *Circ Res.* 46(2), 1–12 (1979).
27. Zafar M, Naqvi SNH. Effects of STZ-induced diabetes on the relative weights of kidney, liver and pancreas in Albino rats: A comparative study. *Int. J. Morphol*. 28(1), 135–142 (2010).