Decreased total antioxidant levels and increased oxidative stress in South African type 2 diabetes mellitus patients

FA Ganjifrockwale**, JT Joseph* and G George*

**Department of Human Biology, Walter Sisulu University, Mthatha, South Africa
*Corresponding author, email: farzanaanis@gmail.com

Introduction

Diabetes mellitus (DM) is a cluster of metabolic disorders characterised by abnormally elevated blood glucose levels (hyperglycaemia), which arise from the body’s inability to produce insulin or to use it to its full potential. DM is a lifetime progressive metabolic disease and, according to recent estimates for the year 2015, 415 million adults aged 20–79 suffer from the disease worldwide. These estimates include 193 million people who are undiagnosed and by the year 2040, if the current rate of increase in cases continues, 642 million people will be suffering from diabetes. DM is the fourth primary reason for death by disease universally and has become a challenging health problem for the twenty-first century.

The incidence of DM is rising at an alarming rate; mainly the type 2 (non-insulin dependent diabetes mellitus (NIDDM)). Sub-Saharan Africa, including South Africa, now faces a double burden of disease, with an epidemiological transition from transmissible diseases to non-communicable or ‘lifestyle’ diseases. The prevalence study by Bertram et al. reported a potential rise in type 2 diabetes mellitus in South Africa from 5.5% in 2000 to 9% in 2009 in people aged 30 or older since the previous approximations. Secondary studies by Bertram et al. furthermore revealed that in South Africa around 55% of cases remained undiagnosed. In a cross-sectional survey of 642 participants aged ≥31 years from an urban South African coloured community in Bellville South, Cape Town, T2DM was evaluated using the World Health Organization (WHO) criteria. The crude prevalence of T2DM was 28.2%, and undiagnosed T2DM was present in 18.1% of participants. In a recent report by International Diabetic Federation (IDF) on the prevalence of diabetes in African countries, South Africa was recorded as having an average 2.3 (1.2–4.6) million people with diabetes.

Several pathological processes are involved in the development of diabetes, which range from autoimmune obliteration of the beta cell of the pancreas causing insulin deficiency (type 1 diabetes mellitus) to abnormalities that result in insulin resistance (T2DM). As a result of chronic hyperglycaemia and insulin resistance, various long-term complications of diabetes develop. These complications include both microvascular and macrovascular irregularities, such as retinopathy, peripheral neuropathy, autonomic neuropathy, cardiovascular symptoms and nephropathy. Oxidative stress is accountable for the development of chronic complications of DM and results from chronic hyperglycaemia, dyslipidaemia and elevated fatty acids in the circulation.

Oxidative stress is an inevitable consequence of life in an atmosphere that is oxygen-rich and arises when a synthesis of reactive oxygen species (ROS) and reactive nitrogen species (RNS) surpasses the capacity of cellular antioxidant defences to eradicate these toxic species. Examples of ROS are superoxide, hydroxyl radical, peroxyl radical, and hydroperoxyl radical. The non-radical ROS are hydrogen peroxide and hypochlorous acid. Examples of RNS include nitric oxide, nitrogen dioxide, peroxynitrite and, nitrous oxide. Most of the free radicals are produced in small reactions of lipid peroxidations. The antioxidant system includes enzymes like SOD, catalase, glutathione peroxidase and molecules like GSH, uric acid, bilirubin, lipoic acid, albumin, transferrin, vitamin E, vitamin C, carotenoid, copper and zinc. The antioxidants scavenge the free radicals by several mechanisms. The enzymes degrade free radicals; proteins such as transferrin can bind to metals that stimulate the synthesis of free radicals; and vitamins C and E act as free radical scavengers. Vitamin C is a water-soluble molecule and usually scavenge hydroxyl radicals, while vitamin E, a lipid soluble vitamin, interferes with chain reactions of lipid peroxidations.
In diabetes and other pathological conditions such as hyperglycaemia in diabetes, these mechanisms include glucose auto-oxidation, increased glucose flux through the polyol pathway, non-enzymatic and progressive glycation of proteins and the formation of advanced glycosylation end products (AGEs). An increase in the polyol pathway depletes the NADPH, which is utilised by the enzyme aldose reductase that catalyses the conversion of glucose to sorbitol.

Numerous studies have reported increased oxidative stress in type 2 diabetes mellitus patients compared with their healthy counterparts. In Africa, studies on oxidative stress and diabetes have also reported similar findings. There are very few to no studies conducted on oxidative stress levels in South African people with type 2 diabetes. This investigation aimed to investigate the oxidative stress and total antioxidant levels in South African T2DM patients compared with healthy volunteers without diabetes.

Materials and methods
Ethical clearance was acquired from the Research Ethics and Biosafety Committee, the Faculty of Health Sciences, Walter Sisulu University (Bioethics clearance No: 012/012).

Research participant recruitment
Inclusion criteria: The cross-sectional observational study was conducted on total of 98 participants (57 black, South African, known T2DM patients attending selected diabetes clinics and 41 healthy volunteers as controls) within the age group 35–75 years, all of Xhosa ethnicity, in Mthatha, Eastern Cape Province of South Africa.

Exclusion criteria: Patients who have HIV infection and other chronic diseases such as tuberculosis, thyroid problems, coronary artery diseases, renal complications and other complications of diabetes, if reported, were not included in this study.

The clinical examination of the T2DM patients was carried out by the clinician of the diabetes clinic. Control participants were selected randomly from the general population, keeping in mind the selection criteria. The participants were sensitised concerning the study, and those who volunteered were asked to sign an informed consent form before blood collection. A questionnaire was used to obtain anthropometric data as well general information (medication, physical activity, family history, duration of diabetes and other chronic illnesses) from each participant.

Sample collection and preparation
Fasting blood (approx. 20 ml) was collected in vacutainer tubes from each participant. Plasma was separated from the specimen within three hours of collection. Serum samples were stored at −70 °C if not analysed on the day of collection and used within a month. Fasting blood samples were used for measurements of plasma glucose, glycated haemoglobin (HbA1c), lipid profile, TAO level, malondialdehyde (MDA), thiobarbituric acid reactive substances (TBARS), oxidised LDL (ox-LDL) levels and superoxide dismutase (SOD) enzyme activity.

Methods
Plasma glucose, HbA1c and lipid profile were measured by routine methods, using the Roche cobas® 6000 chemical auto-analyser (Roche Diagnostics USA, Indianapolis, IN, USA), by NHLS (National Health Laboratory Services) of NMAH (Nelson Mandela Academic Hospital). Different methods for assessing lipid peroxidation and total antioxidant activity for measuring the oxidative stress in diseases have been discussed by various authors. In this study the TAO level in serum was measured using a Sigma-Aldrich kit (ABTS method; Saint Louis, MO, USA). MDA (TBARS) and SOD enzyme activity were measured using Cayman assay kits (colorimetric method; Cayman Chemical Company, Ann Arbor, MI, USA) and ox-LDL was measured by the ELISA technique using a Merckodia kit (Uppsala, Sweden). The BioTek KC, Autoreader (BioTek Instruments, Inc., Winooski, VT, USA) was used for all the analyses referred to above.

Statistical analysis
Statistical analysis was conducted using the IBM Statistical Package for the Social Sciences, version 23 (IBM Corp, Armonk, NY, USA). Data are expressed as mean ± SD and median (IQR) depending on their distribution (normal and not normal) respectively. The statistical significance of differences between the means of quantitative variables across groups was evaluated by Student’s t-test for normally distributed data, and the non-parametric Mann–Whitney U test was used for parameters violating normal distribution. The bivariate correlations were ascertained using Spearman rank correlation to analyse relationships between continuous variables.

Results
Table 1 presents information regarding the general characteristics of participants. The mean age was comparable across groups and showed no significant difference (p = 0.101). The mean BMI for both groups was high, with T2DM patients having higher BMIs compared with individuals in the healthy control group; the difference was not, however, statistically significant (p = 0.378). Biochemical characteristics of participants are presented in Table 2. FPG and HbA1c were significantly higher in T2DM patients compared with those of persons in the control group (p < 0.0005 and p < 0.0005 respectively). Serum triglyceride (TG) levels were substantially higher in the T2DM group as opposed to the controls (p = 0.024), and high density lipoprotein cholesterol (HDL-C) was significantly different between groups (p = 0.008), with the T2DM patients having lower HDL-C compared with the persons in the healthy control group. There was no difference in total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) between the two groups.

Serum TAO, MDA (TBARS) and ox-LDL levels were significantly different in both groups. A statistically significant reduction in

| Parameters                  | Control group, n = 41 | T2DM group, n = 57 | p-value |
|-----------------------------|-----------------------|--------------------|---------|
| Age (years)                 | 54.24 ± 6.05          | 56.61 ± 7.59       | 0.101   |
| Weight (kg)                 | 76.0 (87.8–65.7)      | 80.0 (96.0–70.0)   | 0.125   |
| Height (cm)                 | 159.4 ± 6.20          | 162.1 ± 7.87       | 0.067   |
| BMI (kg/m²)                 | 30.4 ± 7.28           | 31.6 ± 6.49        | 0.378   |
| Duration of diabetes (years)| –                     | 6.87 ± 6.34        |         |

Notes: Data are shown as mean ± SD and median (IQR), BMI = body mass index.
TAO levels was observed in the T2DM patients compared with healthy participants (p = 0.017), whereas median MDA and ox-LDL levels were significantly raised in patients with diabetes compared with controls. There was no significant difference in total SOD activity between the two groups, as shown in Table 3.

An analysis of the correlations between HbA1c, MDA, ox-LDL, SOD and TAO in both groups is shown in Table 4. There was a significant negative correlation between TAO levels and MDA in the T2DM group (r = 0.291, p = 0.029). There was also a significant negative correlation between HDL-C and HbA1c, TG and ox-LDL levels in the control group, whereas in the T2DM patients only TG levels were significantly associated with HDL-C, as presented in Table 5.

**Discussion**

In the present study there was a marked rise in HbA1c and FPG levels in T2DM patients compared with the control population, indicating excessive glycosylation of haemoglobin and poor control of diabetes as reported by other studies. An increase in the serum TG levels and a decrease in HDL-C levels were observed in patients with diabetes, indicating the presence of dyslipidaemia. Since the uptake of free fatty acids (FFAs) by the skeletal muscle and adipose tissue is mediated by insulin, an increase in insulin resistance would result in increased FFAs delivered to the liver. This leads to the overproduction of very low-density lipoprotein (VLDL) and increased VLDL–cholesterol concentrations, clinically manifesting as hypertriglyceridaemia. An accumulation of the TG-rich lipoproteins in plasma can also result due to decreased lipoprotein lipase (LpL) activity. Hypertriglyceridaemia and reduced plasma HDL-C is commonly present in T2DM and has been reported by various studies.

Chronic hyperglycaemia, dyslipidaemia and elevated FFAs results in oxidative stress by stimulating ROS and RNS production, which attacks the lipids found in the plasma membranes, mitochondrial membranes and endoplasmic reticulum membranes and causes peroxidation. Once lipid peroxidation is initiated, propagation chain reactions will occur until termination products are produced, such as lipid hydroperoxide, which further decompose to aldehydes such as MDA and, 4-hydroxy-2 nonenal (4-HNE). Cyclic endoperoxides, isoprostanes and hydrocarbons may also be formed. The observed increase in MDA levels in T2DM patients in the present study is thought to be due to the increased production of lipid peroxides and their release in circulation, which would be consistent with previous studies. In the present study, increased oxidation of LDL particles was observed in the T2DM patients compared with the control group. Several factors, such as glycation, increased TG content and the reduced anti-oxidative properties of HDL are possible stimulators of LDL oxidation in T2DM patients. TGs have an effect on LDL size and HDL-C inhibits the oxidative modification of LDL, so increased TG and decreased HDL-C can result in further oxidation of LDL in diabetes. Similar observations have been reported by other studies.

A significant decrease in TAO levels among T2DM patients was observed in this study and has also been reported by various other authors in their studies. This reduction in TAO levels could be attributed to increased oxidative stress. This is evidenced by increased lipid peroxidation as well as by the excess utilisation of antioxidants against oxidative stress to minimise the damage. The significant negative correlation observed between TAO levels and MDA levels in the T2DM group in this study also explains the decrease in TAO levels with increased lipid peroxidation.
Rani and Mythili showed a significant negative association between TAO levels and MDA levels in their study population.\(^\text{61}\) There was no significant difference in total SOD activity between the two groups, which concurs with the findings of Kesavulu et al.\(^\text{62}\) and Guler et al. in their studies of T2DM patients.\(^\text{63,64}\)

A significant negative correlation was observed between HDL-C and serum TG in the T2DM patients and the control participants. In the T2DM group, no significant correlation was demonstrated between HDL-C and ox-LDL, but the control group showed a significant negative correlation. HDL-C contains enzymes such as paraoxonase, platelet activating factor, acetyhydrolase, and lecithin cholesterol acyltransferase and is involved in the reverse transport of cholesterol from the periphery to the liver. These enzymes prevent the formation of or metabolise the oxidised phospholipids. Evidence exists that HDL can reverse LDL oxidation by removing the oxidised phospholipids that make LDL harmful and lead to atherogenesis.\(^\text{49}\) In the healthy control group, a significant negative association was observed between the HDL and LDL, which indicates that high HDL-C can decrease the oxidation of LDL. In the T2DM group, this correlation was not significant and could be due to the fact that in diabetes the anti-oxidative property of HDL is reduced. This reduction could be promoted by hyperglycaemia and the TG enrichment of lipoprotein.\(^\text{49}\) This may be the reason why no correlation was observed between HDL-C and ox-LDL in the T2DM group.

**Conclusion**

The results of this study suggest that hyperglycaemia and dyslipidaemia seen in the T2DM patients could lead to an increase in lipid peroxidation and oxidative stress and thus a decrease in TAO levels. This decrease in TAO levels could be due to its increased utilisation in order to scavenge the free radicals produced in high amounts due to increased oxidative stress. Early intervention and a diet rich in antioxidants can reduce the risk of developing complications and increase the longevity and quality of life of patients with diabetes.

**Limitations**

The effects of diet and diabetic medication were not considered in this study.

**Author contributions** – All the authors contributed equally in the preparation of this manuscript.

**Conflict of interests** – The authors declare that there is no conflict of interest regarding the publication of this manuscript.

**Acknowledgements** – The authors would like to thank all the research participants who made this study possible and Walter Sisulu University for funding the research project.

**ORCID**

FA Ganijfromkwa D <http://orcid.org/0000-0003-2647-8056>
JT Joseph <http://orcid.org/0000-0001-7404-4178>
G George <http://orcid.org/0000-0002-4662-720X>

**References**

1. Wold LE, Ceylan-ISIK AF, Ren J. Oxidative stress and stress signaling: menace of diabetic cardiomyopathy. Acta Pharmacol Sin. 2005;26(8):908–17. https://doi.org/10.1111/aps.2005.26.issue-8

2. Kowluru RA, Chan PS. Oxidative stress and diabetic retinopathy. Exp Diabetes Res. 2007;1–2.

3. International Diabetes Federation. IDF Diabetes Atlas-Seventh Edition’ [internet]. 2015 [cited 2016 Apr 30]. Available from: http://www.diabetesatlas.org.

4. Maiese K, Daniela Morhan SD, ZhongChong ZZ. Oxidative stress biology and cell injury during type 1 and type 2 diabetes mellitus. Curr Neuro Res. 2007;4(1):63–71. https://doi.org/10.2174/15672020779940653

5. Levitt NS, Bradshaw D, Zwartenstein MF, et al. Audit of public sector primary diabetes care in Cape Town, South Africa: high prevalence of complications, uncontrolled hyperglycaemia, and hypertension. Diabet Med. 1997;14:1073–7. https://doi.org/10.1002/(ISSN)1096-9136

6. Jakus V. The role of free radicals, Oxidative stress and antioxidant systems in diabetic vascular disease. Bratil lek listy. 2000;10(1):541–51.

7. Gning SB, Thiam M, Fall F, et al. Diabetes mellitus in sub-Saharan Africa: epidemiological aspects and management issues. Med Tropicale (Mars). 2007;67(6):607–11.

8. Mayosi BM, Flisher AJ, Lallo UG, et al. The burden of non-communicable disease in South Africa. Lancet. 2009;374(9694):957–9.

9. Bertram MY, Jaswal AVS, Pillay Van Wyk V, et al. The non-fatal disease burden caused by type 2 diabetes in South Africa, 2009. Global Health Action. 2013;6:206–12. doi:10.3402/gha.v6i0.19244.

10. Erasmus RT, Soita DJ, Hassan MS, et al. High prevalence of diabetes mellitus and metabolic syndrome in a South African coloured population: baseline data of a study in Bellville, Cape Town. South Afr Med J. [internet]. 2012 [cited 2016 Apr 30]:102(11):841–4. ISSN 2078-5135. Available from: http://www.sajm.org.za/index.php/sajm/article/view/5670/4761. doi:10.7196/SAMJ.5670.

11. Rahimi R, Nikfar S, Larijani B, et al. A review on the role of antioxidants in the management of diabetes and its complications. Biomed Pharma. 2005;59(7):365–73. https://doi.org/10.1016/j.biopharm.2005.07.002

12. Opara EC. Oxidative stress, micronutrients, diabetes mellitus and its complications. J Royal Soc Promot Health. 2002;122(1):28–34. https://doi.org/10.1177/146462400221200112

13. Kuroki T, Ishiiki K, King GL. Oxidative stress: the lead or supporting actor in the pathogenesis of diabetic complications. J Am Soc Nephrol. 2003;14:5216–20. https://doi.org/10.1097/01.ASN.0000077405.07888.07

14. Davies KJA. Oxidative stress, antioxidant defences and damage removal, repair and replacement systems. Int Union Biochem Mol Biol Life. 2000:50:278–89.

15. Johansen JS, Harris AK, Rychly DJ, et al. Review, oxidative stress and the use of antioxidants in diabetes: Linking basic science to clinical practice. Cardiovas Diabetol. 2005;4:5. https://doi.org/10.1186/1475-2840-4-5

16. Limón-Pacheco J, Gosebatt ME. The role of antioxidants and antioxidant-related enzymes in protective responses to environmentally induced oxidative stress. Mutation Res. 2009;674:137–47. https://doi.org/10.1016/j.mrgentox.2008.09.015

17. Maiese K, Chong ZZ, Shang YC. Mechanistic insights into diabetes mellitus and oxidative stress. Curr Med Chem. 2007;14(16):1729–38.

18. Valko M, Leibfritz D, Moncol J, et al. Free radicals and antioxidants in normal physiological functions and human disease. Int J Biochem Cell Biol. 2007;39:44–84. https://doi.org/10.1016/j.biocel.2006.07.001

19. Figueroa-Romero C, Saddidi M, Feldman EL. Mechanisms of disease: the oxidative stress theory of diabetic neuropathy. Rev Endocrine Metab Disord. 2008;9(4):301–14. https://doi.org/10.1007/s11514-008-9104-2

20. Mossanda KS, Bolajoko EB, Morapane M, et al. Antioxidant and oxidative stress status in type 2 diabetes and diabetic foot ulcer. JEMDSA. 2008;13(2):58–63.

21. Jamuna Rani A, and Mythili SV. Study on total antioxidant status in relation to oxidative stress in type 2 diabetes mellitus. J Clin Diagn Res. 2014;8(3):108–10.

22. Maharjan BR, Jha JC, Adhikari D, et al. A study of oxidative stress, antioxidant status and lipid profile in diabetic patient in western region of Nepal. Kathmandu Univ Med J. 2008;6(6):16–22.

23. Benrebai M, Abidli N, Nasr SM, et al. Oxidative stress status in type 2 diabetic patients in Eastern Algeria. World Appl Sci J. 2008;4(5):714–9.

24. Soliman GZA. Blood lipid peroxidation (superoxide dismutase, malondialdehyde, glutathione) levels in Egyptian type 2 diabetic patients. Singap Med J. 2008;49(2):129–36.

25. Abuja PM, Albertini R. Methods for monitoring oxidative stress, lipid peroxidation and oxidation resistance of lipoproteins. Clin Chim Acta. 2001;306:1–17. https://doi.org/10.1016/S0009-8981(01)00393-X
Decreased total antioxidant levels and increased oxidative stress in South African type 2 diabetes mellitus patients

26. Nourooz-Zadeh J, Rahimi A, Tajaddini-Sarmadi J, et al. Relationships between plasma measures of oxidative stress and metabolic control in NIDDM. Diabetologia. 1997;40:647–53. https://doi.org/10.1007/s001250050729

27. Merzouk S, Hichami A, Sari A, et al. Impaired oxidant/antioxidant status and LDL-fatty acid composition are associated with increased susceptibility to peroxidation of LDL in diabetic patients. Gen Physiol Biophys. 2004;23:387–99.

28. Pasupathi P, Bakhavathalsam G, Saravanan G, et al. Evaluation of oxidative stress and antioxidant status in patients with diabetes mellitus. J Appl Sci Res. 2009;5(7):770–5.

29. Kharroubi AT, Darwish HM, Akkawi MA, et al. Total antioxidant status in type 2 diabetic patients in Palestine. J Diab Res. 2015;2015, Article ID 461271: 7 p. doi:10.1155/2015/461271.

30. Chen S, Tseng C. Dyslipidaemia, kidney disease, and cardiovascular disease in diabetic patients. Rev Diabet Stud. 2013;10:80–100.

31. Pereira EC, Ferderbar S, Bertolami MC, et al. Biomarkers of oxidative stress and endothelial dysfunction in glucose intolerance and diabetes mellitus. Clin Biochem. 2008;41:1454–60. https://doi.org/10.1016/j.clinbiochem.2008.08.074

32. Vincent AM, Russell JW, Low P, et al. Oxidative stress in the pathogenesis of diabetic neuropathy. Endocr Rev. 2004;25:612–28. https://doi.org/10.1210/er.2003-0019

33. Kohen R, Nyska A. Oxidation of biological systems: oxidative stress phenomena, antioxidants, redox reactions, and methods of their quantification. Toxicol Pathol. 2002;30(6):620–50. https://doi.org/10.1080/01926230290166724

34. Kunwar A, Priyadarshini KL. Review: free radicals, oxidative stress and importance of antioxidants in human health. J Med Allied Sci. 2011;1(2):52–60.

35. Noori S. An overview of oxidative stress and antioxidant defensive system. 2012;1:413. doi:10.4172/21610728.1000021

36. Birben E, Sahiner UM, Sackesen C, et al. Oxidative stress and antioxidant defence. World Allergy Organ J. 2012;5:9–19. https://doi.org/10.1097/WOX.0b013e3182439613

37. Rahal A, Kumar A, Singh V, et al. Oxidative stress, pro-oxidants, and antioxidants: the interplay. Biomed Res Int. 2014;1–19. https://doi.org/10.1155/2014/761264

38. Anh Le N. Lipoprotein-associated oxidative stress: a new twist to the postprandial hypothesis. Int J Mol Sci. 2015;16:401–19.

39. Mahboob M, Rahman MF, Grover P. Serum lipid peroxidation and antioxidant enzyme levels in male and female diabetic patients. Singap Med J. 2005;46(7):322–4.

40. Vergès B. Lipid modification in type 2 diabetes: the role of LDL and HDL. Fundam Clin Pharmacol. 2009;23:681–5. https://doi.org/10.1111/j.1472-8206.2009.00739.x

41. Behzadi P, Torabi F, Amini M, et al. Comparison of ox-LDL levels in diabetic patients with normo-, micro-, and macroalbuminuria with their first degree relatives and the healthy control group. Int J Endocrinol. 2012;1–5. https://doi.org/10.1155/2012/167154

42. Nour-Eldin EEM, Almarzouki A, Assiri AM, et al. Oxidized low density lipoprotein and total antioxidant capacity in type 2 diabetic and impaired glucose tolerance Saudi men. Diabetol Metab Syndr. 2014;6:94. https://doi.org/10.1186/1758-5996-6-94

43. Kiranmayi PV, Vivekanand N, Pandit VL. The study of lipid profile and oxidized LDL in type 2 diabetes mellitus. Scholars J Appl Med Sci. 2014;2(3D):1119–22.

44. Kesavulu MM, Giri R, Kameshwara Rao B, et al. Lipid peroxidation and antioxidant enzyme levels in type 2 diabetic and impaired glucose tolerance Saudi men. Diabetol Metab Syndr. 2014;6:94. https://doi.org/10.1186/1758-5996-6-94

45. Vincent AM, Russell JW, Low P, et al. Oxidative stress in the pathogenesis of diabetic neuropathy. Endocr Rev. 2004;25:612–28. https://doi.org/10.1210/er.2003-0019

46. Kohen R, Nyska A. Oxidation of biological systems: oxidative stress phenomena, antioxidants, redox reactions, and methods of their quantification. Toxicol Pathol. 2002;30(6):620–50. https://doi.org/10.1080/01926230290166724

47. Kunwar A, Priyadarshini KL. Review: free radicals, oxidative stress and importance of antioxidants in human health. J Med Allied Sci. 2011;1(2):52–60.

48. Noori S. An overview of oxidative stress and antioxidant defensive system. 2012;1:413. doi:10.4172/21610728.1000021

49. Birben E, Sahiner UM, Sackesen C, et al. Oxidative stress and antioxidant defence. World Allergy Organ J. 2012;5:9–19. https://doi.org/10.1097/WOX.0b013e3182439613

50. Rahal A, Kumar A, Singh V, et al. Oxidative stress, pro-oxidants, and antioxidants: the interplay. Biomed Res Int. 2014;1–19. https://doi.org/10.1155/2014/761264

51. Anh Le N. Lipoprotein-associated oxidative stress: a new twist to the postprandial hypothesis. Int J Mol Sci. 2015;16:401–19.

52. Mahboob M, Rahman MF, Grover P. Serum lipid peroxidation and antioxidant enzyme levels in male and female diabetic patients. Singap Med J. 2005;46(7):322–4.

53. Vergès B. Lipid modification in type 2 diabetes: the role of LDL and HDL. Fundam Clin Pharmacol. 2009;23:681–5. https://doi.org/10.1111/j.1472-8206.2009.00739.x

54. Behzadi P, Torabi F, Amini M, et al. Comparison of ox-LDL levels in diabetic patients with normo-, micro-, and macroalbuminuria with their first degree relatives and the healthy control group. Int J Endocrinol. 2012;1–5. https://doi.org/10.1155/2012/167154

55. Nour-Eldin EEM, Almarzouki A, Assiri AM, et al. Oxidized low density lipoprotein and total antioxidant capacity in type 2 diabetic and impaired glucose tolerance Saudi men. Diabetol Metab Syndr. 2014;6:94. https://doi.org/10.1186/1758-5996-6-94

56. Kiranmayi PV, Vivekanand N, Pandit VL. The study of lipid profile and oxidized LDL in type 2 diabetes mellitus. Scholars J Appl Med Sci. 2014;2(3D):1119–22.

57. Kesavulu MM, Giri R, Kameshwara Rao B, et al. Lipid peroxidation and antioxidant enzyme levels in type 2 diabetic and impaired glucose tolerance Saudi men. Diabetol Metab Syndr. 2014;6:94. https://doi.org/10.1186/1758-5996-6-94

58. Kohen R, Nyska A. Oxidation of biological systems: oxidative stress phenomena, antioxidants, redox reactions, and methods of their quantification. Toxicol Pathol. 2002;30(6):620–50. https://doi.org/10.1080/01926230290166724

59. Kunwar A, Priyadarshini KL. Review: free radicals, oxidative stress and importance of antioxidants in human health. J Med Allied Sci. 2011;1(2):52–60.

60. Noori S. An overview of oxidative stress and antioxidant defensive system. 2012;1:413. doi:10.4172/21610728.1000021

61. Birben E, Sahiner UM, Sackesen C, et al. Oxidative stress and antioxidant defence. World Allergy Organ J. 2012;5:9–19. https://doi.org/10.1097/WOX.0b013e3182439613

62. Rahal A, Kumar A, Singh V, et al. Oxidative stress, pro-oxidants, and antioxidants: the interplay. Biomed Res Int. 2014;1–19. https://doi.org/10.1155/2014/761264

63. Anh Le N. Lipoprotein-associated oxidative stress: a new twist to the postprandial hypothesis. Int J Mol Sci. 2015;16:401–19.