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The Progression of Type-II Diabetes Mellitus With Concurrent Hypertension Influenced By Oxidative Stress

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ABSTRACT— The inactivation of nitric oxide caused by oxidative stress raises the possibility of HT by promoting disruption of endothelial cells. Discussing the development of type-II diabetes mellitus with concurrent hypertension impacted by oxidative stress was the primary goal of this study. The 384 participants were split into four distinct groups based on their illness status: 108 controls (those without T2DM or HT), 48 prediabetes (those without HT), 22 T2DM, and 68 T2DM+ HT (those with coexisting T2DM and HT). We used GSH/GSSG and 8-OHdG as oxidative stress indicators. Because they demonstrate the effectiveness of the antioxidant defense system, GSH, 8-OHdG, and GSSG were chosen. The statistical software SPSS 25 was used for all tests. Sample size estimates were not carried out before statistical assessments because this investigation was conducted using information that had already been gathered. Since it was established that perpetual variables did not follow a normal pattern of distribution, they were represented by the median. To find significant differences between the four groups, Kruskal-Wallis tests were employed. The threshold for significance was $p<0.05$. Compared to the control and prediabetes groups, the HbA1c levels were considerably higher in the T2DM and T2DM-HT groups. The T2DM-HT group's levels for inflammatory biomarkers eventually returned to being equivalent to controls. Regarding OS, GSH first rose from controls to T2DM ($p<0.001$), nearly reaching the threshold for statistical significance, and then significantly decreased when juxtaposed with concurrent T2DM-HT ($p<0.001$). From controls to T2DM, GSSG showed a similar pattern of increase ($p<0.01$), followed by a significant decline in T2DM-HT ($p<0.001$). The study's conclusions suggest that an increased understanding of OS markers is more reliable for distinguishing between the stages of T2DM progression with and without HT. Our results also confirm the usefulness of prescription pharmaceuticals, especially when considering the known functions of OS in the onset of the illness.

KEYWORDS: progression, diabetes mellitus Type-II, hypertension, oxidative stress, biomarkers

1. Introduction

The global population of people with type II diabetes mellitus (T2DM), which is predicted to reach 700.2 million by 2045, constitutes one of the primary contributors of morbidity and early mortality worldwide [1]. By the following year, the incidence of prediabetes, a metabolic disorder that precedes type 2 diabetes, is predicted to increase to 8.3% worldwide [2], [3]. The stage in between normoglycemia and overt type 2 diabetes is known as prediabetes [4]. Even though this illness frequently has no symptoms [5], pathogenic mechanisms and problems related to hyperglycemia are currently apparent [6]. It is currently believed that type 2 diabetes is an immunological and oxidative illness [7]. Oxidative stress (OS) contributes to the progression and aggravation of type 2 diabetes in addition to being a consequence of insulin resistance, the main feature of the disease. Because of their weakened antioxidant defense mechanism, pancreatic β cells are more susceptible to reactive oxygen species (ROS), which can cause malfunction and cell death [8]. Moreover, OS reduces the amount and potency of insulin produced by interfering with the development and functioning of β cells [9- 11]. By interfering with insulin signaling pathways, OS can also impair insulin efficiency. As in prediabetes to diabetes, the advancement of hyperglycemia is largely dependent on the concomitant deterioration of insulin release and functionality [12]. ROS are ineffective as OS indicators because of their significant responsiveness and short half-life. On the other hand, ROS's a detrimental impact and their harm to proteins, lipids, and mitochondria are better indicators of OS [13]. Arachidonic acid peroxidation produces 8-isoprostane, a lipid peroxidation biomarker that is an excellent representation of a biomarker because of its remarkable stability [14].

In addition to oxidative damage, OS may additionally be measured by indicators of the antioxidant defense mechanism. Diminished glutathione (GSH), a non-enzymatic antioxidant found in erythrocytes, detoxifies ROS that penetrate the circulatory system. Glutathione peroxidase 1 oxidizes GSH to glutathione disulfide (GSSG) as part of GSH's electron-scavenger functionality. Because hyperglycemia makes the erythrocyte membrane stiffer, it prevents the transit of its precursor, cysteine, which lowers the quantity of GSH present [15]. Therefore, GSH and GSSG measurements are helpful in assessing the level of oxidative stress. Through enhancing the activity of mitochondria and reacting to OS, research in diabetic animals has shown that HN influences insulin responsiveness and efficiency [16], [17]. In diabetes mellitus, inflammatory factors are primarily generated by visceral white adipose tissue. Multiple processes, including hypoxia and macrophage penetration, facilitate the breakdown of cytokines and chemokines, numerous of resulting in are stimulated by hyperglycemia. Inflammatory variables, alongside oxidative stress, significantly contribute to the progression of diabetes by enhancing insulin resistance by means of modifications in β-cell function and disruption of insulin signaling [18- 20]. Considering the significant role of interleukins in mediating inflammation, encompassing both pro-inflammatory and anti-inflammatory properties, numerous interleukins have been examined in patients with T2DM. Interleukin-6 (IL-6) [21], interleukin-1β (IL-1β) [22], and interleukin-10 (IL-10) [23] have been identified and proposed to play multipurpose contributions to the progression of T2DM. Hypertension (HT) commonly occurs alongside diabetes, and the presence of both disorders elevates the risk of microvascular and macrovascular adverse effects, which includes an exponential rise in the threat of heart failure . Both disorders frequently overlap due to prevalent risk variables, especially insulin resistance, with approximately 75% of T2DM patients experiencing HT. The interplay between oxidative stress and inflammatory responses in diabetes results in blood vessels growth, characterized by changes in vessel framework, beginning with endothelial dysfunction [26]. Oxidative stress contributes to the emergence of endothelial dysfunction by inactivating nitric oxide, thereby increasing the risk of hypertension. This study primarily aimed to examine the progression of type-II diabetes mellitus alongside simultaneously hypertension, with a focus on the consequences of oxidative stress.

2. RESEARCH METHODS

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During the course of a year (October 2022 to February 2024), study participants were selected from the Internal Medicine department of the Combined Military Hospital in Pakistan and approved by the Institutional Ethics (Ethics Approval number: 2024/04281). The study also included experts from the Arabian and Pakistani countries (NMC Royal Hospital, Sharjah, United Arab Emirates). Additionally, prediabetes was diagnosed based on a fasting BGL of 5.6-6.9 mmol/L. We used GSH/GSSG and 8-OHdG as oxidative stress indicators. Because they demonstrate the effectiveness of the antioxidant defense system, GSH, 8-OHdG, and GSSG were chosen. Those who presented with acute inflammation, renal disease, or cardiovascular disease (CVD, etc.) were excluded. The remaining 384 participants were split up into four groups based on their disease status: 48 prediabetes (no HT), 22 T2DM, 68 T2DM+ HT (coexisting T2DM and HT), and 108 controls (no T2DM or HT). Patients taking antihypertensive drugs, such as beta and calcium channel blockers, angiotensin-converting enzyme (ACE) receptor blockers, ACE inhibitors, and hypoglycemic medications, as well as preventive statin use, were not eliminated from this investigation because the data collection was done in a healthcare environment rather than under controlled conditions. The method of collecting biomarkers was employed. Finger prick point of care testing was used to measure the subjects' fasting BGL. An authorized pathological laboratory produced the HbA1c, triglyceride, and cholesterol readings. After a five-minute rest, brachial artery blood pressure was recorded in a supine posture using a Welsh-Allyn BP recorder. If high blood pressure had been suspected, the measurement was performed two days later [27]. Urine specimens were used to evaluate the concentrations of oxidative stress biomarkers. Both GSH and GSSG are determined by dividing the samples. By blocking any free GSH in the sample with 2-vinylpyridine, GSSG is ascertained. Total GSH will be obtained from all specimens that have not undergone treatment with 2-vinylpyridine. The difference between the total GSH measured and the GSH produced from oxidized glutathione for the specimens that were administered 2-vinylpyridine is used to assess the free GSH content in the sample. Calorimetric measurements at 405 nm were used to figure out the GSH concentration [28]. The amounts of 8-OHdG and 8-isoprostane were measured in urine specimens. 8-OHdG levels were measured using the Kit using AChE-substrate for color development monitoring and competitive assay binding. Using the Isoprostane ELISA Kit, competitive assay binding, and color monitoring with horseradish peroxidase, 8-isoprostane was quantified. The statistical application SPSS 25 was used for all assessments. Sample size estimates were not carried out before statistical evaluation because this investigation was conducted using data that had already been gathered. Since it was established that continuous parameters did not follow a standard distribution, they were represented by the median. To find substantial distinctions between the four groups, Kruskal-Wallis tests were employed. The threshold for significance was $p<0.05$.

3. RESULTS AND DISCUSSION

Table 1 shows the number of individuals, biochemical information, and overall clinical characteristics. The control group's respondents were noticeably younger. Significantly more statins were used in the T2DM-HT group than in any other group, and significantly more in the T2DM group than in the control and prediabetes groups. The control, T2DM, and T2DM-HT groups were the only ones whose BMIs differed significantly. Additionally, although there were no differences between the prediabetes, T2DM, and T2DM-HT groups, BGL was significantly greater in the prediabetes, T2DM, and T2DM-HT groups than in the control group, as was to be anticipated. Compared to the control and prediabetes groups, the HbA1c levels were substantially higher in the T2DM and T2DM-HT groups (Table 1). Table 2 displays the OS biomarker values. After then, levels in the T2DM-HT group were once more equivalent to controls. Regarding OS, GSH first rose from controls to T2DM ($p<0.001$), nearly reaching statistical significance, and then significantly decreased when juxtaposed with concurrent T2DM-HT ($p<0.001$). From controls to T2DM, GSSG showed a similar pattern of increase ($p<0.01$), followed by a significant decline in T2DM-HT ($p<0.001$).

Table 1: Demographics and Clinical Characteristics of Patients

Characteristic	Group-I (Controls, n= 108)	Group-II (Prediabetes, n= 48)	Group III (T2DM, n= 22)	Group-IV (T2DM+HT, n= 68)	p-value
Sex (F), (%)	57%	58%	66%	55%	**0.422**
Alcohol, (%)	12%	16%	6.2%	14%	**0.453**
Smoking, (%)	6.7%	9.1%	9.4%	8.0%)	**0.732**
DM-Medications, (%)	0.0	0.0	62%	77%	**<0.001**
Antihypertensive Drugs, (%)	0.0	0.0	0.0	76%	**<0.001**
Statin Use, (%)	1.9%	0%	22%	48%	**<0.001**
Age (Years), Median (Q1-Q3)	52 (45-62)	57 (50-68)	55(49-65)	61(57,70)	**<0.001**
BMI (Kg/m²), Median (Q1-Q3)	25.7 (23.3, 29.1)	28.1 (24.5, 30.4)	29.2 (23.8, 34.1)	29.4 (26.0, 34.5)	**<0.001**
Lying-SBP (mmHg), Median (Q1-Q3)	120 (113, 128)	126 (116, 132)	128 (118, 132)	140 (130, 152)	**<0.001**
Lying-DBP (mmHg), Median (Q1-Q3)	77 (70, 82)	80 (70, 85)	78 (70, 84)	80 (74, 88)	**0.001**
Duration of diabetes (years), Median (Q1-Q3)	---	---	2.0 (1.0,4.2)	4.0 (1.0, 9.5)	**0.032**
Lipid profile and glycemic measurements					
BGL (mmol/L)	4.80 (4.43, 5.10)	5.90 (5.70, 6.25)	6.65 (5.93, 9.25)	7.50 (5.95, 9.60)	**<0.000**
HbA1c (%)	5.65 (5.40, 5.90)	5.80 (5.70, 6.10)	7.40 (6.30, 8.20)	7.60 (6.60, 8.15)	**0.000**
HDL (mmol/L)	1.30 (1.10, 1.40)	1.50 (1.20, 1.70)	1.20 (1.00, 1.52)	1.30 (1.10, 1.50)	**<0.001**
LDL (mmol/L)	3.10 (2.80, 3.40)	3.00 (2.50, 3.50)	2.70 (1.90, 2.82)	2.70 (2.10, 3.30)	**<0.001**
Triglycerides (mmol/L)	1.10 (0.90, 1.40)	1.00 (0.80, 1.30)	1.80 (1.23, 3.30)	2.00 (1.50, 2.20)	**0.000**
TC (mmol/L)	4.95 (4.50, 5.57)	5.00 (4.70, 5.50)	4.50 (3.90, 5.03)	4.60 (4.10, 5.50)	**0.000**

BGL, Fasting blood glucose levels; HDL, High density lipoprotein; LDL, Low density lipoprotein; TC, Total cholesterol.

a Significant difference between control and prediabetes group (p<0.05); b significant difference between control and T2DM group (p<0.05); c significant difference between control and T2DM

+HT group (p<0.05); d significant difference between prediabetes and T2DM group; e significant difference between prediabetes and T2DM+HT group; f significant difference between T2DM and T2DM+HT group

Table 2: Biomarkers Level in Four Groups

Characteristic	Group-I (Controls)	Group-II (Prediabetes)	Group III (T2DM)	Group-IV (T2DM+HT)	p-value
GSH (mM)	1,584 (1,524, 1,720)	1,629 (1,388, 1,827)	1,740 (1,666, 1,740)	1,314 (1,299, 1,682)	**<0.001**
GSSG (mM)	270 (243, 318)	345 (249, 358)	351 (275, 412)	261 (215, 357)	**<0.001**
GSH/GSSG	5.85 (5.01, 6.57)	4.81 (3.95, 7.13)	4.66 (4.23, 5.74)	4.97 (4.23, 7.38)	**<0.001**
8-OHdG (ng/mL)	143 (103, 212)	153 (153, 204)	110 (83, 144)	90 (49, 114)	**<0.001**

The precise processes separating normotensive and hypertensive individuals with T2DM remain enigmatic, and this field of research is still underdeveloped despite the increased consequences in patients with coexisting T2DM and HT [29]. In Australia, 15.5% of those aged 65 to 69 have type 2 diabetes, and 16% of adults over 25 have prediabetes [30]. Additionally, as was previously mentioned, about 25% of those with type 2 diabetes

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have normotension. It is therefore reasonable to anticipate variations in the sizes of the participant groups. There were variations in medication use among the groups, which probably affected a large number of the biomarker levels found in this investigation. For instance, the T2DM and T2DM-HT groups had lower LDL values, which were probably caused by a higher percentage of statin use in these groups. By accelerating the rate at which LDL is absorbed by hepatic cells, statin medication reduces intrahepatic cholesterol levels and increases the density of LDL receptors on hepatic cell surfaces [32]. In addition to being a result of insulin resistance, the primary characteristic of type 2 diabetes, oxidative stress (OS) also plays a role in the development and exacerbation of the condition. Pancreatic β cells are more vulnerable to reactive oxygen species (ROS), which can lead to dysfunction and cell death, due to their compromised antioxidant defense system. Furthermore, by disrupting the growth and function of β cells, OS lowers the quantity and strength of insulin generated. OS can also reduce insulin efficiency by disrupting insulin signaling pathways. Similar to the progression of prediabetes to diabetes, the concurrent decline in insulin secretion and function is a major factor in the development of hyperglycemia. Due to their high responsiveness and brief half-life, ROS are not useful as OS indicators. However, ROS's negative effects and damage to mitochondria, lipids, and proteins are better markers of OS. Because of its exceptional stability, 8-isoprostane, a lipid peroxidation biomarker produced by arachidonic acid peroxidation, is a great example of a biomarker. The global population of people with type II diabetes mellitus (T2DM), which is predicted to reach 700.2 million by 2045, constitutes one of the primary contributors of morbidity and early mortality worldwide. By the following year, the incidence of prediabetes, a metabolic disorder that precedes type 2 diabetes, is predicted to increase to 8.3% worldwide [2], [3]. The stage in between normoglycemia and overt type 2 diabetes is known as prediabetes [4]. Even though this illness frequently has no symptoms, pathogenic mechanisms and problems related to hyperglycemia are currently apparent [6]. Contrary to earlier findings, 8-OHdG levels did vary by group, with T2DM having lower levels than controls and prediabetes. This could affect the effects of statins, antihypertensive drugs, and antidiabetic medications. By scavenging ROS, preventing the production of advanced glycation end products, and upregulating antioxidants, hypoglycemic medications such as metformin, sulfonylureas, and thiazolidinediones demonstrate antioxidant qualities [33]. Furthermore, statin medication is thought to affect levels of oxidative DNA damage by reducing dyslipidemia, which lowers 8-OHdG, however studies have not confirmed this effect [34]. The much lower levels of 8-OHdG in the T2DM+HT group, where a significantly higher proportion of individuals were on statin medication, serve as additional evidence of this. Our data demonstrate the efficacy of ACE inhibitors and a number of antihypertensive drugs, such as the beta-blockers metoprolol, carvedilol, and bisoprolol, as well as ACE inhibitors, which have been shown to lower OS [35], [36]. To confirm if the reduction in oxidative stress improves the course of the patient's illness, longer follow-up research is required. The current results further confirm earlier findings [37] that T2DM causes increased GSH synthesis in response to rising OS, which is reflected in growing GSSG levels. The declining GSH levels as they approach T2DM+HT are consistent with findings that indicate a reduction in the effectiveness of GSH synthesis when coexisting conditions are present [38]. The actions of the aforementioned antihypertensive medications may lead to reduced levels of OS, which in turn may result in lower GSSG levels. Additionally, GSH is not just produced by recycling GSSG; it is also produced from the precursors glycine and cysteine, both of which have been shown to be significantly decreased in type 2 diabetes (T2DM) [39]. The examination of mitochondrial biomarkers at different phases of the disease was one of the study's novel discoveries. Going from controls to T2DM, HN significantly dropped, which is consistent with a prior finding by [40]. The pattern was reversed, though, as T2DM+HT levels rose once more, surpassing the control group by a significant margin. When paired with the results of the oxidative and inflammatory biomarkers, our results of a significant rise in systolic blood pressure in the DM+HT group can help doctors select the right drugs to lower blood pressure in this population. As a proactive therapy approach, the little elevations in blood pressure for the groups with prediabetes and type 2 diabetes can be analyzed similarly. When taken together, the observed changes in inflammatory markers and

OS show significant differences in the progression of diabetes from no diabetes to DM+HT in a clinical setting where patients must take medication. This suggests that adding more biomarkers to the patient review could be beneficial. T2DM and its co-occurring comorbidities, such HT, are becoming more common. The significance that oxidative stress plays in the development of diabetes has been emphasized by current understanding of disease progression in general [41].

4. CONCLUSION

It is possible to draw some significant implications. The research has validated earlier findings of increased oxidative stress in type II diabetes and prediabetes. Furthermore, oxidative stress biomarkers could be useful for tracking how well antihypertensive drugs are working. Additionally, it seems to be a trustworthy biomarker for HT even when medicine is used, and it could be a useful predictor in long-term, follow-up research. The assessments of inflammatory processes and OS in healthcare settings provided in the current investigation are the first of their kind and can serve as the foundation for additional investigations into to determine thresholds and customized treatment determined by these parameters.

5. REFERENCES

[1] Huang K, Liang Y, Ma Y, Wu J, Luo H, Yi B. The variation and correlation of serum adiponectin, nesfatin-1, IL-6, and TNF-a levels in prediabetes. Front Endocrinol (2022) 13:1–10. doi: 10.3389/fendo.2022.774272

[2] Abhilasha, Mitra P, Suri S, Saxena I, Shukla RKG, Shukla KK, et al. Downregulation of interleukin-10 receptor (IL-10R) along with low serum IL-10 levels in newly diagnosed type 2 diabetes mellitus patients. Gene Rep (2021) 24:101251. doi: 10.1016/j.genrep.2021.101251

[3] Wang Z, Shen XH, Feng WM, Ye GF, Qiu W, Li B. Analysis of inflammatory mediators in prediabetes and newly diagnosed type 2 diabetes patients. J Diabetes Res (2016) 2016. doi: 10.1155/2016/7965317

[4] Nemati F, Rahbar-roshandel N, Hosseini F, Mahmoudian M, Shafiei M. Anti- inflammatory effects of anti-hypertensive Agents : influence on interleukin-1 b secretion by peripheral blood polymorphonuclear leukocytes from patients with essential hypertension. Clin Experiment Hypertens (2011) 33:69–76. doi: 10.3109/ 10641963.2010.496521

[5] Rabkin SW, Langer A, Ur E, Calciu CD, Leiter LA. Inflammatory biomarkers CRP, MCP-1, serum amyloid alpha and interleukin-18 in patients with HTN and dyslipidemia: impact of diabetes mellitus on metabolic syndrome and the effect of statin therapy. Hypertens Res (2013) 36(6):550–8. doi: 10.1038/hr.2012.214

[6] Cortez A, Muxfeldt E. Monocyte chemoattractant protein-1 and hypertension: an overview. Hipertens y Riesgo Vasc (2022) 39(1):14–23. doi: 10.1016/j.hipert.2021.11.003

[7] Komiyama M, Takanabe R, Ono K, Shimada S, Wada H, Yamakage H, et al. Association between monocyte chemoattractant protein-1 and blood pressure in smokers. J Int Med Res (2018) 46(3):965–74. doi: 10.1177/0300060517723415

[8] Gallo G, Volpe M, Rubattu S. Angiotensin receptor blockers in the management of hypertension: a real-world perspective and current recommendations. Vasc Health Risk Manag (2022) 18:507–15.

ISSN: 1311-1817
Volume 26, Issue 12, December, 2024

[9] Saavedra JM. Angiotensin receptor blockers are not just for hypertension anymore. Physiology. (2021) 36(3):160–73. doi: 10.1152/physiol.00036.2020

[10] Castiñeiras-Landeira MI, Rodiño-Janeiro BK, Paradela-Dobarro B, Batista- Oliveira AL, Raposeiras-RoubıńS, González-Peteiro M, et al. Change of concept about the regulation of angiotensin II-induced monocyte chemoattractant protein-1 production in human endothelial cells. Vascul Pharmacol (2016) 80:20–34.

[11] Prakash Chandra Bhatta, Upendra Chand, Ramesh Kanbargi & Priya Nandimath (2024). The Assessment of Demographic & Socio-economic barriers associated with Disuse of Contraceptive Methods among Married Women of Dhangadhi, Nepal. Dinkum Journal of Medical Innovations, 3(03):240-256.

[12] Rakesh Kumar Mahato, Sagar Pokharel & Avinash Sahani (2024). Knowledge & Practice Regarding Neonatal Resuscitation among Health Care Providers in Tertiary Care Hospitals of Nepal. Dinkum Journal of Medical Innovations, 3(03):257-270.

[13] Ribha Verma, Ramakant Lamichhane & Joshna Shrestha (2024). Formulation & In Vitro Evaluation of Effect of Polymer in Gastro-Retentive Drug Delivery System Using Ciprofloxacin Hydrochloride as A Model Drug. Dinkum Journal of Medical Innovations, 3(03):271-289.

[14] Rukmani Kafle (2024). Medication Adherence to Psychotropic Drugs among Patient Attending OPD of Teaching Hospital Chitwan Medical College Teaching Hospital, Nepal. Dinkum Journal of Medical Innovations, 3(04):321-336.

[15] Raksha Rimal, Anu Kafle, Arju Sah, Ankur Bista, Anshu Yadav & Sampada Khatiwada (2024). Comparative Study of Hematological Parameters among First-Time Blood Donors & Repeat Blood Donors of Kathmandu Valley. Dinkum Journal of Medical Innovations, 3(04):302-312.

[16] Rences G. Gardose (2024). The Experimental Study of C. Papaya Leaf Extract & Its Effect on the Platelet Count: A Potential Treatment of Dengue Patients. Dinkum Journal of Medical Innovations, 3(04):313-320.

[17] Rukmani Kafle (2024). Medication Adherence to Psychotropic Drugs among Patient Attending OPD of Teaching Hospital Chitwan Medical College Teaching Hospital, Nepal. Dinkum Journal of Medical Innovations, 3(04):321-336.

[18] Dr. Surendra Prasad Bhatta, Dr. Binita Pradhan & Dr. Pratibha Mishra (2024). Relationship between Screening and Diagnostic Performance of 50gm GCT vs. 75gm DIPSI test of Gestational Diabetes Mellitus: A Cross Sessional Study of Paten Hospital, Lalitpur. Dinkum Journal of Medical Innovations, 3(05):416-423.

[19] Charissa Rosamond D. Calacday (2024). Patient Safety Culture in Selected Government Hospitals in the National Capital Region (NCR) Towards Improved Healthcare Practices. Dinkum Journal of Medical Innovations, 3(05):349-357.

[20] Dr. Amit Singh, Dr. Ashok Yadav & Dr. Anish Ahemad (2024). Correlation between expulsion rate of distal ureteric calculus up to 8mm in size with CRP level, WBC count and Neutrophil percentage. Dinkum Journal of Medical Innovations, 3(05):358-365.

[21] Dr. Kul Raj Shahi, Dr. Ujjwol Arayal & Dr. Sandesh Pandit (2024). Study on Risk Factors of Non Alcoholic Fatty Liver Disease in Patients Attending NGMCTH. Dinkum Journal of Medical Innovations, 3(05):367-378.

[22] Schöttker B, Xuan Y, Gào X, Anusruti A, Brenner H. Oxidatively damaged DNA/RNA and 8-isoprostane levels are associated with the development of type 2 diabetes at older age: results from a large cohort study. Diabetes Care (2020) 43(1):130– 6. doi: 10.2337/dc19-1379

[23] Ma E, Ingram KH, Milne GL, Timothy Garvey W. F2-isoprostanes reflect oxidative stress correlated with lean mass and bone density but not insulin resistance. J Endocr Soc (2017) 1(5):436. doi: 10.1210/js.2017-00006

[24] Il'yasova D, Wong BJ, Waterstone A, Kinev E, Okosun IS. Systemic F2-isoprostane levels in predisposition to obesity and type 2 diabetes: emphasis on racial differences. Divers Equal Heal Care (2017) 14(2):0–0. doi: 10.21767/2049-5471.100098

[25] Choi SW, Ho CK. Antioxidant properties of drugs used in type 2 diabetes management: could they contribute to, confound or conceal effects of antioxidant therapy? Redox Rep (2018) 23(1):1–24. doi: 10.1080/13510002.2017.1324381

[26] Donmez-Altuntas H, Bayram F, Coskun-Demirkalp AN, Baspınar O, Kocer D, Toth PP. Highlight article: therapeutic effects of statins on chromosomal DNA damage of dyslipidemic patients. Exp Biol Med (2019) 244(13):1089–95. doi: 10.1177/ 1535370219871895

[27] Ciciliot S, Fadini GP. Modulation of obesity and insulin resistance by the redox enzyme and adaptor protein p66shc. Int J Mol Sci (2019) 20(4):1–11.

[28] Mousavi S, Khazeei Tabari MA, Bagheri A, Samieefar N, Shaterian N, Kelishadi R. The role of p66Shc in diabetes: a comprehensive review from bench to bedside. J Diabetes Res (2022) 2022. doi: 10.1155/2022/7703520

[29] 75. Pan Z, Dong H, Huang N, Fang J. Oxidative stress and inflammation regulation of sirtuins: new insights into common oral diseases. Front Physiol (2022) 13:1–20. doi: 10.3389/fphys.2022.953078

[30] Bartoli-Leonard F, Wilkinson FL, Schiro A, Inglott FS, Alexander MY, Weston R. Suppression of SIRT1 in diabetic conditions induces osteogenic differentiation of human vascular smooth muscle cells via RUNX2 signalling. Sci Rep [Internet]. (2019) 9 (1):1–16.

[31] Shi S, Chen Y, Luo Z, Nie G, Dai Y. Role of oxidative stress and inflammation- related signaling pathways in doxorubicin-induced cardiomyopathy. Cell Commun Signal (2023) 21(1):1–20.

[32] Whitsed R, Horta A, Jelinek HF. Assessing representativeness of a rural Australian clinical database using a spatial modelling approach. In: Eskola H., Väisänen O., Viik J., Hyttinen J. (eds) EMBEC & NBC 2017. EMBEC NBC 2017 2017. IFMBE Proceedings (2018) 65. Singapore: Springer.

[33] Nguyen TTU, Yeom JH, Kim W. Beneficial effects of vitamin e supplementation on endothelial dysfunction, inflammation, and oxidative stress biomarkers in patients receiving hemodialysis: a systematic

ISSN: 1311-1817
Volume 26, Issue 12, December, 2024

review and meta-analysis of randomized controlled trials. Int J Mol Sci (2021) 22(21)11923.

[34] Kochlik B, Grune T, Weber D. New findings of oxidative stress biomarkers in nutritional research. Curr Opin Clin Nutr Metab Care (2017) 20(5):349–59.

[35] Sivitz WI, Yorek MA. Mitochondrial dysfunction in diabetes: from molecular mechanisms to functional significance and therapeutic opportunities. Antioxidants Redox Signal (2010) 12(4):537–77.

[36] Sandra Rumi Madhu (2024). A Study on Anemia in Adolescent Girls Due to Food Habit at Gazipur District in Bangladesh. Dinkum Journal of Medical Innovations, 3(06):469-482.

[37] Dr. Bikram Duwal, Dr. Biraj Singh Karki, Dr. Lok Bahadur Kathayat & Dr. Dishan Maharjan (2024). A Study on Gallbladder Retrieval via Epigastria V/S Supraumbilical port in Laparoscopic Cholecystectomy. Dinkum Journal of Medical Innovations, 3(06):424-433.

[38] Jami Parvin Nitu, Kamrun Nahar, G. R. M. Shafy Parvez, Sumaiya Sabrin, Mahbub Ur Rahim & ANM Shamsul Islam (2024). Experiences of Dental Surgeon in Providing Dental Health Care during Covid-19 Pandemic. Dinkum Journal of Medical Innovations, 3(06):434-441.

[39] Yeung RO, Al Jundi M, Gubbi S, Bompu ME, Sirrs S, Tarnopolsky M, et al. Management of mitochondrial diabetes in the era of novel therapies. J Diabetes Complications (2021) 35(1):107584.

[40] Vassalle C, Gaggini M. Type 2 diabetes and oxidative stress and inflammation: pathophysiological mechanisms and possible therapeutic options. Antioxidants. (2022) 11(5):11–4.

[41] Darenskaya MA, Kolesnikova LI, Kolesnikov SI. Oxidative stress: pathogenetic role in diabetes mellitus and its complications and therapeutic approaches to correction. Bull Exp Biol Med (2021) 171(2):179–89.

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