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ABSTRACT:

Background. Diabetes mellitus (DM) is a prevalent disease that, if not managed properly, can lead to a variety of problems, including diabetic foot. Glycated hemoglobin A1c (HbA1c), FBS, amylase, and lipase are important diabetic management indicators that are now employed as diagnostic tests.

Objective. To evaluate the value of amylase lipase as a predictive marker in diabetic foot

Patients and methods. This study included 30 patients who reported to Baghdad Hospital with diabetic feet between November 2023 and November 2024. All patients had their HbA1c, amylase, lipase, and FBS levels tested. Means, independent t-tests, and the F-test were used in the statistical analysis.

Results. Thirty patients aged 35-75 years were evaluated, with significant differences (P = 0.001). People with diabetic feet had a high percentage of Hba1c and FBS, as well as a substantial drop in amylase and lipase measures, with a difference value of (P=0.001).

Conclusion. HbA1c amylase lipase is an important prognostic factor in diabetic foot patients. Levels greater than eight were related with a poor prognosis and prolonged hospitalization. Thus, diabetes management is a critical role in preventing and treating diabetic complications.

Keywords: diabetic foot, hemoglobin A1c, FBS, amylase, lipase

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Abbreviations (in alphabetical order)

DFU – diabetic foot ulcer

DM – diabetes mellitus

FBS – fasting blood sugar

HbA1c – hemoglobin A1c

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder with a high global prevalence and is a significant public health concern. According to estimates, 425 million people will have diabetes by 2025, accounting for roughly 10% of the world's population, with type 2 diabetes accounting for 90% [1]. Acute and chronic diabetes complications, including nephropathy, retinopathy, cardiovascular disease, and diabetic foot, are related to hospitalization and death [2,3]. These precautions may generate undue concern, particularly in younger patients [4] and those with neuropsychiatric illnesses [5,6]. Glycated proteins such as HbA1C have been reported to raise serum cortisol levels, salivary cortisol levels, plasma and prolactin levels [7], as well as other assumed diabetes indicators [8]. Salivary indicators include the first glycemic control enzyme in food digestion (salivary Amylase) [9]. Furthermore, in diabetic patients, fasting blood glucose and salivary glucose test values are significantly correlated [10,11], salivary glucose test values and HbA1c [10,12], and other salivary markers, such as fructosamine glycoprotein, have a significant correlation with HbA1c and blood glucose levels [13]. Diabetic foot problems are the most common long-term complication of diabetes, accounting for roughly half of all diabetes-related hospital days. Diabetic feet are particularly susceptible to issues due to their inability to resist stress. Diabetic foot ulcers (DFUs) are one of the most prevalent and dangerous consequences of diabetes. They affect 15% of all diabetic patients. and place a significant financial burden [14, 15]. Diabetic patients account for around 50% of lower extremity amputations. Diabetes-related lower extremities problems have become a significant public health concern in both developing and affluent countries. People with diabetes have a 25% lifetime risk of getting foot ulcers [16], which is mainly caused by vascular insufficiency and peripheral neuropathy. Approximately 20% of diabetic individuals with foot ulcers have primarily arterial insufficiency, 50% have mainly neuropathy, and roughly 80% have both diseases [17], [18]. Neuropathy, peripheral vascular disease, and a decreased resistance to infection are all known risk factors for the development of DFU, which resembles a chronic wound. Hyperglycemia is caused by a negative result and its activity, which might impact external production and secretions. Some generate enzymes such as Amylase, lipase, and protease. [19] When blood is collected from the proximal islets, secretory afferent cells are exposed to high levels of endocrine hormones. Evidence indicates that endocrine pancreatic hormones, particularly insulin, influence pancreatic exocrine function. Insulin negatively impacts secretory cells. Amylase and lipase are among the enzymes found in the secretory acinar

cells that aid in the digestion of specific food components [.20]. Amylase is the primary enzyme responsible for breaking down starch into maltose and malt triose while also removing dextrins during digestion. Lipase is a digestive enzyme generated in the pancreas and transferred to the gut, where it converts triglycerides to fatty acids and monoglycerides. A lack of pancreatic enzymes causes poor digestion and hunger. [21] Low serum amylase levels have long been thought to indicate deteriorating pancreatic damage caused by advanced illness. However, recent research has found that low serum amylase levels are connected with metabolic syndrome and diabetes. Hemoglobin A1c (HbA1c) also indicates a patient's glycemic state for the last three months [22].

METHODS AND MATERIALS

Study design

Patients with diabetes mellitus and foot ulcers were seen at the outpatient clinic of Baghdad Teaching Hospital, Medical City, between November 2023 and November 2024. A total of 30 diabetic foot ulcer patients and 20 healthy individuals. The patients ranged in age from 35 to 75 years (mean age 52); a specialist physician detected the presence of foot ulcers after a physical and x-ray examination. Documenting the patient's medical history.

Blood sampling

Venous blood was taken from all participants with disposable syringes. The blood was gently expelled and separated into two portions. The first was discharged into a tube containing an anticoagulant used in hematological assays, such as HBA1C. The second part was emptied into plain tubes, allowing the blood to coagulate before being centrifuged to separate the serum components. The first was utilized immediately for a regular test, which comprised serum FBS, amylase, and lipase.

Outcome measurements

Fasting blood sugar, amylase, and lipase levels were measured using a fully automated chemistry analyzer, the BS240Pro instrument. Using an EDTA tube. HBA1C was measured using a Clover device, which uses an immunological assay approach.

Statistical analysis

A statistical application, SPSS version 24.0, was used. The variations in variable means between the control and sick groups were analyzed using a one-way ANOVA test. The data were expressed as mean ± SD. Pearson's correlation coefficient (r) was used to examine correlations between all variables under research, and data analytic methods included linear regression analyses. Statistics were considered significant when the p-value was less than 0.001. The study variables' cut-off values, sensitivity,

specificity, and area under the curve were displayed using the receiver operating characteristic (ROC) curve.

RESULTS

Table (1) shows the incidence rates of diabetic foot ulcers in patients aged less than 70 and over 35. While Table (2) shows diabetes patients who are most impacted by the foot, Table (3) reveals that the most significant areas of foot ulcers are at the bottom of the big toe and the least at the ball of the foot. There is a substantial difference between FBS and HbA1c amylase lipase levels in diabetic foot ulcer patients and the control group. Problems caused the gap between healthy people and patients. A. Retinopathy (reduced vision, exudation, and retinal hemorrhage). To Neuropathy (pain, numbness, loss of feeling) C. Nephropathy (pleural effusion, ascites, subcutaneous edema in the legs, increased amylase levels, blood, and albuminuria). D - Gastropathy. The figure depicts the percentage difference in ages between them. Table (4) represents the distribution of the average percentage of HbA1c, FBS, amylase, and lipase among patients with foot ulcers.

Table 1: Age distribution

Age group	Percentage of diabetic foot ulcer
35-45	11.5 %
46-55	23.5 %
56-65	29.5 %
66-75	35.5 %
Total	100 %

Table 2: The site of foot ulcers distribution

Site	Number of patients	Percent
Ball of the foot	13	40%
Bottom of the big toe	17	60%
Total	30	100%

Table 3: Fasting blood sugar levels Hemoglobin, glycosylated amylase and lipase in control subjects and diabetic foot ulcers

	Control (n=20)	Diabetic foot ulcer (n=30)
FBS (mg/dL)	51.23 ± 6.25	310.5 ± 8.09
HBA1c %	3.89 ± 1.26	10.78 ± 2.37
Amylase (U/L)	13.52 ± 3.14	2.13 ± 0.41
Lipase (U/L)	15.34 ± 1.99	3.01 ± 1.19

Table 4: Distribution of mean HbA1c, FBS, amylase and lipase among the patients with foot ulcer

Age group	HbA1c%	FBS (mg/dl)	Amylase (U/L)	Lipase (U/L)
35-45	8.18 ± 0.12	205 ± 5.25	15.79 ±3.87	12.5 ± 2.97
46-55	8.56 ± 0.13	218.66 ± 6.67	13.78 ± 2.79	9.18 ± 3.21
56 - 65	9.79 ± 0.29	275.5 ± 13.07	9.72 ± 1.24	7.14 ± 1.45
66 - 75	11.01 ± 0.27	354.5 ± 41.07	7.85± 0.26	3.98± 1.64

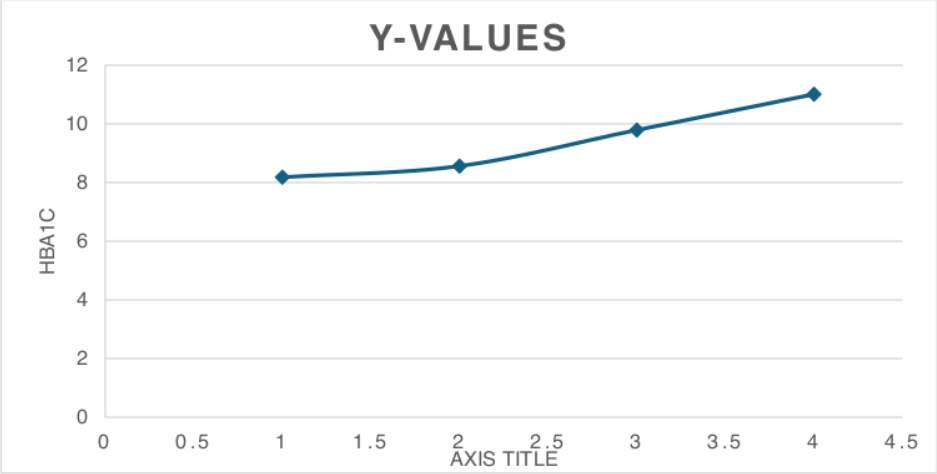

Figure1: The relationship between Hba1c and Age

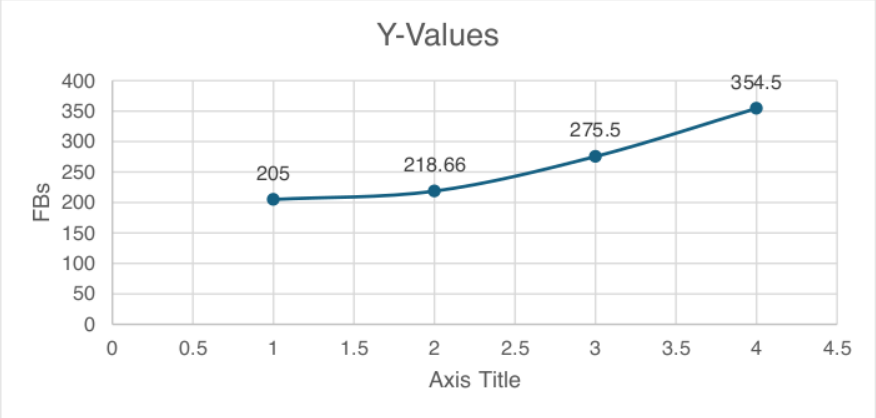

Figure 2: The relationship between FBS and Age

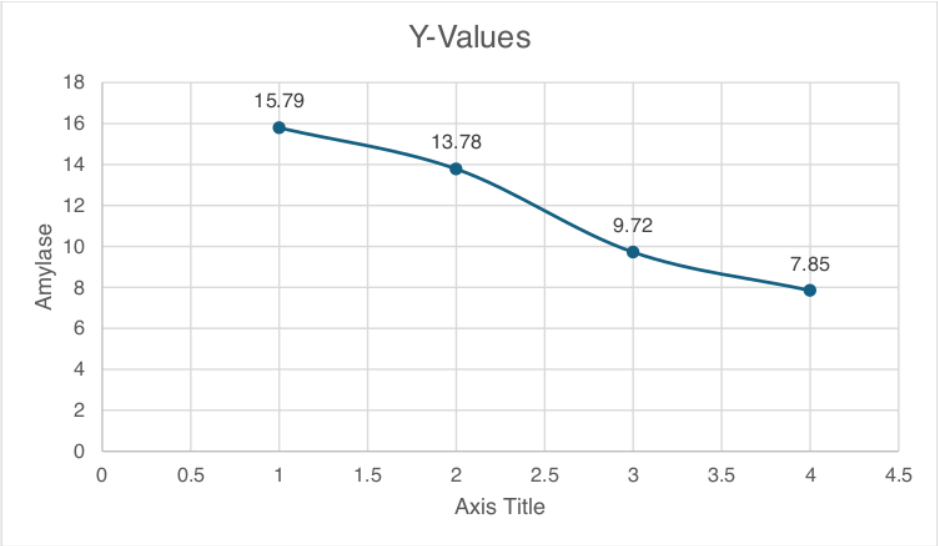

Figure3: The relationship between Amylase and Age

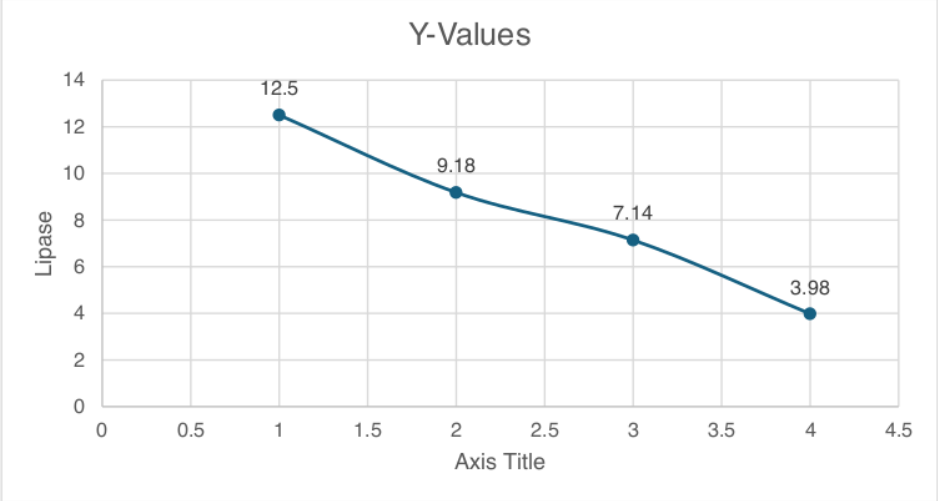

Figure 4: The relationship between lipase and Age

DISCUSSION

This study found a linear association between HbA1c levels and Wagner classification grades: patients classified as grades 0-2 had somewhat higher HbA1c levels, while those classified as grades 3-5 had the highest HbA1c values. Diabetic foot syndrome

comprises a variety of diabetic foot lesions, such as infections, neuropathic osteoarthritis, and diabetic foot ulcers. Diabetic foot lesions comprise roughly 15% of all diabetic foot lesions. They are expected to rise to 25% in the future, making it the most serious disorder that can result in limb amputation [23]. Diabetic foot is caused by tiny injuries that people with diabetes may overlook for a long period owing to peripheral nerve damage. Furthermore, peripheral nerve dysfunction is frequently coupled with peripheral artery disease, resulting in insufficient blood supply to the extremities, a condition known as diabetic vasculopathy, which can lead to diabetic foot. Thus, the diabetic foot might be neuropathic, neuroischemic, or ischemic [24]. Zubair et al. and Ozenc et al. found inconsistent associations between HbA1c levels and the Wagner classification; Zubair et al. found a statistically significant correlation, but Ozenc et al. found a statistically negligible link [25,26]. Sarinnapakorn et al. discovered that whereas HbA1c levels and fasting blood glucose values are not substantially associated with diabetic foot, nearly half of DM patients are at moderate or high risk for diabetic foot. Almost all of the patients in this study had uncontrolled diabetes, as shown by a mean HbAC1 of 8.55% and a mean FBS of 292 mg/dl. However, no significant link was found between amputation risk and numerous parameters, including cumulative blood glucose levels, FBS, and other variables. First, FBS and HbAC1 levels did not differ across study participants with modest amputations, large amputations, or DFU. All individuals (dead or living) had poorly managed diabetes with different degrees of complications at the time. of admission to an orthopedic unit [27]. Fungal infections of the foot can be superficial or intricate deep tissue lesions. *Candida* species *and Fusarium solani* are both commonly affected. [28]. In this study, fungus-positive patients had a mean diabetes duration of 7.89 ± 6.14 years. While Al-Rubeaan et al. [29] found a link between diabetic foot ulcers and diabetes duration, no significant correlation was found between fungal infection and diabetes duration in the current study. Fungal infections in the foot can range from superficial to deep tissue diseases. Candida species and *Fusarium solani* are both commonly affected. The incidence of fungal infections is directly proportional to the length of diabetes. Patients had an average duration of diabetes of 7.7 years. had fungal infections [28]; Al-Rubeaan et al. [29] showed a tight relationship between diabetic foot ulcers and diabetes duration, while our investigation revealed no significant link between fungal infection and diabetes length. The authors ascribe these levels to hormonal and metabolic alterations in diabetes patients, including microvascular problems and

autonomic neuropathy, both of which can impact salivary secretions [30]. Hertz [31], using mass spectrometry data, proposed that poor buildup of α-amylase speckles in diabetes patients may be connected to alterations in oral anti-inflammatory status. They also imply that diabetes will only impact a subset of alpha-amylase isoforms. These apparent disparities might be attributed to the manner of saliva collection and other variables that can influence salivary amylase levels, such as diabetes duration [32] and comorbidities [33], such as Parkinson's disease [34]. Other illnesses that affect saliva flow include gastroesophageal reflux [35]. Other relevant variables include the use of parasympathetic system-active drugs such as pilocarpine, muscle relaxants, and antiepileptic and antipsychotic medications. Anticholinergic medications, for example, interfere with acetylcholine's activity. antihistamines and cytostatics. In studies with identical saliva sample collecting conditions, salivary amylase, and blood glucose were found to be positively associated. Salivary amylase has a high connection with total salivary proteins [36] and serum amylase [37]. It should be noted that, according to the studies mentioned above, not all parameters show a good correlation between saliva and blood, as well as differences in concentration depending on saliva flow in the case of polar or ionic compounds of high molecular weight transported by saliva or excreted through excretion. [38]. Nakajima et al. discovered that insulin-dependent diabetics have reduced blood lipase. and amylase levels. These findings might be explained by the reduced activity of adenoblast cells in the proximity of insulin-depleted islets. In another study. Other pancreatic enzymes, including elastase, trypsin, and chymotrypsin, were lowered. Analyzing pure pancreatic secretions embedded in the pancreatic duct lumen in diabetic individuals with uncontrolled hyperglycemia revealed considerably lower amylase concentrations and somewhat higher bicarbonate and lipase levels. Diabetes is one of the most common chronic illnesses, threatening the lives of millions of people globally [39]. Dyslipidemia, which is characterized by hyperglycemia and low blood insulin, is a significant risk factor for diabetes complications and has been extensively researched [40, 41].

CONCLUSION AND RECOMMENDATIONS

HbA1c, FBS Amylase, and lipase are key prognostic markers in diabetic foot patients. Levels greater than eight were linked to worse prognoses, complications, longer hospital stays, and more severe and costly therapy and surgical interventions. This

raises the strain on the health-care budget. Controlling diabetes is a critical aspect in preventing diabetic complications. If it happens, appropriate control may lessen the impact.

Authors contributions:

All authors made significant contributions to the development of the first and amended versions of this manuscript. They accept full responsibility for the integrity of all parts of their work.

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Conflict of interest:

The authors declare no conflict of interest.

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References

1.Peters SAE, Woodward M. Sex Differences in the Burden and Complications of Diabetes. Current Diabetes Reports [Internet]. 2018 Apr 18;18(6). Available from: http://dx.doi.org/10.1007/s11892-018-1005-5

2.Boulton AJ, Vileikyte L, Ragnarson-Tennvall G, Apelqvist J. The global burden of diabetic foot disease. The Lancet [Internet]. 2005 Nov;366(9498):1719–24. Available from: http://dx.doi.org/10.1016/s0140-6736(05)67698-2 references

3.Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Research and Clinical Practice [Internet]. 2018 Apr;138:271–81. Available from: http://dx.doi.org/10.1016/j.diabres.2018.02.023

4.McLenon J, Rogers MAM. The fear of needles: A systematic review and meta-analysis. Journal of Advanced Nursing [Internet]. 2018 Sep 11;75(1):30–42. Available from: http://dx.doi.org/10.1111/jan.13818

5.Kanehisa M, Kawashima C, Nakanishi M, Okamoto K, Oshita H, Masuda K, et al. Gender differences in automatic thoughts and cortisol and alpha-amylase responses to acute psychosocial stress in patients with obsessive-compulsive personality disorder. Journal of Affective Disorders [Internet]. 2017 Aug;217:1–7. Available from: http://dx.doi.org/10.1016/j.jad.2017.03.057

6.Kawano A, Tanaka Y, Ishitobi Y, Maruyama Y, Ando T, Inoue A, et al. Salivary alpha-amylase and cortisol responsiveness following electrical stimulation stress in obsessive–compulsive disorder patients. Psychiatry Research [Internet]. 2013 Aug;209(1):85–90. Available from: http://dx.doi.org/10.1016/j.psychres.2012.11.010

7.Deneva T, Ianakiev Y, Keskinova D. Burnout Syndrome in Physicians—Psychological Assessment and Biomarker Research. Medicina [Internet]. 2019 May 24;55(5):209. Available from: http://dx.doi.org/10.3390/medicina55050209

8.Tiongco REG, Arceo ES, Rivera NS, Flake CCD, Policarpio AR. Estimation of salivary glucose, amylase, calcium, and phosphorus among non-diabetics and diabetics: Potential identification of non-invasive diagnostic markers. Diabetes & Metabolic S

yndrome: Clinical Research & Reviews [Internet]. 2019 Jul;13(4):2601–5. Availa ble from: http://dx.doi.org/10.1016/j.dsx.2019.07.037

9.Malathi L. Estimation of Salivary Amylase in Diabetic Patients and Saliva as a Diag nostic Tool in Early Diabetic Patients. JOURNAL OF CLINICAL AND DIAGNOSTI C RESEARCH [Internet]. 2013; Available from: http://dx.doi.org/10.7860/jcdr/2013/7 574.3634

10.Malhotra SL. On the causation of diabetes mellitus (effect of saliva on blood gluco se levels in oral glucose tolerance tests). Medical Hypotheses [Internet]. 1982 Mar;8(3):311–8. Available from: http://dx.doi.org/10.1016/0306-9877(82)90128-1

11.Ephraim RKD, Anto EO, Acheampong E, Fondjo LA, Barnie RB, Sakyi SA, et al. Fasting salivary glucose levels is not a better measure for identifying diabetes mellitus than serum or capillary blood glucose levels: comparison in a Ghanaian population. H eliyon [Internet]. 2019 Mar;5(3):e01286. Available from: http://dx.doi.org/10.1016/j.h eliyon.2019.e01286

12.Patel BJ, Mehta DN, Vaghani A, Patel K. Correlation of Body Mass Index (BMI) w ith Saliva and Blood Glucose Levels in Diabetic and Non-Diabetic Patients. Journal of Pharmacy and Bioallied Sciences [Internet]. 2023 Jul;15(Suppl 2):S1204–7. Available from: http://dx.doi.org/10.4103/jpbs.jpbs_159_23

13.Nakamoto I, Morimoto K, Takeshita T, Toda M. Correlation between saliva glycate d and blood glycated proteins. Environmental Health and Preventive Medicine [Intern et]. 2003 Jul;8(3):95–9. Available from: http://dx.doi.org/10.1007/bf02897922

14.Boulton AJ, Vileikyte L, Ragnarson-Tennvall G, Apelqvist J. The global burden of diabetic foot disease. The Lancet [Internet]. 2005 Nov;366(9498):1719–24. Available f rom: http://dx.doi.org/10.1016/s0140-6736(05)67698-2

15.Varani J, Warner RL, Gharaee-Kermani M, Phan SH, Kang S, Chung J, et al. Vitam in A Antagonizes Decreased Cell Growth and Elevated Collagen-Degrading Matrix M etalloproteinases and Stimulates Collagen Accumulation in Naturally Aged Human Sk in1. Journal of Investigative Dermatology [Internet]. 2000 Mar;114(3):480–6. Availabl e from: http://dx.doi.org/10.1046/j.1523-1747.2000.00902.x

16.Zubair M, Malik A, Ahmad J. Clinico-microbiological study and antimicrobial drug resistance profile of diabetic foot infections in North India. The Foot [Internet]. 2011 Mar;21(1):6–14. Available from: http://dx.doi.org/10.1016/j.foot.2010.10.003

17.Economic Costs of Diabetes in the U.S. in 2007. Diabetes Care [Internet]. 2008 Ma r 1;31(3):596–615. Available from: http://dx.doi.org/10.2337/dc08-9017

18.Singh N. Preventing Foot Ulcers in Patients With Diabetes. JAMA [Internet]. 2005 Jan 12;293(2):217. Available from: http://dx.doi.org/10.1001/jama.293.2.217

19.Daniel V, Daniel K. Perception of Nurses' Work in Psychiatric Clinic. Clinical Med icine Insights [Internet]. 2020 Sep 19;27–33. Available from: http://dx.doi.org/10.5284 5/cmi/2020v1i1a5

20.McGurk S. Ganong's Review of Medical Physiology – 23rd edition Kim E Barratt Ganong's Review of Medical Physiology – 23rd editionet al |McGraw Hill Medical|72 6pp|£41.99978 0 07160567 00071605673. Nursing Standard [Internet]. 2010 Jan 20;2 4(20):30–30. Available from: http://dx.doi.org/10.7748/ns.24.20.30.s35

21.Ambad R, Jha RK, Chandi DH, Hadke S. Association of leptin in diabetes mellitus and obesity. RESEARCH JOURNAL OF PHARMACY AND TECHNOLOGY [Inter net]. 2020;13(12):6295–9. Available from: http://dx.doi.org/10.5958/0974-360x.2020. 01095.1

22 Scherm MG, Daniel C. miRNA Regulation of T Cells in Islet Autoimmunity and T ype 1 Diabetes. Current Diabetes Reports [Internet]. 2020 Jul 28;20(9). Available from : http://dx.doi.org/10.1007/s11892-020-01325-9

23.Lauterbach S, Kostev K, Kohlmann T. Prevalence of diabetic foot syndrome and its risk factors in the UK. Journal of Wound Care [Internet]. 2010 Aug;19(8):333–7. Avai lable from: http://dx.doi.org/10.12968/jowc.2010.19.8.77711

24Andrews KL, Houdek MT, Kiemele LJ. Wound management of chronic diabetic foo t ulcers. Prosthetics & Orthotics International [Internet]. 2015 Feb;39(1):29–39. A vailable from: http://dx.doi.org/10.1177/0309364614534296

25.Zubair M. Glycosylated Hemoglobin in Diabetic Foot and its Correlation with Clin ical Variables in a North Indian Tertiary Care Hospital. Journal of Diabetes & Me tabolism [Internet]. 2015;06(07). Available from: http://dx.doi.org/10.4172/2155-6156 .1000571

26.Özenç S, Simsek K, Yildirim AO, Arslan E, Sari S, Ince M, et al. Association betw een the development of diabetic foot and serum fetuin-A levels. Polish Archives of Int ernal Medicine [Internet]. 2013 Aug 19;123(10):513–8. Available from: http://dx.doi.o rg/10.20452/pamw.1921

27.Smith-Strøm H, Iversen MM, Igland J, Østbye T, Graue M, Skeie S, et al. Severity and duration of diabetic foot ulcer (DFU) before seeking care as predictors of healing t ime: A retrospective cohort study. Sambhara S, editor. PLOS ONE [Internet]. 2017 Ma y 12;12(5):e0177176. Available from: http://dx.doi.org/10.1371/journal.pone.0177176

28 Raymundo M, Mendoza MT. The microbiologic features and clinical outcome of diabetic foot infections among patients admitted at UP-PGH. Phil J Microbiol Infect Dis. 2002;31(2):54-63.

29 .Al-Rubeaan K, Al Derwish M, Ouizi S, Youssef AM, Subhani SN, Ibrahim HM, et al. Diabetic Foot Complications and Their Risk Factors from a Large Retrospective Co hort Study. Santanelli, di Pompeo d'Illasi F, editor. PLOS ONE [Internet]. 2015 May 6 ;10(5):e0124446. Available from: http://dx.doi.org/10.1371/journal.pone.0124446

30.Newrick PG, Bowman C, Green D, O'Brien IAD, Porter SR, Scully C, et al. Paroti d salivary secretion in diabetic autonomic neuropathy. Journal of Diabetic Complicatio ns [Internet]. 1991 Jan;5(1):35–7. Available from: http://dx.doi.org/10.1016/0891-663 2(91)90008-d

31.Hirtz C, Chevalier F, Sommerer N, Raingeard I, Bringer J, Rossignol M, et al. Saliv ary protein profiling in type I diabetes using two-dimensional electrophoresis and mas s spectrometry. Clinical Proteomics [Internet]. 2006 Mar;2(1–2):117–27. Available fro m: http://dx.doi.org/10.1385/cp:2:1:117

32.Peyrot des Gachons C, Breslin PAS. Salivary Amylase: Digestion and Metabolic S yndrome. Current Diabetes Reports [Internet]. 2016 Sep 17;16(10). Available from: ht tp://dx.doi.org/10.1007/s11892-016-0794-7

33.Nater UM, Rohleder N. Salivary alpha-amylase as a non-invasive biomarker for th e sympathetic nervous system: Current state of research. Psychoneuroendocrinology [I nternet]. 2009 May;34(4):486–96. Available from: http://dx.doi.org/10.1016/j.psyneue n.2009.01.014

34.Tumilasci OR, Cersósimo MG, Belforte JE, Micheli FE, Benarroch EE, Pazo JH. Q uantitative study of salivary secretion in Parkinson's disease. Movement Disorders [In ternet]. 2006 May;21(5):660–7. Available from: http://dx.doi.org/10.1002/mds.20784

35.Valdez IH, Fox PC. Interactions of the Salivary and Gastrointestinal Systems. Dige stive Diseases [Internet]. 1991;9(3):125–32. Available from: http://dx.doi.org/10.1159/ 000171298

36.Chandrashekar P, Indira M, Kattappagari K, Chandra LP, Chitturi R, BV R. Evaluat ion of salivary glucose, amylase, and total protein in Type 2 diabetes mellitus patients. Indian Journal of Dental Research [Internet]. 2015;26(3):271. Available from: http://d x.doi.org/10.4103/0970-9290.162883

37.Tiongco R, Bituin A, Arceo E, Rivera N, Singian E. Salivary glucose as a non-inva sive biomarker of type 2 diabetes mellitus. Journal of Clinical and Experimental Denti stry [Internet]. 2018;0–0. Available from: http://dx.doi.org/10.4317/jced.55009

38.Romero AS, Gómez S, Agudo P, Sánchez de Puerta C. HIPERTRANSAMINASEM IA COMO SIGNO GUÍA EN EL DIAGNÓSTICO DE ENFERMEDAD NEUROMU SCULAR. 37 Congreso Nacional de la Sociedad Española de Pediatría y Atención Pri maria - SEPEAP 2023 Abstracts Publication [Internet]. 2023 Jun 27; Available from: http://dx.doi.org/10.48158/sepeap2023.pd082

39.Maheshwari S, Jaan A, Vyaasini CVS, Yousuf A, Arora G, Chowdhury C. Laser an d its Implications in Dentistry : A Review Article. Journal of Current Medical Researc h and Opinion [Internet]. 2020 Aug 14;3(08). Available from: http://dx.doi.org/10.155 20/jcmro.v3i08.323

40.Nakajima K, Nemoto T, Muneyuki T, Kakei M, Fuchigami H, Munakata H. Low se rum amylase in association with metabolic syndrome and diabetes: A community-base

d study. Cardiovascular Diabetology [Internet]. 2011;10(1):34. Available from: http://dx.doi.org/10.1186/1475-2840-10-34

41.Lorini R, Cortona L, Scotta MS, Melzi d'Eril GV, Severi F. Exocrine pancreatic function in children and adolescents with insulin-dependent diabetes mellitus. Diabetes Research and Clinical Practice [Internet]. 1990 Jan;8(3):263–7. Available from: http://dx.doi.org/10.1016/0168-8227(90)90125-d