International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 1s, 2025
https://www.theaspd.com/ijes.php

The relationship between the salivary level of Glucosyl transferase-B with Ferritin, Transferrin, and Lactoferrin levels in patients suffering from Beta-Thalassemia major

Saba S. Abd Al Wahab[1] and Maha A. Mahmood [2]
[1,2] Department of Basic Sciences, College of Dentistry, University of Baghdad, Baghdad, Iraq.
[1]https://orcid.org/0009-0008-8874-769X
[2]https://orcid.org/0000-0003-3516-1309
Corresponding author: Saba Sami Abd Al Wahab, Maha Adel Mahmood,
Email Address:
[1]Saba.abd2307m@codental.uobaghdad.edu.iq, [2]adelmaha70@codental.uobaghdad.edu.iq

Abstract : Background: Thalassemia major (T major), a severe hereditary hematological condition, typified by inadequate synthesis of the hemoglobin chain, which causes anemia, iron overload, and related problems.

Objectives: The present work explores the relationship between the salivary glucosyltransferase B levels and serum ferritin, serum transferrin and salivary lactoferrin levels in T major patients.

Methods: This study included sixty participants, of whom thirty were diagnosed with thalassemia major and thirty were healthy controls. Salivary GtfB, serum ferritin, serum transferrin, and salivary lactoferrin levels were appraised through enzyme-linked immunosorbent assays (ELISA) and immunoturbidimetry.

Results: Remarkable differences were evident in the ferritin and glucosyltransferase levels between the T major and control groups ($p = 0.000$). The T major patients presented higher ferritin levels implying iron overload and lower glucosyltransferase levels. No significant changes were noted in the lactoferrin and transferrin levels. Association analysis indicated a strong positive association between lactoferrin and glucosyltransferase in both groups ($p < 0.05$), inferring an identical biological mechanism.

Conclusion: The findings highlight the presence of T major and stress-related metabolic disturbances and the need for further studies to clarify the role of biomarkers like glucosyltransferase in iron overload management and disease development. This work offers critical insights into the biomarkers that can be investigated for prospective diagnostic and treatment lines for T major.

Keywords: Ferritin, glucosyltransferase, lactoferrin, thalassemia major, transferrin

INTRODUCTION

Thalassemia comprise an assortment of hereditary hematologic disorders caused by aberrations in the production of one or more of the hemoglobin chains (1). Alpha-thalassemia occurs due to a lowered or complete lack of production of the alpha-globin chains, whereas beta-thalassemia arises from a reduced or total absence of production of the beta-globin chains (2). Imbalances in the globin chains result in hemolysis and hinder erythropoiesis (3). Beta-thalassemia major results in hemolytic anemia, impaired growth, and infant skeletal deformities (4). Most experts estimate that approximately 5.2% of the global population (around 300-360 million people) possess structurally abnormal hemoglobin (5). Nearly 80-90 million individuals are β-thalassemia carriers, representing 1.5% of the global population. Furthermore, reports reveal that approximately 68,000 newborns are born annually with β-thalassemia, which includes both minor and significant cases (6).

Glucosyltransferase B (GtfB), an enzyme synthesized by *Streptococcus mutans*, catalyzes the formation of insoluble glucans from sucrose, which contributes to the structural integrity of the biofilm (7). It is one of the prime virulence factors in the development of dental caries (8). Nonetheless, its function continues to be ambiguous in caries-free individuals who harbor the bacterium (9). GtfB is considered a diagnostic indicator for dental caries activity, and its significance in the development of the disease has prompted the development of many prevention strategies, including vaccines and the use of natural substances like apigenin, which regulate the expression of the genes for GtfB and GtfC (10).

The sole treatment for anemia in beta-thalassemia individuals is the administration of numerous blood transfusions, which causes iron overload and heart, liver, and bone damage (11). Chelation therapy is done to reduce the high iron levels, thus averting rapid clinical decline or potential mortality (12). After the iron is absorbed from different sites of the small intestine, the iron transporters associate with transferrin, which is then sequestered in the reticuloendothelial cells of the spleen, liver, and bone marrow, where it binds to the hemosiderin and ferritin (13). Iron serves as a metallic cofactor for several enzymes (such as ribonucleotide reductase, mitochondrial aconitase, and the oxidases, peroxidases, and catalases) and is a component of the hemoproteins, including cytochromes and hemoglobins (14). The chemical properties of iron can adversely affect biological systems (15). Ferritin, an intracellular iron storage protein, seen in both eukaryotes and prokaryotes, sequesters iron in a non-toxic and soluble form (16). The global protein complex with 450 kDa molecular weight has twenty-four protein components (17). The iron load on the body is assessed using serum iron, total iron-binding capacity (TIBC), and ferritin concentrations. The serum ferritin estimation is crucial to the assessment of iron overload in β-thalassemia major patients (18). The primary objective is to examine the correlation between the concentration of salivary glucosyl transferase-B and the ferritin, transferrin, and lactoferrin levels in individuals with Thalassemia major, to elucidate the potential biomarker interactions and implications for disease progression and management.

MATERIAL AND METHODS

Subject selection

Saliva and sera samples were obtained from sixty participants (males and females) in the 18- to 60-year age range, from December 2023 to March 2024. The subjects were enlisted and segregated into two groups: the first group included thirty individuals diagnosed with Beta Thalassemia major at the Thalassemia centers of Ebn-Al Balidy and Al-Karama hospitals in Baghdad, while the second group comprised thirty healthy subjects, as controls. This study was granted ethical approval from the Ethics Committee of the College of Dentistry, University of Baghdad.
The inclusion criteria consist of stable Beta Thalassemia major (T major) patients without concomitant diseases or drug effects for the patient group, and healthy persons without any types of blood disorders or chronic illnesses that impact iron metabolism, for the control group. The exclusion criteria included individuals from age 18 to 60 years of age who were unable to provide informed permission, pregnant or lactating women, and individuals affected with other diseases or on medication or receiving treatments that could influence the biomarkers under investigation.

Serum and saliva collection

Using the by the spitting method, 3 ml of unstimulated saliva was obtained from each participant (19), and transferred to sterile tubes. The samples were centrifuged at 4000 rpm for 3 minutes to separate the cellular debris. For blood samples, 5 mL was drawn via venipuncture into sterile tubes, centrifuged for 15 minutes at 3000 rpm, and the serum was extracted with an automated pipette. Both serum and saliva were preserved at -20^{o} C for later usage.

Measurement of human ferritin by Chemistry Analyzers

The technique employed utilizes microparticle-enhanced immunoturbidimetry with a Thermo Scientific chemical analyzer from Finland. Serum samples from both patients and controls were used and processed with microparticles coated with rabbit antibodies specific to human ferritin or iron. The quantification of the immunocomplex formation for Ferritin was performed by assessing the absorbance changes at 700 nm, within a detection range of 0.32–20 ng/ml.

Measurement of Human salivary Glucosyltransferase (GTFB), serum Transferrin (TRF), and salivary Lactoferrin (LTF)

The commercially available Enzyme-linked immunosorbent Assay (ELISA) kits were used to measure Human Glucosyltransferase (GTFB), Human Transferrin (TRF), and Human Lactoferrin (LTF). For both GtfB and LTF analyses, saliva samples were used. The Human Glucosyltransferase (GTFB) ELISA Kit (Wuhan Feiyue Biotechnology Co., Ltd., China) and the Human Lactoferrin ELISA Kit (ELK Biotechnology, USA) were employed to quantify the GtfB and LTF levels, respectively. In contrast, the Human Transferrin ELISA Kit was used to detect TRF from the serum samples. The conventional Sandwich ELISA protocol was used; the final reaction was terminated with a stop solution after the TMB substrate solution was added to the wells, causing a color transition from blue to yellow. The absorbance of optical density (OD) at 450 nm was carefully recorded, and the findings were computed by comparing the absorbance values to a standard curve, and the quantities of the target proteins in the samples were determined.

Statistical analysis

Statistical analyses were done using the SPSS 15 software (SPSS Inc., IL, USA). The Shapiro-Wilk test, Kruskal-Wallis H test, and Pairwise test were performed. A p-value of less than 0.05 was considered of statistical significance.

RESULT

The present study included sixty subjects (males and females) segregated into two groups; in the first group were thirty patients suffering from T major, with a mean age of 23.233 ± 7.398 years, while in the second group were thirty healthy individuals, with a mean age of 29.667 ± 9.517 years.

Measurement of Glucosyltransferase, Ferritin, Transferrin, and Lactoferrin in Thalassemia major patients

As demonstrated in Table (1), this study analyzed the presence of Glucosyltransferase (GTFB) enzyme and the biochemical parameters, including Human Ferritin (FE), Transferrin (TRF), and Lactoferrin (LTF), across the Thalassemia major and control groups. Descriptive statistics, comprising the median and chi-square (X2), were computed for each parameter, and the statistical analysis revealed substantial differences across the groups.

Table (1): Descriptive statistics for glucosyltransferase-B, ferritin, transferrin, and lactoferrin across Thalassemia major and control groups.

Parameters	Groups	Descriptive Statistics		
		Median	X^2	p-value
Glucosyltransferase pg/mL	T major	30.158	18.488	0.000
	Control	40.829		
Ferritin	T major	2783.800	**59.376**	0.000

ng/mL	**Control**	63.150		
Transferrin ng/mL	**T major**	84.119	2.610	0.271
	Control	82.589		
Lactoferrin ng/mL	**T major**	1.271	**3.852**	**0.146**
	Control	1.422		

Table (2): Multiple comparisons for glucosyltransferase-B, ferritin, transferrin, and lactoferrin between Thalassemia major and control groups using pairwise test.

Parameters	Groups	Pairwise test	P-value
Glucosyltransferase Bpg/mL	T major x control	28.25	0.000
Ferritin ng/mL	T major x control	-44.367	0.000

From the analytical results in Table 1 significant differences were observed between the T major and control groups for ferritin and glucosyltransferase-B, with p-values of 0.000 for both parameters, demonstrating a huge discrepancy in their distribution. Although the control group reveals a median glucosyltransferase level (40.829), which is higher than in the T major group (30.158), the median ferritin level in the T major group (2783.800) appreciably exceeds that of the control group (63.150). In contrast, for lactoferrin (p-value = 0.146) and transferrin (p-value = 0.271) no significant differences were noted between both groups, as the T major and control groups showed comparable median values for transferrin (84.119 vs. 82.589) and lactoferrin (1.271 vs.1.422), respectively. The pairwise test also revealed significant differences for the glucosyltransferase-B between the T major and control groups, which was also true for ferritin, as demonstrated in Table 2.

Correlation between parameters in T major and control groups

Lactoferrin and glucosyltransferase display a strong positive correlation in both the T major (r = 0.429, p = 0.018) and control groups (r = 0.411, p = 0.024), as shown in the Tables (3,4). However, the groups exhibit variations in other correlations. Further, transferrin and glucosyltransferase show a substantial negative connection (r = -0.427; p = 0.019) in the control group, which is absent in the T major group. However, no significant correlations were identified between the other markers tested in both groups. Both groups reveal a noticeable link between lactoferrin and glucosyltransferase but, the control group displays deeper correlations, especially between transferrin and glucosyltransferase.

Table (3) Correlation among markers investigated in the T major group

Parameters ng/mL		**Glucosyl-transferase**	**Transferrin**	**Lactoferrin**
Ferritin	**r**	-0.058	-0.008	0.027
	p	0.760	0.966	0.888
Transferrin	**r**	-0.307		
	p	0.099		
Lactoferrin	**r**	0.429	-0.210	
	p	0.018	0.265	

Table (4) Correlation among the markers studied in the control group

Parameters ng/mL		Glucosyl - transferase	Transferrin	Lactoferrin
Ferritin	r	-0.199	0.071	-0.046
	p	0.291	0.709	0.807
Transferrin	r	-0.427		
	p	0.019		
Lactoferrin	r	0.411	-0.312	
	p	0.024	0.093	

DISCUSSION

An examination of this study at present, indicated notable disparities in the glucosyltransferase and ferritin distributions, as both showed p-values of 0.000. These findings suggest that the concentration levels of these two biomarkers are significantly modified in thalassemia major patients, relative to the healthy controls.

In the T major group the ferritin level, on average, is much higher than that in the control group. This implies that the T major group has increased iron levels. It is a well-recognized fact that thalassemia major patients who receive regular blood transfusions as part of the anemia treatment end up with excessive iron in their bloodstream (20). As the severity of the iron overload escalates, the ferritin levels show a corresponding rise, indicating that the body has large quantities of stored iron. This is a highly accurate situation, unless proper iron chelation treatment is provided (21). The median quantity of GtfB in the control group is higher than that in the T major group compared to the ferritin, with a p-value of 0.000 considered significant. The distribution of the GtfB enzyme is evident in several streptococcal species present in the oral cavity. It is recognized as an essential enzyme that contributes to the oral biofilm formation, including dental plaque. (22, 23). The current research corroborates the findings of Dwivedi et al. (2014), which indicated that photodynamic antimicrobial therapy produces singlet oxygen which causes the speedy deterioration of the microbial cell components, including the DNA, consequently diminishing the expression of the gtfB gene (24).

The reduced GtfB-B levels identified in this study may correlate with the modified physiological parameters in individuals affected with Beta Thalassemia. One possible explanation for this outcome is that the chronic anemia and recurrent blood transfusions associated with Beta Thalassemia may adversely affect the overall metabolic and enzymatic functions in the body, including those pertinent to dental health (25). Furthermore, Beta Thalassemia patients frequently contract infections and therefore need to undergo treatments and take antibiotics, which may help in reducing tooth decay and related germs (26). Similarly, Al-Kazirragy (2010) reported that the glucan binding proteins exert a strong effect on biofilm formation by *Streptococcus mutans*, thus indicating that various systemic circumstances can differentially alter the analogous enzymes (27). Also, the lower median GtfB levels in the T major group could imply changes in the cellular or metabolic processes. This is most likely because of the ongoing inflammation and oxidative stress that accompany very high iron levels. According to previous studies iron-related oxidative stress may adversely affect glucosyltransferase activity, which is perhaps one reason for the lower levels in T major patients (28). Some studies reported that the presence of too much iron could alter the regular cellular processes like protein glycosylation. It is possible that too much iron could prevent the GtfB or other enzymes involved in glycosylation from working well, which could change the way the proteins are glycosylated (29). This finding could indicate that further study is needed to consider GtfB as a potential biomarker to assess the metabolic effects of iron overload in individuals with thalassemia.

The data obtained in the present study revealed no major modifications between the two groups for lactoferrin ($p = 0.146$) and transferrin ($p = 0.271$), as both parameters gave comparable median values in the T major and control groups. Lactoferrin is a glycoprotein that binds iron and participates in iron metabolism and the immune system (30). Transferrin is a protein that binds to iron and facilitates the movement of iron through the body (31, 32). The absence of substantial differences in these two markers indicates that despite iron dysregulation being a notable characteristic of thalassemia major, the regulatory mechanisms for lactoferrin and transferrin may not be as significantly affected by the condition, at least not to the degree observed with ferritin and glucosyltransferase. This discovery may imply that lactoferrin and transferrin are influenced by a broader range of physiological mechanisms, including inflammation and iron requirements, rather than exclusively by excess iron (33).

The correlation analysis of biochemical indicators in the T major and control groups reveals notable relationship patterns, highlighting both common patterns and substantial variances between the groups. Both groups display an important positive correlation between lactoferrin and GtfB. This finding suggests that, in both groups, lactoferrin, an iron-binding glycoprotein possessing antimicrobial functions (34), is intimately linked to GtfB, an enzyme that participates in the glycosylation processes (35). The uniformity of this beneficial correlation between the groups may be indicative of a shared biological mechanism connecting these two proteins, most likely related to iron metabolism, immunological response, or cellular stress responses. The notable link indicates that any rise in the lactoferrin levels corresponds to elevated GtfB levels, potentially reflecting the adaptive response of the body to preserve homeostasis under conditions of iron modifications (36). Significant variations arise when alternative correlations are examined.

In the control group, a negative association is evident between the transferrin and GtfB, which is not observed in the T major group. This indicates that in healthy individuals, elevated transferrin levels may correlate with reduced GtfB activity, perhaps caused by iron-dependent control. The absence of this link in T major may be indicative of iron overload (21), wherein transferrin is saturated with iron, thus affecting the normal regulatory processes. The principal function of transferrin is to sequester iron, a vital resource for both the host and pathogenic microorganisms (37). High transferrin activity in the control group may decrease the availability of free iron by binding to it, thus potentially inhibiting bacterial growth. This may affect the function of the bacterial enzymes, such as the glucosyltransferases, which could be dependent on iron availability or integral to those bacterial metabolic pathways that require iron. Furthermore, the control group shows a non-significant negative association between lactoferrin and transferrin, a link completely absent in the T major group. While lactoferrin and transferrin sequester iron (38), lactoferrin further plays a crucial role in immunological response and microbial growth regulation (39).

The negative correlation observed in the control group may point to a compensating mechanism, in which elevated lactoferrin levels coincide with diminished transferrin levels, caused by either the modified iron requirements or immunological responses in healthy subjects. This interaction may be reduced in the T major group, where the excess iron possibly saturates the transferrin, lowering its ability to bind and transport the iron (40). Considering their distinct physiological environments, transferrin in the bloodstream and lactoferrin in the tissues possibly do not have a direct or positive interaction, particularly under circumstances of iron overload, as in the case of β-thalassemia (41). Another reason could be the fact that in people with β-thalassemia, the variations in iron overload, transferrin, and lactoferrin can vary and thus hide a clear link between them; some patients may have higher transferrin levels or lower lactoferrin levels because they are either at different stages of iron overload or because of their differences in inflammation or immune reactions. Therefore, the link between lactoferrin and transferrin might not be apparent in T major, due to the impairment of iron transport caused by transferrin saturation (42).

CONCLUSION

This study investigates some important biomarkers in thalassemia major (T major) individuals with a focus on ferritin, glucosyltransferase, lactoferrin, and transferrin. In the T major patients, high ferritin levels indicate the presence of too much iron in the body, while low glucosyltransferase levels show alterations in the metabolic processes, due to long-term reactive stress. No significant variations were evident between the T major and control groups in the lactoferrin or transferrin levels. This suggests that these proteins may be affected by more than just iron dysregulation in the body. Regular patterns were observed in the correlations between the lactoferrin and glucosyltransferase, which imply a shared regulatory mechanism. However, the differences noted in other correlations imply that iron overload affects the regulatory processes in T major. The results clarify the biochemical changes in T major and indicate the need for more study to fully comprehend the effects of iron dysregulation and its repercussions in therapeutic approaches.

Declaration by Authors

We confirm that all Tables given in the manuscript belong to the current study. Authors sign on ethical considerations Approval — Ethical Clearance: The project was approved by the local ethical committee (University of Baghdad, College of Dentistry, Research Ethics Committee) according to **Ref. number: 889** on **Date: 11-1-2024.**

Funding

The authors assert that no financial resources, grants, or additional assistance were obtained during the development of the manuscript.

Declaration of conflicts of interest

The authors report no conflicts of interest.

Authors' contributions

Study conception & design: (Maha Adel Mahmood). Literature search: (Maha Adel Mahmood & Saba Sami Abd Al Wahab). Data acquisition: (Saba Sami Abd Al Wahab). Data analysis & interpretation: (Maha Adel Mahmood & Saba Sami Abd Al Wahab). Manuscript preparation: (Saba Sami Abd Al Wahab). Manuscript editing & review: (Maha Adel Mahmood).

REFERENCES

1. Kattamis A, Kwiatkowski JL, Aydinok Y. Thalassaemia. The lancet. 2022;399(10343):2310-24. https://doi.org/10.1016/S0140-6736(22)00536-0
2. Shafique F, Ali S, Almansouri T, Van Eeden F, Shafi N, Khalid M, et al. Thalassemia, a human blood disorder. Brazilian Journal of Biology. 2021;83:e246062. https://doi.org/10.1590/1519-6984.246062
3. Kristiansson A, Gram M, Flygare J, Hansson SR, Åkerström B, Storry JR. The role of α1-microglobulin (A1M) in erythropoiesis and erythrocyte homeostasis-therapeutic opportunities in hemolytic conditions. International Journal of Molecular Sciences. 2020;21(19):7234. https://doi.org/10.3390/ijms21197234
4. Ali S, Mumtaz S, Shakir HA, Khan M, Tahir HM, Mumtaz S, et al. Current status of beta-thalassemia and its treatment strategies. Molecular genetics & genomic medicine. 2021;9(12):e1788. https://doi.org/10.1002/mgg3.1788
5. Mohammed BJ. TNF-alpha gene polymorphism and its relation to vitamin D, calcium, alkaline phosphatase and ferritin status in Iraqi beta thalassemia patients. Biomedicines. 2022;5(45):906-11.

https://doi.org/10.51248/.v42i5.1848
6. Forni GL, Grazzini G, Boudreaux J, Agostini V, Omert L. Global burden and unmet needs in the treatment of transfusion-dependent β-thalassemia. Frontiers in Hematology. 2023;2:1187681.
https://doi.org/10.3389/frhem.2023.1187681
7. Fathallh AA, Mahmood MA. The estimation of the viable count of mutans streptococcus in waterpipe smokers and cigarette smokers. Journal of Baghdad College of Dentistry. 2021;33(3):23-9.
https://doi.org/10.26477/jbcd.v33i3.2950
8. Flayyih AS, Hassani HH, Wali MH. Detection of biofilm genes (gtf) in Streptococcus mutans isolated from human dental caries. Iraqi Journal of Science. 2016;57(1A):104-8.
9. Hoshino T, Fujiwara T. The findings of glucosyltransferase enzymes derived from oral streptococci. Japanese Dental Science Review. 2022;58:328-35.
https://doi.org/10.1016/j.jdsr.2022.10.003
10. Peritore-Galve FC, Shupe JA, Cave RJ, Childress KO, Washington MK, Kuehne SA, et al. Glucosyltransferase-dependent and independent effects of Clostridioides difficile toxins during infection. PLoS Pathogens. 2022;18(2):e1010323.
https://doi.org/10.1371/journal.ppat.1010323
11. Sadiq IZ, Abubakar FS, Usman HS, Abdullahi AD, Ibrahim B, Kastayal BS, et al. Thalassemia: Pathophysiology, Diagnosis, and Advances in Treatment. Thalassemia Reports. 2024;14(4):81-102.
https://doi.org/10.3390/thalassrep14040010
12. Hussein SZ. Evaluation of thyroid hormones and ferritin level in patients with β-thalassemia. Medicine and Pharmacy Reports. 2022;95(2):152.
https://doi.org/10.15386/mpr-2053
13. Aisen P. Iron metabolism in the reticuloendothelial system. Iron transport and storage: CRC Press; 2024. p. 281-95.
https://doi.org/10.1201/9781003574811-22
14. Cammack R, Wrigglesworth JM, Baum H. Iron-dependent enzymes in mammalian systems. Iron transport and storage. 2024:17-39.
https://doi.org/10.1201/9781003574811-3
15. Ezealigo US, Ezealigo BN, Aisida SO, Ezema FI. Iron oxide nanoparticles in biological systems: Antibacterial and toxicology perspective. JCIS Open. 2021;4:100027.
https://doi.org/10.1016/j.jciso.2021.100027
16. Zyara AM, Aldoori AA, Samawi FT, Kadhim SI, Ali ZA. A relationship study of coronavirus (COVID-19) infection, blood groups, and some related factors in Iraqi patients. Baghdad Science Journal. 2023;20(4 (SI)):1459-68.
https://doi.org/10.21123/bsj.2023.8871
17. Gehrer CM, Mitterstiller A-M, Grubwieser P, Meyron-Holtz EG, Weiss G, Nairz M. Advances in ferritin physiology and possible implications in bacterial infection. International journal of molecular sciences. 2023;24(5):4659.
https://doi.org/10.3390/ijms24054659
18. Matar BM, Sakr MMA, Alsehaimy LA, Al-samee A, Samir H. Evaluation of Serum Insulin, Glucose and Liver Function in β-Thalassemia Major and Their Correlation with Iron Overload. International Journal of Medical Arts. 2021;3(1):1088-96.
19. Alyaseen HA, Aldhaher ZA. The effect of new trend electronic cigarettes on dental caries in relation to glucosyltransferase b and secretory immunoglobulin A (a case-control study). Cell Biochemistry and Biophysics. 2024;82(3):2865-71.
https://doi.org/10.1007/s12013-024-01401-x
20. Hokland P, Daar S, Khair W, Sheth S, Taher AT, Torti L, et al. Thalassaemia-A global view. British Journal of Haematology. 2023;201(2):199-214.

https://doi.org/10.1111/bjh.18671
21. Gattermann N, Muckenthaler MU, Kulozik AE, Metzgeroth G, Hastka J. The evaluation of iron deficiency and iron overload. Deutsches Ärzteblatt International. 2021;118(49):847.
https://doi.org/10.3238/arztebl.m2021.0290
22. Lairson L, Henrissat B, Davies G, Withers S. Glycosyltransferases: structures, functions, and mechanisms. Annu Rev Biochem. 2008;77(1):521-55.
https://doi.org/10.1146/annurev.biochem.76.061005.092322
23. Nussrat RL, Aldhaher ZA. Evaluation of Statherin and ß-Defensin-3 in saliva of children with dental caries: Case control study. Journal of Emergency Medicine, Trauma & Acute Care. 2024;2024(2):7.
https://doi.org/10.5339/jemtac.2024.uncidc.7
24. Dwivedi S, Wahab R, Khan F, Mishra YK, Musarrat J, Al-Khedhairy AA. Reactive oxygen species mediated bacterial biofilm inhibition via zinc oxide nanoparticles and their statistical determination. PloS one. 2014;9(11):e111289.
https://doi.org/10.1371/journal.pone.0111289
25. Sankar V, Villa A. Hematologic diseases. Burket's Oral Medicine. 2021:627-64.
https://doi.org/10.1002/9781119597797.ch17
26. Wanachiwanawin W. Infections in E-β thalassemia. Journal of pediatric hematology/oncology. 2000;22(6):581-7.
https://doi.org/10.1097/00043426-200011000-00027
27. Al-kazirragy S. The effect of glucan binding protein on Streptococcus mutans biofilm formation and determination of chemical inhibitors: Thesis, College of Science, University of Baghdad, Baghdad, Iraq; 2010.
28. Velliyagounder K, Chavan K, Markowitz K. Iron Deficiency Anemia and Its Impact on Oral Health-A Literature Review. Dentistry Journal. 2024;12(6):176.
https://doi.org/10.3390/dj12060176
29. von Brackel FN, Oheim R. Iron and bones: effects of iron overload, deficiency and anemia treatments on bone. JBMR plus. 2024;8(8):ziae064.
https://doi.org/10.1093/jbmrpl/ziae064
30. Kell DB, Heyden EL, Pretorius E. The biology of lactoferrin, an iron-binding protein that can help defend against viruses and bacteria. Frontiers in immunology. 2020;11:1221.
https://doi.org/10.3389/fimmu.2020.01221
31. Talib HJ, Ahmed MA. Assessment of Salivary Lactoferrin and pH Levels and Their Correlation with Gingivitis and Severity of Chronic Periodontitis (Part: 2). Journal of Baghdad College of Dentistry. 2018;30(1):46-52.
https://doi.org/10.12816/0046311
32. Talukder J. Role of transferrin: an iron-binding protein in health and diseases. Nutraceuticals: Elsevier; 2021. p. 1011-25.
https://doi.org/10.1016/B978-0-12-821038-3.00060-4
33. Artym J, Zimecki M, Kruzel ML. Lactoferrin for prevention and treatment of anemia and inflammation in pregnant women: A comprehensive review. Biomedicines. 2021;9(8):898.
https://doi.org/10.3390/biomedicines9080898
34. Cao X, Ren Y, Lu Q, Wang K, Wu Y, Wang Y, et al. Lactoferrin: A glycoprotein that plays an active role in human health. Frontiers in Nutrition. 2023;9:1018336.
https://doi.org/10.3389/fnut.2022.1018336
35. Mikolajczyk K, Kaczmarek R, Czerwinski M. How glycosylation affects glycosylation: the role of N-glycans in glycosyltransferase activity. Glycobiology. 2020;30(12):941-69.
https://doi.org/10.1093/glycob/cwaa041

36. Srivastava NK, Mukherjee S, Mishra VN. One advantageous reflection of iron metabolism in context of normal physiology and pathological phases. Clinical Nutrition ESPEN. 2023.
https://doi.org/10.1016/j.clnesp.2023.10.006
37. Ullah I, Lang M. Key players in the regulation of iron homeostasis at the host-pathogen interface. Frontiers in Immunology. 2023;14:1279826.
https://doi.org/10.3389/fimmu.2023.1279826
38. Ianiro G, Rosa L, Bonaccorsi di Patti MC, Valenti P, Musci G, Cutone A. Lactoferrin: From the structure to the functional orchestration of iron homeostasis. Biometals. 2023;36(3):391-416.
https://doi.org/10.1007/s10534-022-00453-x
39. Sienkiewicz M, Jaśkiewicz A, Tarasiuk A, Fichna J. Lactoferrin: An overview of its main functions, immunomodulatory and antimicrobial role, and clinical significance. Critical reviews in food science and nutrition. 2022;62(22):6016-33.
https://doi.org/10.1080/10408398.2021.1895063
40. Ajayi ND, Ajayi SA, Oladoyinbo OB, Olaniyi OO. A review of literature on transferrin: deciphering its complex mechanism in Cellular Iron Regulation and Clinical Implications. Available at SSRN 4690424. 2024.
https://doi.org/10.2139/ssrn.4690424
41. Pirotte M. Detailed investigation of erythropoiesis and iron metabolism in the context of allogeneic hematopoietic stem cell transplantation. 2024.
42. Campos-Escamilla C. The role of transferrins and iron-related proteins in brain iron transport: applications to neurological diseases. Advances in protein chemistry and structural biology. 2021;123:133-62. https://doi.org/10.1016/bs.apcsb.2020.09.002