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Original Article

Comparative and Predictive Analysis of Clinical and Metabolic Features of Anorexia Nervosa and Bulimia Nervosa

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Abstract

Background: Eating disorders have become increasingly prevalent over the years; the age at which they appear has decreased, and they can lead to serious illness or death. Therefore, the number of studies on the matter has increased. Eating disorders like anorexia nervosa (AN) and bulimia nervosa (BN) are affected by many factors including mental illnesses that can have serious physical and psychological consequences. Accordingly, the present study aimed to compare the clinical and metabolic features of patients with AN and BN and identify potential biomarkers for distinguishing between the two disorders.

Methods: Clinical data of 41 participants who sought treatment for eating disorders between 2012 and 2022, including 29 AN patients and 12 BN patients, were obtained from NPIstanbul Brain Hospital in Istanbul, Turkey. The study included the clinical variables of both outpatient and inpatient treatments. Principal component analysis (PCA) was utilized to gain insights into differentiating AN and BN patients based on clinical characteristics, while machine learning techniques were applied to identify eating disorders.

Findings: The study found that thyroid hormone levels in patients with AN and BN were influenced by non-thyroidal illness syndrome (NTIS), which could be attributed to various factors, including psychiatric disorders, substance abuse, and medication use. Lipid profile comparisons revealed higher triglyceride levels in the BN group ($P<0.05$), indicating increased triglyceride synthesis and storage as an energy source. Liver function tests showed lower levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in BN patients ($P<0.05$), while higher prolactin levels ($P<0.05$) suggested an altered hypothalamic-pituitary-gonadal axis. Imbalances in minerals such as calcium and magnesium ($P<0.05$) were observed in individuals with eating disorders. PCA effectively differentiated AN and BN patients based on clinical features, and the Naïve Bayes (NB) model showed promising results in identifying eating disorders.

Conclusion: The findings of the study provide important insights into AN and BN patients' clinical features and may help guide future research and treatment strategies for these conditions.

Keywords: Eating disorder, Anorexia, Bulimia, Laboratory diagnosis, Machine learning

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Introduction

Eating disorders are psychiatric or brain disorders that commonly impact individuals; extreme attitudes and behaviors toward food and weight control lead to significant physical and psychological consequences. Feeding and eating disorders encompass a spectrum of abnormal eating habits, ranging from mild to life-threatening chronic conditions, characterized by disruptions in eating behavior and the body's food absorption process.[1] Patients with eating disorders, including anorexia nervosa (AN) and bulimia nervosa (BN), often exhibit disruptions in biochemical parameters, hormone levels, vitamin levels, and organ dysfunctions, potentially leading to various associated diseases.

An intense fear of getting fat or gaining weight defines AN, which results in a severe self-induced loss in body weight. The distortion in perceiving body shape and weight is also a mark of this condition.[2] Those with AN often show eating restrictions that cause noteworthy weight loss and malnutrition. Metabolic indices, dyslipidemia included, are altered in individuals with AN, resulting in psychological, psychiatric, and physical

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consequences.[3]

Dyslipidemia is frequently observed in AN,[4] characterized by a decline in total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides. One reason for these lipid imbalances is energy conservation in response to severe food restriction. The body enters a state of catabolism and then breaks down stored fats for energy. The outcome is a reduction in lipid levels [5]. It is known that the levels of high-density lipoprotein (HDL), LDL, very-low-density lipoprotein (VLDL), and triglycerides (TG) measurements characterize lipid profiles. Fatty acids influence plasma lipids and lipoprotein levels in the bloodstream.[6] Changing plasma lipids and lipoproteins may also be influenced by complex mechanisms, such as increased triglyceride-rich lipoprotein synthesis with an unchanged rate of cholesterol synthesis.[7] A significant example of an unbalanced fat ratio in the body is low HDL cholesterol which activates LDL cholesterol, paving the way for atherogenesis to trigger pro-atherogenic factors due to hyperlipidemia.[8] Patients with AN may have a metabolic disorder that could potentially be treated by pharmacologically modulating the endogenous ghrelin system.

AN patients typically exhibit elevated B12 levels and reduced folic acid levels, which may be attributed to the B12-dependent utilization of folic acid and its subsequent accumulation.[9] This might be explained by the metabo-psychiatric feature of AN (folic acid decrease) and the fact that vitamin B12 elevation is an important indicator determining liver damage.[10] In AN, the correlation between vitamin D, Ca^{2+}, and Mg^{2+}, along with their physiological interactions in immune system functions and bone metabolism, indicates increased susceptibility to infectious diseases, canc..er, and complications like weakness, fatigue, psychiatric diseases, and major depression due to nutrient deficiency, unbalanced lipid profile, and malabsorption of vitamin D.[11,12] Eating disorders have notable impacts on the digestive and endocrine systems, disrupting pathways, particularly the hypothalamic-pituitary axis, and exerting long-term effects on overall body health, with AN receiving more research attention compared to BN and AN exhibiting more pronounced endocrine disorders than BN.[13] Thyroid hormones (thyroxine (T4), 90% inactive, and triiodothyronine (T3), 10% active) control metabolism in the body and also control cardiac, respiratory, skeletal muscles, etc.[14] They have effects that regulate many mechanisms.[15,16] Furthermore, nutrient deficiency leads to the reduction of insulin-like growth factor 1 (IGF-1) levels, thus resulting in atrophy of the thyroid gland with a delayed response to stimulants such as thyrotropin.[17] AN patients show elevated blood glucose, protein catabolism, imbalanced lipids, increased liver enzymes from internal energy source utilization, and a correlation between decreased body mass index (BMI) and increased AST levels,[18] proving the disease is related to metabo-psychiatric characterization.

Symptoms of BN include repeated binge eating episodes. It is usually followed by compensatory behaviors such as self-induced vomiting, excessive exercise, or excessive use of diuretics or laxatives[19] Those with BN typically exhibit no variation from the standard weight range or might be marginally overweight.[20] Dyslipidemia can be caused by the intake of significant quantities of fats and carbohydrates resulting from frequent episodes of binge eating in BN.[3] Elevated triglyceride levels in BN are primarily associated with dyslipidemia caused by episodes of binge eating and excess calorie intake. However, it is not consistent across all individuals[21]; the frequency and presence of compensatory behaviors can vary. Addressing dyslipidemia in AN often involves comprehensive treatment strategies focusing on nutritional rehabilitation, weight restoration, and reestablishing healthy eating patterns that may exhibit elevated triglyceride levels due to binge eating. Regular monitoring of lipid profiles and other relevant laboratory markers can help guide the management and treatment of dyslipidemia in individuals with AN.

Dyslipidemia in AN and BN may have a reciprocal association, as individuals with AN may develop binge eating and purging behaviors contributing to dyslipidemia.[22] Alternatively, individuals with BN might undergo periods of limited food intake or switch to AN-type actions that decrease lipid levels.[3] AN patients have a lower weight and metabolic rate than BN patients. AN involves weight loss, amenorrhea, and psychiatric disorders. In contrast, BN manifests as inappropriate behaviors like vomiting and diuretic and laxative use to counteract overeating episodes, all of which are characteristic features of these eating disorders.[23]

Recent studies revealed that some trace elements are essential in diagnosing and treating AN or BN. The main elements are B12, vitamin D, Ca^{2+}, and Mg^{2+}.[11] Furthermore, nutrient deficiency leads to the reduction of IGF-1 levels, thus resulting in atrophy of the thyroid gland with a delayed response to stimulants such as thyrotropin.[17] Eating disorders can cause sudden and severe weight loss, leading to liver dysfunction and disease. This can be seen in increased transaminase (AST, ALT) levels, disrupted liver function, and decreased prothrombin time. Gamma-glutamyl transferase (GGT) levels also have a complex relationship with eating disorders. Liver biopsies often reveal autophagy, which impacts glucose, protein, and lipid metabolism. Decreased BMI is associated with increased AST levels.[24,18] Proving the disease is related to metabo-psychiatric characterization. Recent studies indicated that some trace elements are essential in diagnosing and treating AN or BN. The main elements are B12, vitamin D, Ca^{2+}, and Mg^{2+}.[11]

Certain traits of AN and BN bear a resemblance to addictive behaviors.[25] Compulsive behaviors surrounding food, body weight, and shape are present in these eating disorders, and patterns observed in substance abuse disorders bear a resemblance to them.[26] Eating disorders and addictive behaviors may intersect, as indicated by these common behavioral patterns. Comprehensive treatment approaches addressing both aspects are highlighted by this.[27,28]

To classify individuals into AN and BN groups, machine learning methods based on specific features and biomarkers were employed. Principal component analysis (PCA) simplified complex datasets, while the Naïve Bayes (NB) algorithm predicted AN or BN classification. The diagnostic efficacy of biomarkers in differentiating between AN and BN was assessed using receiver operating characteristic (ROC) curve analysis, which comprehensively assessed the model's discrimination ability through the area under the curve (AUC) value.

This study aimed to identify biomarkers, metabolic differences, and correlations in patients with AN and BN and assess clinical characteristics and mineral imbalances in comparison with addictive behaviors. The study used statistical and machine learning techniques, such as PCA, NB, and ROC curve analysis, to classify individuals and evaluate the diagnostic performance of biomarkers in eating disorders.

Methods

Study Population and sample collection

This was a retrospective study. The clinical data of the participants with complaints of eating disorders from 2012 to 2022 were obtained from NPIstanbul Brain Hospital. The inclusion criteria were being diagnosed with eating disorders (n = 41), AN (n = 29) or BN (n = 12), and having received outpatient or inpatient treatments. The eating disorder was defined based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV or V) criteria for AN and BN. Before any drug treatments, the participants' laboratory data from the initial stage of hospitalization were used to minimize the influence of drug interventions on the metabolic indices under investigation. Examining patients before drug treatment initiation aimed to identify potential clinical or metabolic biomarkers that could differentiate between AN and BN individuals. Patients with pituitary adenomas (pituitary tumors) that develop due to the high level of prolactin hormone were excluded from the study. All patients were assessed depending on the measurement of their blood biochemistry and hormone levels. Blood biochemistry analyses were performed by Cobas Integra 400 Plus device, and hormone analyses were performed using Cobas E-411 device. The patients were selected based on routine analyses. The parameters commonly used to assess the metabolic indices of patients, including LDL, HDL, VLDL, TG, TSH, T3, T4, AST, ALT, GGT, prolactin, Ca, and Mg were chosen based on their relevance to metabolic markers and routine clinical practice use. All participants gave written informed consent. The patients' demographic data (age, sex) and biochemical parameters such as lipid or protein profile, blood parameters, hormone levels, and vitamin levels were all noted before and after drug treatments.

Statistical analysis

IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The Kolmogorov-Smirnov and Shapiro-Wilk tests, as well as histogram curves were used to determine the normality of data distribution. Mean values with standard deviation (SD) were also used to report customarily distributed numerical data. Independent samples *t* test was used to evaluate the differences between the two groups for normally distributed numerical variables. Mann-Whitney U test was applied for non-normally distributed variables. Then, the Bonferroni post-hoc test and a series of *t* tests were conducted on each pair of groups. This test was performed to reduce the risk of type I errors (false positives) through controlling the overall family-wise error rate by adjusting the significance level based on the number of tests conducted. Correlations between numerical variables were analyzed using Pearson correlation tests. Moreover, $P < 0.05$. was considered statistically significant.

Principal component analysis and classification analysis

The unsupervised technique known as PCA reduces the dimensionality of high-dimensional datasets by processing them.[29] The clinical features were analyzed separately using PCA, which can identify relationships without any assumption of priority among the multiple data. PC1, PC2, and PC3 were the principal components (PCs) that were extracted from the data. These components, which indicate particular patterns or directions of variation in the data, are produced by a linear combination of the dataset's original variables. PC1 often represents the most prevalent pattern or factor in the data, while PC2 accounts for the second-largest share of variation and contains discriminatory information after PC1. A specific pattern or direction of variation is captured by PC3, which accounts for the third-largest amount of variance. The recorded data is differentiated in detail by PC1 and PC2, and PC3 adds additional detail. People were categorized into the diagnostic groups AN and BN based on biomarkers using the NB model. ROC curve analysis is a visual technique for evaluating a binary classifier system's performance. Plotting different categorization thresholds against the genuine positive rate (sensitivity) and false positive rate (specificity) is required.

The AUC is used to assess the classifier's performance. In the present study, ROC curve analysis was used to assess the diagnostic efficacy of the NB model as well as the AN and BN biomarkers. Greater discriminating power for the model or biomarkers is indicated by a higher AUC value. The NB model's performance indices were evaluated for identifying eating disorders using the 5-fold cross-validation technique. A ROC analysis was conducted to further assess the NB classifier's robustness, and the AUC were calculated. The computational models were performed using MATLAB V2021a software.

Results

Clinical results

This study compared the clinical features of patients with AN and BN. As shown in Figure 1a, TSH levels tended to increase, and T4 levels decreased but not significantly. However, T3 levels were significantly increased in the BN group compared to the AN group ($P<0.05$). Besides, to compare the lipid profile of the groups, the LDL, HDL, VLDL, and TG levels were compared (Figure 1b). As presented, triglyceride levels were higher in BN than in the AN group ($P<0.05$). Additionally, AST and ALT levels in the BN group tended to be lower, and GGT levels were higher in BN than in the AN group but the difference was not statistically significant (Figure 1c). Finally, prolactin levels were compared between AN and BN. The results showed that the prolactin level was higher in BN than in the AN group (Figure 1d).

As shown in Figure 2, calcium and magnesium levels were compared between the AN and BN groups. There was a decreased amount of Ca^{2+} ($P<0.05$) and Mg levels in the BN group compared to the AN group. The findings from Figure 2 suggest a significant difference in calcium and magnesium levels between the AN and BN groups. Specifically, the BN group had lower levels of both Ca^{2+} and Mg^{2+} compared to the AN group.

The results showed a milder decrease in levels of these minerals in AN than in BN patients. Among all parameters, only the Mg levels showed a significant difference between the groups ($P<0.05$). Furthermore, Mg levels showed a negative correlation between T3 and TG levels and a positive correlation with HDL and GGT. The statistical results of the two groups are presented in Table 1.

There were significant differences in the levels of triglycerides, T3, and Mg between the two groups, with p-values less than 0.05. This indicates that these biomarkers are potentially helpful in distinguishing between AN and BN patients. Some biomarkers such as VLDL and GGT showed a trend towards significance with p-values less than 0.10 but more significant than 0.05. On the other hand, some biomarkers, such as LDL, TSH, AST, ALT, prolactin, and Ca did not show significant differences between the two patient groups.

Notably, most of the significant biomarkers' effect sizes (ε^2) were relatively low, indicating that they may not have a strong practical significance in distinguishing between the two patient groups.

The correlation matrix between and among groups is presented in Table 2. Based on the results, in the AN group, there was a negative correlation between T4 and

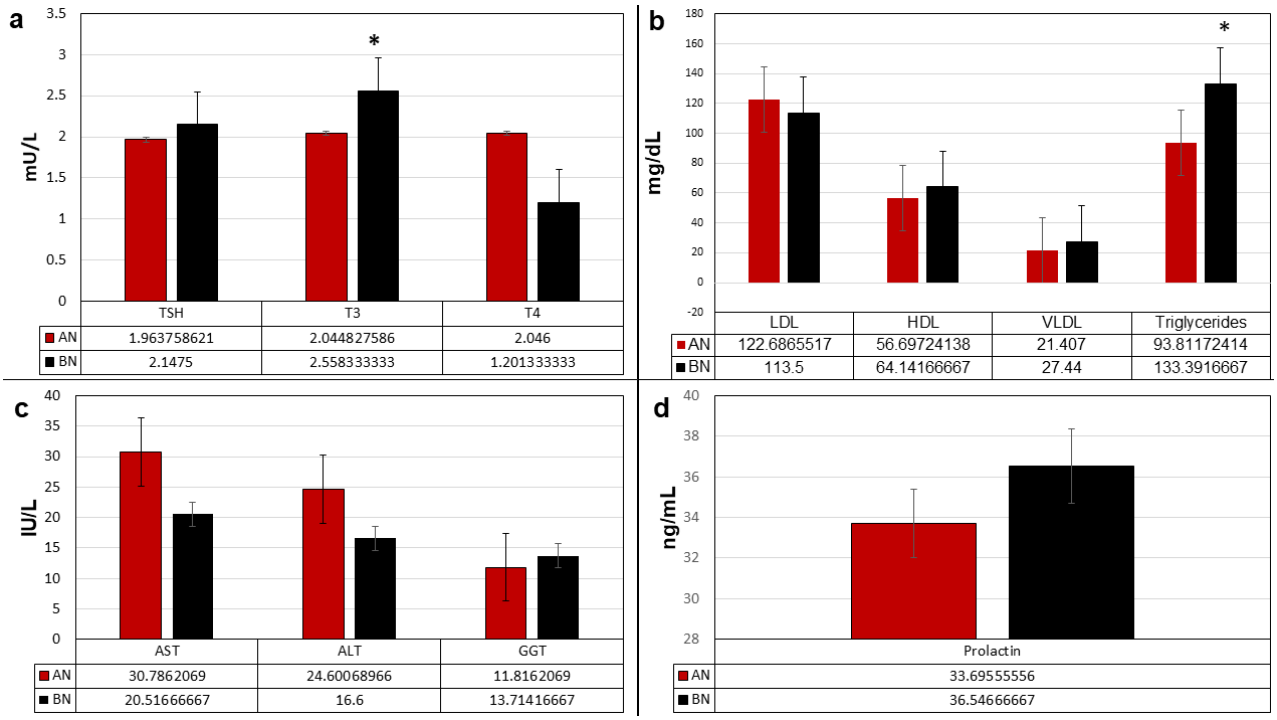

Figure 1. Comparisons of clinical characteristics of AN and BN patients (a) TSH, T3, and T4 levels (b) LDL, HDL, VLDL, and TG levels (c) AST, ALT, and GGT levels and (d) Prolactin levels

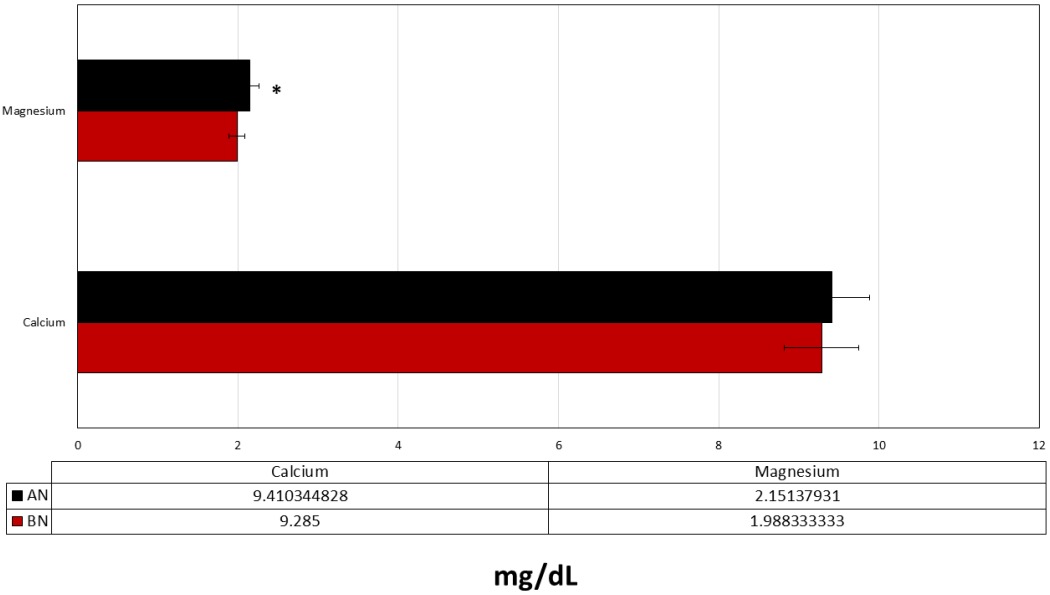

Figure 2. Comparisons of calcium and magnesium levels in AN and BN patients

Table 1. Bonferroni post-hoc test results between AN and BN groups

	χ^2	Df	*P*	ε^2
LDL	0.1886	1	0.664	0.00496
HDL	20.121	1	0.156	0.05030
VLDL	31.832	1	0.074	0.10976
TG	53.872	1	*0.020	0.13468
TSH	0.1388	1	0.710	0.00347
T3	41.976	1	*0.040	0.10494
T4	21.791	1	0.140	0.05448
AST	0.1848	1	0.667	0.00462
ALT	0.0462	1	0.830	0.00116
GGT	27.643	1	0.096	0.06911
Prolactin	11.343	1	0.287	0.02985
Ca	0.1735	1	0.677	0.00434
Mg	49.620	1	*0.026	0.12405

TSH ($P<0.05$).

T3 levels negatively correlated with LDL ($P<0.001$) and Mg levels ($P<0.05$), while T4 levels correlated positively ($P<0.001$). There was a negative correlation between LDL and prolactin levels ($P<0.05$). HDL levels positively correlated with $Ca^{2+}$and Mg^{2+}levels ($P<0.05$) but negatively with VLDL levels ($P<0.05$). TG levels positively correlated with GGT ($P<0.01$) but negatively with Mg levels ($P<0.05$). Moreover, AST levels were positively correlated with ALT, GGT, and prolactin levels ($P<0.01$). Besides, ALT and GGT were positively correlated with GGT levels ($P<0.001$). In the BN group, LDL and TSH levels were negatively correlated ($P<0.05$). TG and VLDL were positively correlated ($P<0.01$), and Mg and GGT were also positively correlated ($P<0.01$). Finally, the features were compared between the groups. The results showed that T4 and T3 levels were positively correlated ($P<0.05$). TG levels were negatively correlated with T3 ($P<0.05$) and positively correlated with T4 levels ($P<0.001$). LDL and GGT levels were positively correlated ($P<0.05$). Furthermore, there was a negative correlation between both LDL and prolactin levels and Ca levels ($P<0.05$).

Machine learning results

Principal component analysis results

Figure 3a presents two components, and Figure 3b presents three components of PCA results. As seen in Figure 3a, the total variance contribution rates of PC1 and PC2 were 76.70% and 15.0%, respectively. The cumulative contribution rate was 91.70%, which is more significant than the typical threshold of 80%. In addition, as seen in Figure 3b, the total variance contribution rates of PC1, PC2, and PC3 were 76.70%, 15.0%, and 5.13%, respectively. The cumulative contribution rate was 96.83%, which is more significant than the typical threshold of 80%.

Classification analysis results

The performance indices for the NB model to identify eating disorders using the 5-fold cross-validation technique are shown in Figure 4a. The NB algorithm provided an accuracy of 82.9% (95% CI: 67.9%-92.9%) to predict patients with AN and BN eating disorders. The recall was higher for the AN patient (86.7%, 95% CI: 74.3%-93.6%), indicating that very few AN patients predicted by the NB model were BN patients. The precision was also higher for the AN patient (89.7%, 95% CI: 72.7%-97.8%), indicating that the model produced fewer false-negative predictions than BN patients (66.7%, 95% CI: 34.9%-90.1%). ROC analysis was also performed

Table 2. Correlation matrix between and among groups

	TSH	T3	T4	LDL	HDL	VLDL	TG	AST	ALT	GGT	Ca	Mg
AN group												
T4	*-0.384	0.726***										
LDL		-0.422*										
VLDL					*-0.475							
ALT								0.517**				
GGT							0.516**	0.562**	0.650***			
Ca					0.380*							
Mg		-0.380*			0.400*		-0.382*					
Prolactin				-0.413*				0.496**				
BN group												
LDL	-0.658*											
TG						**0.815						
GGT												0.804**
Between groups												
T3							-0.704*					
T4							0.824***			0.628*		
LDL											-0.675*	
TG			0.638*									
Prolactin											-0.605*	

Note: * $P<0.05$, ** $P<0.01$, *** $P<0.001$ is significant. Only significant values are presented.

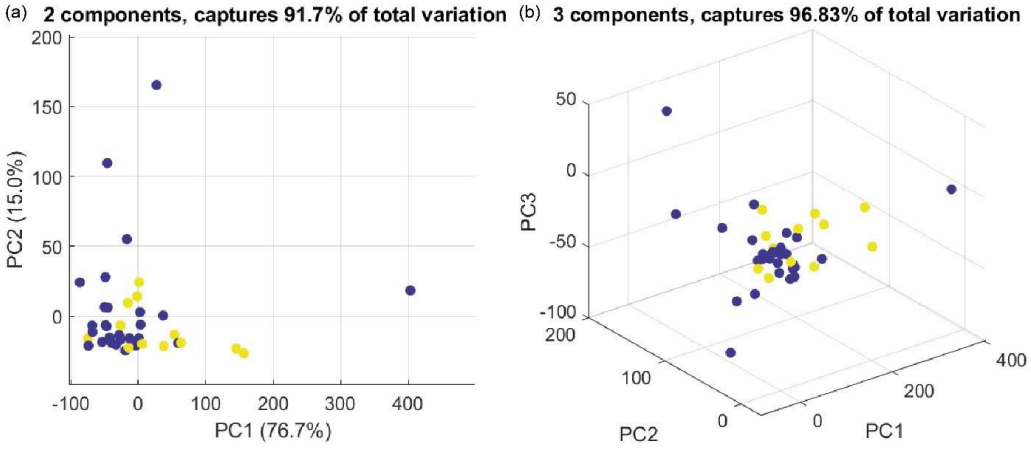

Figure 3. PCA results between AN and BN groups. a) two components, b) three components

to examine further the robustness of the NB classifier (Figure 4b). The value of the AUC was calculated as 0.72 (95% CI: 0.69-0.76).

Discussion

This retrospective study collected 10-year data from AN and BN patients and utilized PCA to yield valuable insights into the clinical features of both disorders. This section discusses changes in thyroid hormone levels, non-thyroidal illness syndrome (NTIS) influenced by factors such as psychiatric disorders, substance abuse, and medication use. Lipid profiles, liver function, prolactin levels, mineral imbalances as well as PCA and machine learning applications for discriminating AN and BN diseases are also discussed.

Thyroid abnormalities are common in psychiatric patients and those with malnutrition-related conditions like AN. However, caution is necessary when interpreting results as up to one-third of patients may have NTIS due to factors like psychiatric disorders, substance abuse, and medication use.[30,31] TSH levels tend to increase, T4 levels decrease but not significantly, and T3 levels increase significantly in the BN group compared to the AN group (Figure 1 and Table 1).

These changes are attributed to adaptations developed against the low metabolic rate in patients with AN. The changes in thyroid hormone values observed in AN patients can be explained by NTIS, a condition in which

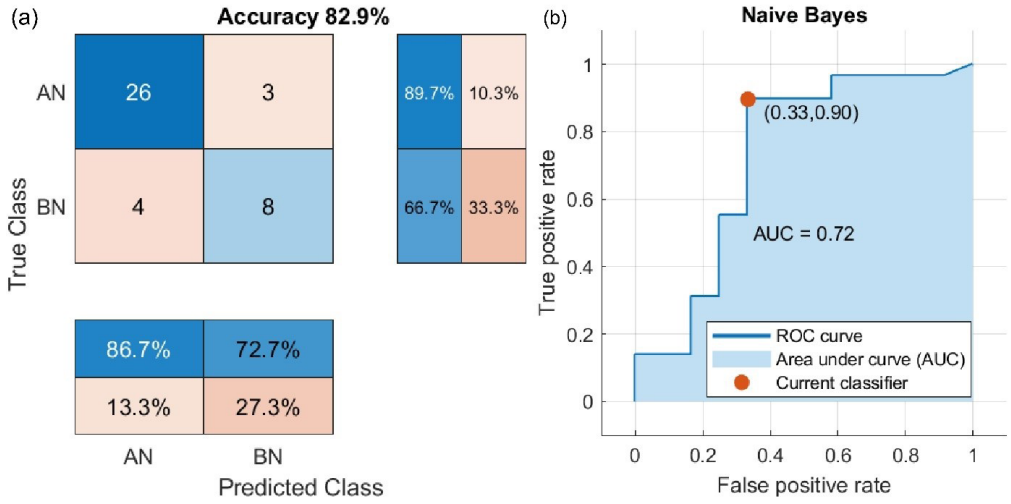

Figure 4. Development of a diagnostic model for identifying eating disorders. (a) A confusion matrix describes the NB classifier's accuracy, precision, and recall performance, (b) the ROC curve

T3 levels are lower than average, and T4 and TSH levels are standard or lower than average.[32,33] NTIS is influenced by various factors, such as psychiatric disorders, substance abuse, and medication use. All these changes are adaptations developed against the low metabolic rate in AN patients.[14] In a study on BN patients, initial T3 levels were lower than the control group but still within the normal range, and after 3 weeks of avoiding bulimic behaviors, TSH levels increased, and T3/T4 levels decreased, potentially due to the high metabolic rates during binge eating attacks and low-calorie intake during the avoidance period.[34] However, despite no weight loss, a low basal metabolic rate may have caused a physiological adaptation by reducing basal serum TSH and T3/T4 levels. As a result, hypothalamic-pituitary-thyroid axis disorders can be seen in BN patients even if there is no weight loss. The exact mechanisms that cause these disorders are unknown.[35]

In the comparison of lipid profiles between the groups, BN showed higher levels of triglycerides than the AN group ($P<0.05$) (Figure 1b), indicating increased triglyceride synthesis and storage as an energy source in adipose tissue and liver cells, which are consistent with the results of the previous studies.[36] Starvation and secondary hyperlipoproteinemia accompany AN disease. Lipoproteins and plasma lipids are affected by plasma fatty acid patterns.[37] Plasma lipid and lipoprotein alterations in AN cause an increase in the synthesis of triglyceride-rich lipoproteins while maintaining unchanged cholesterol synthesis, and potential contribution from enhanced exogenous cholesterol resorption, leading to severe yet reversible hypercholesterolemia.[38] A similar study observed that total cholesterol, triglyceride, and HDL-cholesterol concentrations increased in patients with AN compared to a control group.[39] Changes in these physiological processes can result in modifications in mental functioning, such as mood, cognition, and conduct (for instance, behaviors that resemble depression). Recent studies indicate that administering metreleptin to AN patients increases leptin levels and improves symptoms such as hyperactivity, repetitive thoughts of food, restlessness, fear of gaining weight, and depression.[4] Therefore, remarking dyslipidemia profile, as was done in the present study, and using these values as a marker may be useful for diagnosing and treating patients.

Furthermore, the liver function (AST, ALT, and GGT; Figure 1c) and prolactin levels were evaluated in the two groups. The present study showed differences in liver function tests between AN and BN patients noting lower AST and ALT levels in the BN group. Moreover, higher prolactin levels in the BN group suggest an altered hypothalamic-pituitary-gonadal axis. Hence, one might consider the potential influence of dopamine and its role in prolactin regulation.[40] Starvation-induced liver cell damage and elevated aminotransferases are common in individuals with AN. Still, they can be differentiated from hepatic steatosis through ultrasonography, refeeding, and weight restoration and can rapidly normalize elevated enzyme levels.[41] Liver function tests may also be elevated due to malnutrition before refeeding begins and improve as the refeeding process progresses. This is a manifestation of excessive calories and fat deposition in the liver.[42] In Figure 1d, higher prolactin levels were observed in individuals with BN compared to AN, indicating its influence on the gonadal axis and central nervous system neurohormones. At the same time, dopamine acts as the primary inhibitor and plays a role in lactation. Still, no significant difference in prolactin levels was found in a study on prepubertal girls with eating disorders compared to those without. However, lower leptin and IGF-1 levels were observed in children with eating disorders.[43] It has been reported that prolactin inhibits lipoprotein lipase in the body preventing triglyceride breakdown during lactation, which explains the positive

correlation with LDL.[44] Patients with eating disorders, especially BN, exhibit reduced dopamine receptors due to continuous stimulation of the dopamine center through binge eating behavior, leading to diminished inhibitory effect of dopamine on prolactin and consequently higher prolactin levels, as indicated by decreased dopamine and down-regulation of D2 receptors in the striatal pathway.[45]

Moreover, the present study pointed to imbalances in minerals (Figure 2), such as calcium and magnesium in individuals with eating disorders.[46] In addition, this difference can also be attributed to the increase in AN caused by "refeeding syndrome".[47] In other words, the impact of vomiting in BN on ion imbalance and laxative use may be relevant. The study also showed the role of laxative use in magnesium loss and its effects on electrolyte levels, with a higher frequency of use observed in AN than BN patients, independent of vomiting behavior.[48] Repeated laxative use leads to magnesium loss from the gastrointestinal tract, preserved magnesium levels in the kidneys due to increased renin-angiotensin-aldosterone system (RAAS) activity, blurring the disease distinction, and positive correlations between prolactin and AST levels in the anorexia group, along with a negative correlation with LDL (Table 2).

Finally, PCA differentiates AN and BN patients based on clinical features. PCA effectively captures data variability. Besides, the NB model is a promising approach for identifying eating disorders, with high accuracy, precision, and recall for AN patients. PCA results showed AN and BN patients can be differentiated based on clinical features, with PC1 representing lipid profile and thyroid function and PC2 representing electrolyte levels ($Ca^{2+}$and Mg^{2+}), indicating that PCA effectively captures data variability and provides insights for distinguishing these disorders (Figure 3). Machine learning approaches provide unbiased, data-driven information to healthcare practitioners, helping them distinguish between various eating problems, supplement their therapeutic competence, diagnose patients, create individualized treatment plans, and ultimately improve patient outcomes. The NB model showed promising results in identifying eating disorders, with an accuracy of 82.9% and higher precision and recall values.

The study sample size was reasonable, but it may not fully represent the diversity of individuals with eating disorders. The identification of these disorders could be improved by a larger and more diverse sample. Although clinical features, biomarkers, and eating disorders were investigated in the study, limited causality was established and causal relationships between these factors need to be determined through further research. Moreover, treatment modalities were not specifically assessed for their effects on clinical characteristics and biomarkers for AN and BN. There is a possibility of future research examining the effect of specific interventions on these parameters. This study's findings might not be generalizable to populations outside its geographic and demographic scope. Various factors, such as culture, genetics, and geography, could influence the presentation of eating disorders and related biomarkers. Additionally, while the machine learning models show promise in distinguishing between eating disorder groups, they should be validated in larger and more diverse datasets to assess their reliability and generalizability.

Conclusion

Metabolic profiles, including dyslipidemia, thyroid functions, and mineral imbalances, serve as significant markers for distinguishing between patients with AN and BN. Machine learning algorithms show promise as useful tools for this discrimination. A larger and more diverse population will need to be studied to ensure the robustness and reliability of the results and gain a comprehensive understanding of the metabolic disparities between individuals with AN and BN.

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Competing Interests

The authors have no conflict of interest to declare.

Data Availability Statement

Data will be made available on request.

Ethical Approval

This was a retrospective study. The study received full ethical approval from the non-invasive clinical research ethics committee of the Üsküdar University in Istanbul, Turkey (date: 15.10.2020, decision number 16/02). Informed consent was obtained from the participants.

The research conformed to the principles of the 2013 Declaration of Helsinki and was approved by the non-invasive clinical research ethics committee of the Üsküdar University (date: 15.10.2020, decision number 16/02).

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