ORIGINAL ARTICLE

Correlation between eosinophils and aminotransferases among patients with and without diabetes from a polyclinic in the district of Villa El Salvador, Lima, Peru

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ABSTRACT

Objective: To determine the correlation between eosinophil differential counts and aminotransferase levels among patients with and without diabetes from a polyclinic in the district of Villa El Salvador. **Materials and methods:** An observational, analytical and correlational study was conducted on 767 individuals, out of which 500 were patients without diabetes and 267 were patients diagnosed with diabetes mellitus (DM) for at least six months and undergoing treatment. The study variables included age, sex, basal glycemia, eosinophil differential counts, aspartate aminotransferase (AST) levels and alanine aminotransferase (ALT) levels. The Kolmogorov–Smirnov test was used to assess normality and Spearman's correlation coefficient was applied. The cut-off point for statistical significance was set at α = 0.05. Data analysis was performed using IBM Statistical Package for Social Sciences (SPSS) Statistics 25 software for Windows. **Results:** Among patients without diabetes, elevated AST and ALT levels were observed in 46.40 % and 27.20 %, respectively. In contrast, 62.50 % of patients with diabetes had elevated AST levels, while 35.50 % had elevated ALT levels. Among patients with diabetes, a moderate and negative correlation between eosinophil differential counts and AST (Rho = -0.665) and ALT (Rho = -0.586) levels was found, whereas the group of patients without diabetes showed a weak or null correlation. **Conclusions:** Eosinophil differential counts are moderately and negatively correlated with aminotransferase levels among patients with diabetes. Given the study limitations and the lack of direct precedents, further research with larger populations are needed. The interaction between polymorphonuclear cells, such as eosinophils, and hepatic and systemic inflammatory markers, such as aminotransferases, may serve as an early pathophysiological indicator of DM, potentially years or decades before the onset of micro- and macrovascular systemic complications of this endocrinopathy.

Keywords: Blood Glucose; Eosinophils; Statistics, Nonparametric (Source: MeSH NLM).

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INTRODUCTION

Diabetes is a metabolic disorder characterized by elevated blood glucose levels (hyperglycemia), primarily resulting from insufficient insulin production by the pancreas or the body's ineffective use of insulin [1]. It has a high global prevalence, with approximately 500 million people currently living with the condition. This figure is projected to rise by 25 % in 2030 and 50 % in 2045 [2]. The disease is associated with sedentary behavior and poor dietary habits, and is more prevalent in urban than rural areas [3], as well as in high-income countries compared to low-income ones. Moreover, one in two individuals with diabetes is unaware of their diagnosis [4]. Type 2 diabetes mellitus (T2DM), the most common form of the disease, arises from increased peripheral insulin resistance and impaired insulin secretion, which together affect glucose uptake in peripheral tissues [5]. A small proportion of individuals with T2DM also exhibit autoimmune processes affecting the pancreatic islets, similar to those observed in type 1 diabetes (T1DM) [6]. Obesity and weight gain play a central role in the pathogenesis of diabetes, as the expansion of adipose tissue elevates circulating levels of free fatty acids, which in turn disrupt insulin-mediated glucose uptake [7]. Additionally, adipose tissue acts as an endocrine organ, releasing proinflammatory mediators—such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), leptin and resistin—that may impair glucose metabolism [8].

Eosinophils are white blood cells whose cytoplasm contains granules rich in major basic protein and eosinophil cationic protein [9]. Like monocytes, macrophages and basophils, eosinophils originate from the myeloid lineage and are part of the innate immune system [10]. They contribute to host defense against parasitic and intracellular bacterial infections and play a role in modulating immediate

hypersensitivity reactions [11]. Prolonged eosinophilia has been shown to cause tissue damage, likely due to the presence of toxic proteins within eosinophilic granules, which are detrimental not only to parasites but also to host tissues, thus contributing to chronic inflammation and organ dysfunction when exposure persists over extended periods [12]. Eosinophil differential count may vary according to circulating cortisol levels and tend to decrease in response to stress, beta-blocker or corticosteroid use, and increase in allergic conditions and parasitic infections [13].

Aminotransferases—formerly referred to as transaminases—are a component of the most frequently ordered liver function tests in primary care [14]. These protein enzymes are involved in transamination processes and the synthesis of nonessential amino acids. They are continuously released from damaged cells and therefore serve as markers of acute and chronic liver injury or inflammation. The most relevant aminotransferases are aspartate aminotransferase (AST) and alanine aminotransferase (ALT) [15]. Elevated levels of these enzymes may occur in various conditions, including viral liver disease, Budd-Chiari syndrome, liver cancer and chronic alcohol consumption [16].

Metabolic regulation in the human body involves complex, dynamically interacting neuroendocrine and humoral immunity mechanisms. In diabetes mellitus (DM), autoimmune processes and inflammatory mediators contribute to both short- and long-term vascular and neurological hemodynamic disorders [17]. Accordingly, cells involved in inflammatory and immune responses may play a role in the pathogenesis of DM. Chronic hyperglycemia has been associated with elevated aminotransferase levels; for example, Miyake et al. (2003) reported that glucose intolerance was linked to mildly increased aminotransferase levels in Japanese men without diabetes [18]. Similarly, González et al. (2011) found that aminotransferase levels were associated with fasting glucose intolerance and suggested that such elevations may constitute a risk factor for DM [19]. In a study examining aminotransferase levels and unhealthy dietary habits, Mirmiran et al. (2019) observed that a diet high in fast-food carbohydrates not only promoted the long-term development of non-alcoholic fatty liver disease but also led to elevated aminotransferase levels, along with increased serum glucose and lipid concentrations [20].

The association between aminotransferases and hyperglycemia has been extensively explored across countries and research contexts, generating a substantial body of literature [21]. However, the potential interaction between aminotransferases and conventional complete blood count (CBC) parameters, such as eosinophils, has received comparatively little attention. Some evidence suggests that eosinophils may play a role in the pathophysiology of DM. For instance, Gilbert et al. (1978) reported that patients with asthma had a lower likelihood of developing DM [22], while Wu et al. (2011) observed in animal models that eosinophilia in adipose tissue improved glucose tolerance, suggesting that eosinophils may play a role in the pathophysiology of DM [23].

The relationship between aminotransferases and eosinophils has been examined in various clinical contexts, particularly in systemic inflammatory conditions such as preeclampsia [24], drug reaction with eosinophilia and systemic symptoms (DRESS) [25], eosinophilic hepatitis [26], Kawasaki disease [27] and neoplastic disorders such as chronic myeloid leukemia [28]. These studies consistently report that elevations in AST and/or ALT are accompanied by increases in CBC markers, including eosinophils. Such increases and decreases appear to be driven by chemotactic factors, cytokines and other proinflammatory mediators. However, whether DM influences the correlation between eosinophil differential counts and aminotransferase levels among patients with or without diabetes remains unknown, as no studies specifically addressing this question have been identified.

Accordingly, this study aimed to determine the correlation between eosinophil differential counts and aminotransferase levels among patients with and without diabetes, based on the hypothesis that this potential interaction remains an underexplored aspect of the pathophysiology of the disease.

MATERIALS AND METHODS

Study design and population

This observational, analytical and correlational study was conducted on patients attending a parish polyclinic in the district of Villa El Salvador, Lima, Peru, either for routine medical checkups or as part of a health promotion and disease prevention campaign. The campaign included a physical examination, CBC and liver function tests. Patients with current or prior parasitic infections, asthma or moderate-to-severe atopy were excluded, as well as those undergoing corticosteroid or immunomodulatory treatment at the time of evaluation. The study population consisted of approximately 1,200 individuals with normal fasting blood glucose levels and 500 individuals with fasting glucose levels ≥ 126 mg/dL and a confirmed diagnosis of DM for at least six months. A non-probability convenience sampling method was employed. Based on the inclusion criteria, data were collected from 500 individuals with normal glucose levels and 267 individuals with DM. All participants were 18 years or older and had no other endocrine-metabolic or autoimmune disorders, such as thyroid disease, systemic lupus erythematosus or rheumatoid arthritis.

Variables and measurements

Data were collected from laboratory reports documented in patients' medical records. The qualitative variable was sex. Quantitative variables included age (by age group), patients with fasting blood glucose levels ≥ 126 mg/dL (regardless of comorbidities or glycemic control treatment regimen) and patients without diabetes, including those with normal fasting glucose (70–110 mg/dL) and prediabetes (111–125 mg/dL), also regardless of comorbidities. These parameters were based on the clinical practice recommendations of the American Diabetes Association (ADA) [29]. Other variables included eosinophil differential counts and aminotransferase levels—AST (reference range: 5–40 mg/dL) and ALT (reference range: 7–56 mg/dL)—as

defined by the specimen processing laboratory's standards.

Data collection procedures were coordinated with the polyclinic's administrative board. Records were obtained from routine medical checkups and health promotion and disease prevention campaigns held on the third Thursday of each month between January 2021 and July 2022. The relevant information was compiled into an anonymized Excel 2016 database. Upon completion of the data collection period, the dataset was imported into IBM Statistical Package for Social Sciences (SPSS) Statistics 25 for processing and analysis.

Statistical analysis

Data were processed using IBM SPSS Statistics 25. Descriptive statistics were calculated for categorical variables, such as sex and age, and for numerical variables, including erythrocyte sedimentation rate (ESR), hemoglobin, hematocrit and red blood cell count. Variables were dichotomized and analyzed using 2×2 contingency tables, and the results were summarized in tables. For inferential statistical analysis, bivariate correlation was performed. Pearson's correlation coefficient was used to assess the relationship between numerical variables after assessment of normality with the Kolmogorov–Smirnov test, which indicated non-normal distribution. The cut-off point for statistical significance was set at $\alpha = 0.05$.

Ethical considerations

The study was approved by the polyclinic's administrative board. Patient data were coded and recorded in an anonymized database; no personally identifiable information was collected, as only quantitative clinical record data were used. Therefore, informed consent was not required. Data access was restricted to the principal researcher to ensure confidentiality. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

RESULTS

A greater number of individuals without diabetes were included in the study, as this group comprised the apparently healthy population that regularly attended medical checkups as part of a health promotion and disease prevention campaigns. However, sufficient data were also obtained from individuals with diabetes during the study period to allow for the planned correlation analyses. Additionally, Pearson's chi-square test showed a statistically significant association by sex for both male ($p = 0.000$) and female ($p = 0.000$) participants (Table 1).

Table 1. Sex, age group and fasting blood glucose levels among patients with and without diabetes

Sex				Age group			Total
				Young adult	Middle-aged adult	Older adult	
Male	Fasting blood glucose ranges (mg/dL)	70-110	*n*	30	57	53	140
			%	56.60	37.50	56.20	37.01
		111-125	*n*	8	45	57	110
			%	15.09	30.26	16.80	28.41
		≥ 126	*n*	15	50	59	124
			%	28.31	32.24	27.00	34.58
	Total		*N*	53	152	159	374
			%	100	100	100	100
Female	Fasting blood glucose ranges (mg/dL)	70-110	*n*	33	52	63	148
			%	40.24	37.41	34.63	37.67
		111-125	*n*	33	38	41	102
			%	40.24	27.34	22.52	25.95
		≥ 126	*n*	16	49	78	143
			%	19.52	35.25	42.85	36.38
	Total		*N*	82	139	182	393
			%	100	100	100	100

Among patients without diabetes, elevated AST levels (46.40 %) were more frequent than elevated ALT levels (27.20 %). Normal eosinophil differential counts were observed in the majority of cases (85.10 %) (Table 2).

Table 2. Aminotransferase levels and eosinophil differential counts among patients without diabetes

	Reference range	Frequency	Percentage (%)
AST	5-40	268	53.60
	≥ 41	232	46.40
	Total	500	100
ALT	7-56	364	72.80
	≥ 57	136	27.20
	Total	500	100
Eosinophil differential count	1-4	425	85.10
	≥ 5	75	14.90
	Total	500	100

AST: aspartate aminotransferase; ALT: alanine aminotransferase.

Among patients with diabetes, a higher proportion exhibited elevated AST levels (62.50 %), while the majority had ALT levels within the normal range (64.50 %). Likewise, most patients had eosinophil differential counts within the normal reference range (90.30 %) (Table 3).

Table 3. Aminotransferase levels and eosinophil differential counts among patients with diabetes

	Reference range	Frequency	Percentage (%)
AST	5-40	100	37.50
	≥ 41	167	62.50
	Total	267	100
ALT	7-56	172	64.50
	≥ 57	95	35.50
	Total	267	100
Eosinophil differential count	1-4	241	90.30
	≥ 5	26	9.70
	Total	267	100

AST: aspartate aminotransferase; ALT: alanine aminotransferase.

Among patients with fasting blood glucose levels ≤ 125 mg/dL, no correlation was observed between eosinophil differential counts and AST levels, whereas a weak and negative correlation was found with ALT levels. In contrast, a strong and positive correlation was observed between ALT and AST (Rho = 0.806) (Table 4).

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Table 4. Spearman's correlation between eosinophil differential counts and aminotransferase levels among patients with normal or prediabetic fasting glucose

			AST	ALT	Eosinophil differential count
Spearman's Rho	AST	Correlation coefficient	1.000	0.806**	-0.174*
		Two-tailed significance		0.000	0.032
		N	250	250	250
	ALT	Correlation coefficient	0.806**	1.000	-0.119
		Two-tailed significance	0.000		0.146
		N	250	250	250
	Eosinophil differential count	Correlation coefficient	-0.174*	-0.119	1.000
		Two-tailed significance	0.032	0.146	
		N	250	250	250

AST: aspartate aminotransferase; ALT: alanine aminotransferase.
*Correlation is significant at the 0.05 level (two-tailed).
**Correlation is significant at the 0.01 level (two-tailed).

Among patients with diabetes, a moderate and negative correlation was observed between eosinophil differential counts and ALT levels (Rho = –0.867), as well as between eosinophil differential counts and AST levels (Rho = –0.665). The correlation between ALT and AST remained strong and positive in patients with and without diabetes (Table 5).

Table 5. Spearman's correlation between eosinophil differential counts and aminotransferase levels among patients with diabetes

			AST	ALT	Eosinophil differential count
Spearman's Rho	AST	Correlation coefficient	1.000	0.867**	-0.665**
		Two-tailed significance		0.000	0.001
		N	267	267	267
	ALT	Correlation coefficient	0.867**	1.000	-0.586**
		Two-tailed significance	0.000		0.005
		N	267	267	267
	Eosinophil differential count	Correlation coefficient	-0.665**	-0.586**	1.000
		Two-tailed significance	0.001	0.005	
		N	267	267	267

AST: aspartate aminotransferase; ALT: alanine aminotransferase.
**Correlation is significant at the 0.01 level (two-tailed).

DISCUSSION

A higher proportion of patients with diabetes exhibited elevated AST levels compared to ALT levels. In a review of 13 large-scale prospective cohort studies, Kunutsor et al. (2014) confirmed that AST levels are elevated in patients with diabetes and concluded that the relationship between this enzyme and T2DM may be complex [30]. This finding is consistent with physiological principles: although both AST and ALT are found in various tissues, AST is more abundant in peripheral tissues, whereas ALT is primarily—though not exclusively—concentrated in the liver. Therefore, elevated AST levels among patients with diabetes may reflect chronic inflammation, hyperglycemia and insulin resistance. By contrast, a high proportion of patients without diabetes exhibited ALT levels above the normal range, while AST levels largely remained within normal limits. Aggarwal et al. (2020) reported persistently elevated ALT levels among asymptomatic, healthy adults in a community in northern India, suggesting the presence of underlying liver damage [31]. Given that ALT is closely associated with liver function—and that the liver is particularly susceptible to poor dietary habits and sedentary behavior—it is likely that the elevated ALT levels observed among participants without diabetes in the present study are attributable to these factors.

A strong and positive correlation was observed between aminotransferase levels among patients with and without diabetes. The physiological proximity of these enzymes accounts for this association, as both enzymes are involved in glycogen synthesis, transamination, nonessential amino acid synthesis and amino acid degradation. This relationship is commonly expressed as the AST/ALT ratio, which serves as a diagnostic tool for evaluating liver disorders [32].

Regarding the correlation between eosinophils and aminotransferases among patients without diabetes, a weak and negative correlation was found with AST, while no significant association was observed with ALT. Among patients with diabetes, however, a moderate and negative correlation was identified between eosinophil differential counts and aminotransferase levels. The pathophysiological mechanisms underlying this association are beyond the scope of this study, and the absence of direct prior experimental or descriptive-observational evidence only leads to conjecture. Nonetheless, observational and experimental studies have indicated that elevated eosinophil levels may improve glucose tolerance, suggesting a potential protective or modulatory role against hyperglycemia in DM [33]. At the same time, elevated AST levels has been identified as a key mediator of inflammatory processes in DM [34]. It is therefore plausible that the action of AST—or the metabolic pathways associated with it—may partially suppress eosinophil differential count, thereby reducing their potential protective effect in hyperglycemia. In other scenarios, eosinopenia has been documented in systemic inflammatory states. For example, Orozco Araujo, Guerra Malaver (2012) reported that eosinopenia may present as a marker of systemic inflammation [35].

This study has several limitations. These include the use of convenience sampling rather than randomization, a limited sample size, and the potential influence of bias and confounding variables in patients with and without diabetes, such as comorbidities and concomitant medications. In conclusion, a moderate and negative correlation was found between eosinophil differential counts and aminotransferase levels among patients with a confirmed diagnosis of DM for at least six months, whereas no correlation was observed among patients without diabetes attending a polyclinic in the district of Villa El Salvador. Further studies are warranted to explore the strength of the association and interdependence between these variables in larger populations. In addition, more complex study designs—such as case-control or cohort studies—are needed to assess the relationship between these two laboratory markers in the context of DM. The confirmation of these findings could contribute to a better understanding of the pathophysiology of systemic and hepatic inflammatory changes associated with this disease, which may occur years or even decades before the development of micro- and macrovascular complications. This would underscore the possible role of polymorphonuclear cells in such alterations and in the expression of hepatic inflammatory markers. These findings may also support the development of pharmacological and preventive strategies and, more importantly, of surveillance or follow-up approaches involving the routine monitoring of CBC among patients with diabetes from the time of diagnosis, in parallel with the periodic assessment of fasting glucose and glycated hemoglobin levels.

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