



Association Between Procalcitonin and Lymphocyte Counts Post-Cupping Therapy in Patients With Diabetes Mellitus

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Abstrak

Diabetes mellitus (DM) is a long-term metabolic condition that arises when the pancreas fails to produce insulin properly, typically marked by blood glucose readings above the normal threshold of 200 mg/dL. This condition activates an inflammatory response within the body, and procalcitonin is among the biomarkers used to detect such inflammation in DM patients. Beyond this marker, hematological parameters, particularly lymphocyte counts, can also serve as useful indicators. Persistent hyperglycemia experienced by DM patients can give rise to systemic inflammation, which in turn alters both the quantity and function of lymphocytes. Cupping therapy is believed to help improve blood circulation and reduce blood glucose levels in patients with DM. This study aimed to determine the correlation between procalcitonin levels and lymphocyte counts in patients with DM after undergoing cupping therapy. This study employed a quasi-experimental method with a one-group posttest-only design. The study involved 22 patients with type 2 diabetes mellitus who underwent wet cupping therapy at Griya Bekam Lebah Emas Banyumas. Procalcitonin levels and lymphocyte counts were analyzed using the Spearman Rho correlation test. The result of the Spearman Rho correlation test showed a p-value of 0.257 and an r-value of 0.253. Based on these results, no significant correlation was found between procalcitonin levels and lymphocyte counts in DM patients post cupping therapy.

Keywords: Cupping therapy, Diabetes mellitus, Lymphocyte, Procalcitonin



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INTRODUCTION

Diabetes mellitus (DM) represents a chronic metabolic disorder marked by elevated blood glucose levels resulting from disturbances in pancreatic insulin secretion (Maulida et al., 2025). According to the World Health Organization, the global DM population has risen sharply, climbing from roughly 200 million cases in 1990 to about 830 million by 2022 (WHO, 2024). The International Diabetes Federation further reports that 11.1% of individuals aged 20-79 years live with DM, yet over 40% of these cases remain undiagnosed (IDF, 2025). In Indonesia, the Ministry of Health noted in 2023 that DM prevalence among the population aged 15 years and above, as measured through blood glucose testing, reached 11.7% (Kemenkes RI, 2023). At the regional level, the Central Java Provincial Health Office recorded 618,546 diabetic patients aged 15 years and older in 2021, of whom 91.5% had accessed standard healthcare services (Dinkes Prov Jateng, 2021). More specifically, Banyumas Regency documented 23,388 diabetes cases in 2024, with 23,910 patients (102.2%) receiving services that met the established standards (Dinkes Kab Banyumas, 2024).

Over time, persistent hyperglycemia in diabetic patients contributes to the development of complications and weakens immune function, leaving patients more vulnerable to infection (Wang et al., 2025). Procalcitonin (PCT) is one of the biomarkers commonly used to detect infection and inflammation. Structurally, it is a 116-amino-acid precursor of the hormone calcitonin, synthesized by neuroendocrine cells such as the thyroid's C cells. Under normal

physiological conditions, its serum concentration remains extremely low or even undetectable, but it rises markedly once a systemic inflammatory response to infection occurs (Mistry *et al.*, 2022). In healthy individuals, serum procalcitonin typically stays <0.05 ng/mL (PT Akurat Intan Madya, 2018). Whereas during infection its concentration climbs in proportion to disease severity (Abbas & El-yassin, 2022). In Indonesian patients with type 2 DM, a positive relationship has been observed between procalcitonin and fasting blood glucose levels, pointing to the biomarker's usefulness in tracking diabetes-related complications. Similarly, patients with diabetic foot ulcers tend to show elevated procalcitonin, illustrating the link between chronic infection and the metabolic disturbances characteristic of diabetes (Purwanto *et al.*, 2024).

Repeated bouts of inflammation coupled with ongoing metabolic disturbance in DM patients can alter macrophage activity, which may in turn intensify tissue-level inflammatory responses (Junior *et al.*, 2024). Circulating leukocytes, among other inflammatory factors, are recognized as indicators of subclinical inflammation (Kheradmand *et al.*, 2021). and lymphocytes represent one leukocyte subtype closely tied to DM. As key immune cells driving the inflammatory response (Zhongyuan *et al.*, 2023). lymphocytes normally range between 20% and 40% (equivalent to $1.0\text{--}3.0 \times 10^9/\text{L}$) of total leukocyte count (Kemenkes RI, 2020). A drop in this count typically signals an ongoing immune reaction to infection; such lymphopenia arises when activated lymphocytes migrate less into inflamed tissue and undergo greater apoptosis. Notably, procalcitonin and lymphocyte count tend to move in opposite directions—as procalcitonin rises in response to inflammation or bacterial infection, lymphocyte count tends to fall as part of the body's immune defense (Wardhani *et al.*, 2019).

The interplay between procalcitonin levels and lymphocyte counts mirrors the broader interaction between systemic inflammation and adaptive immunity. When infection or inflammation occurs, a surge in proinflammatory cytokines can substantially raise procalcitonin concentrations, while the same inflammatory cascade lowers lymphocyte counts through apoptosis, redistribution toward inflamed sites, and suppression of adaptive immune activity—collectively producing lymphopenia. Because chronic inflammation is a hallmark of diabetes mellitus, this relationship may be more pronounced in DM patients, suggesting that procalcitonin and lymphocyte count could jointly serve as complementary indicators of inflammatory severity (Wang *et al.*, 2019).

Cupping therapy is one approach used to help lower blood glucose in diabetic patients. It is thought to enhance blood flow and boost nutrient delivery to pancreatic β -cells, which supports insulin regulation and helps reduce glucose levels (Indriani & Nazmi, 2024). Mechanistically, cupping stimulates the skin and alters the surrounding tissue microenvironment, thereby activating the neuroendocrine-immune axis. This process is associated with several beneficial outcomes, including strengthened immunity, improved circulation, reduced inflammation, cellular changes, and a higher pain threshold (Alamin *et al.*, 2023). Previous findings have shown a significant relationship between procalcitonin levels and fasting blood glucose among type 2 diabetes patients ($p = 0.024$, $r = 0.205$), with elevated PCT considered a possible sign of chronic inflammation in this population (Purwanto *et al.*, 2024). Other reports indicate that type 2 DM patients tend to have a lower total lymphocyte percentage compared with healthy individuals (Allahyani *et al.*, 2023). However, whether procalcitonin and lymphocyte count are correlated specifically among DM patients who have undergone cupping therapy has not yet been established. Accordingly, this study set out to investigate the association between procalcitonin levels and lymphocyte counts in diabetes mellitus patients post cupping therapy.

RESEARCH METHODS

This study is a quasi-experimental, one-group posttest-only design and enrolled 22 diabetes mellitus patients who received wet cupping therapy at Griya Bekam Lebah Emas, Banyumas. Participants were recruited through accidental sampling based on predetermined inclusion and exclusion criteria. To be eligible, participants had to be type 2 DM patients between 18 and 75 years old who underwent wet cupping therapy on a regular basis, had blood glucose levels of at least 200 mg/dL, and provided signed informed consent. Individuals were excluded if their blood samples were hemolyzed or lipemic, if they withdrew before the study concluded, if they were pregnant or breastfeeding, or if they had a history of heart disease, liver disease, kidney disease, coagulation disorders, anemia, cancer, or severe bone fractures. Data collection took place at the Hematology Laboratory of Medical Laboratory Technology and the Banyumas District Health Laboratory in December 2025 - January 2026, after obtaining ethical approval from the Health Research Ethics Committee (KEPK) of Universitas Muhammadiyah Purwokerto, No. KEPK/UMP/161/II/2026.

Cupping Therapy Procedure

The wet cupping procedure was carried out by certified therapists from Griya Bekam Lebah Emas who hold accreditation from the Indonesian Cupping Association (PBI). The process began with identifying cupping points following Islamic tradition, followed by a 5-10 minute massage using habbatussauda oil or olive oil. Cupping glasses were then positioned over the designated points, and a hand pump was used to create suction 3-5 times, which was maintained for 2-3 minutes. The treated skin area was subsequently disinfected and punctured 15-20 times with a lancet. The cupping glasses were reattached and suction was reapplied 2-5 times for a duration of 5-10 minutes, adjusted according to each patient's condition. Finally, an antiseptic was applied to the cupping site to reduce the risk of infection (Sapada, 2018).

Specimen Collection Procedure

Following the cupping session, venous blood was drawn from each participant to determine procalcitonin levels and lymphocyte counts. Prior to blood collection, the participant's identity was confirmed, equipment was readied, and gloves were worn by the phlebotomist. A tourniquet was tied 7-10 cm above the intended puncture site, and the median cubital vein was located by palpation while the patient's fist was clenched. The puncture area was cleaned with 70% alcohol, left to dry, and the needle was inserted at an angle of 30 degrees or less. Blood was drawn into red-top and purple-top vacuum tubes, which were then gently mixed; the tourniquet was released, the needle withdrawn, and a plaster placed over the puncture site. Needles were discarded into a designated safety box, and samples were sent for immediate laboratory analysis (Marsudi *et al.*, 2023).

Procalcitonin Level Testing Procedure

Procalcitonin concentrations were measured using a quantitative immunochromatographic assay read on an easy reader device. Each test cassette was taken out of its packaging, placed on a flat surface, and labeled with the respondent's code. Using a micropipette held upright to avoid air bubbles, 25 μ L of serum or plasma was drawn and dispensed into the cassette's sample well, followed by the addition of 150 μ L (four drops) of diluent to initiate the reaction. After a 15-minute incubation period, the cassette was inserted into the easy reader device to obtain the result. Results were interpreted according to standard reference ranges: values below 0.05 ng/mL were classified as normal, 0.05–0.49 ng/mL indicated local infection, 0.50–1.99 ng/mL suggested possible systemic infection (sepsis), 2.00–



9.99 ng/mL denoted systemic infection, and values exceeding 10 ng/mL were associated with severe sepsis or septic shock (*PT Akurat Intan Madya, 2018*).

Lymphocyte Count Testing Procedure

To ensure accurate results, quality control (QC) procedures were carried out once daily prior to hematology testing, using three levels of control material (low, normal, and high). Parameters assessed through this QC process included erythrocyte count (RBC), hemoglobin (Hb), hematocrit (HCT), leukocyte count (WBC), and platelet count, with all measurements logged onto a monitoring chart for automated evaluation (*Prasetya et al., 2024*). Control materials were left at room temperature for 10-15 minutes before use, and the hematology analyzer was checked to confirm it was functioning properly, alongside verification of reagent quality. Lymphocyte count testing itself was performed by loading blood specimens into the HA sample rack, after which results were generated and printed automatically by the analyzer (*Jaenuddin et al., 2024*).

Data Analytics

Procalcitonin levels and lymphocyte counts were analyzed using Spearman's correlation coefficient.

RESEARCH RESULTS AND DISCUSSION

Research Result

The characteristics of research subjects in patients with DM post-cupping therapy are presented in Table 1.

Table 1. Characteristics Data of Research Subjects in DM Patients After Cupping Therapy

Characteristics	Frequency (n)	Percentage(%)	Mean $\pm$ SD	Median (Minimum-Maximum)
Age (y.o)	22	100	61.00 $\pm$ 8.552	64.50 (42-72)
Gender				
Male	4	18.2		
Female	18	81.8		
Duration of diabetes				
$\leq$ 5 years	14	63.6		
$>$ 5 years	8	36.4		
Oral medication				
Yes	11	50		
No	11	50		
Use of insulin				
Yes	2	9.1		
No	20	90.9		
Frequent urination				
Yes	11	50		
No	11	50		
Frequent hunger				
Yes	7	31.8		
No	15	68.2		
Frequent thirst				
Yes	7	32		
No	15	68		
Experiencing wounds				
Yes	2	9.1		
No	20	90.9		

Experiencing diabetic ulcers				
Yes	0	0		
No	22	100		
Cigarette Consumption				
Yes	2	9.1		
No	20	90.9		
Exercise				
Yes	22	100		
No	0	0		
Exercise routine in a week				
1 – 2 times	11	50		
3 – 4 times	11	50		
Frequency of cupping therapy each week				
Once a week	10	45.5		
Once every two weeks	12	54.5		
Relaxation after cupping therapy				
Yes	22	100		
No				
Therapies other than cupping therapy				
Yes	0	0		
No	22	100		
Procalcitonin level (ng/mL)	22	100	0.323± 0.0869	0.300 (0.3-0.7)
Lymphocyte count (%)	22	100	32.27 ± 5.700	33.50 (22 - 40)

Most participants (16 patients, or 73%) were aged 57 years or older, with a mean age of 61.00 ± 8.552 years. Female patients made up the larger share of the sample (18 people, 82%), and 14 patients (64%) had been diagnosed with DM for less than five years. Regarding treatment and symptom patterns, 11 patients (50%) were taking oral antidiabetic medication, 2 patients (9%) used insulin, 11 patients (50%) reported frequent urination, 7 patients (32%) experienced frequent hunger, and another 7 patients (32%) reported frequent thirst. Wounds were present in 2 patients (9%), 2 patients (9%) were smokers, and all 22 patients (100%) engaged in regular exercise and reported relaxation after cupping sessions. Association Between Procalcitonin and Lymphocyte Counts Post-Cupping Therapy in Patients With Diabetes Mellitus is presented in Table 2.

Table 2. Association Between Procalcitonin and Lymphocyte Counts Post-Cupping Therapy in Patients With Diabetes Mellitus

	Lymphocyte count
Procalcitonin levels	$r = 0.253$ $p = 0.257$ $N = 22$

Table 2 shows that there is no relationship between procalcitonin levels and lymphocyte counts ($p = 0.257$) in patients with diabetes mellitus post-cupping therapy.

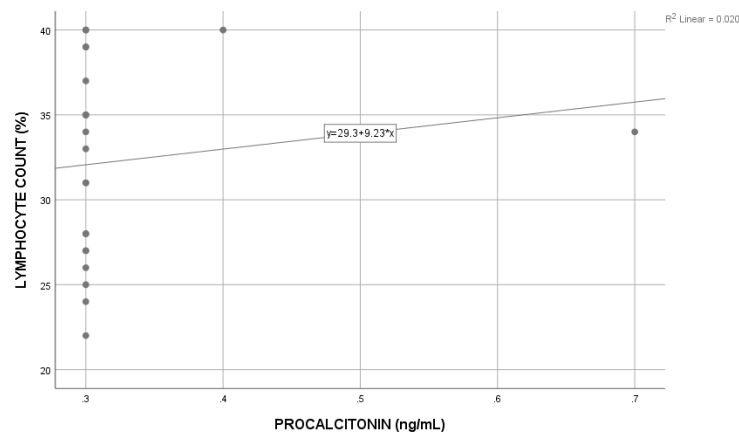


Figure.1. Association Between Procalcitonin and Lymphocyte Counts Post-Cupping Therapy in Patients With Diabetes Mellitus

The scatter plot in figure 1 illustrates a weak positive association between procalcitonin levels and lymphocyte counts, evidenced by the shallow slope of the regression line and the low coefficient of determination (R^2). This pattern suggests that the two parameters are not meaningfully related within this group of respondents.

Discussion

The demographic profile of the study participants revealed that most patients with diabetes mellitus were aged 57 years or above, with a mean age of 61.00 ± 8.552 years, consistent with earlier evidence that DM is more common among adults aged 55 and older (Yu *et al.*, 2025). Globally, DM prevalence continues to climb, with developed nations experiencing steeper increases; notably, cases rise sharply from age 50 onward, particularly within the 50-69 age bracket, and peak incidence has been reported around age 55 (Khan *et al.*, 2020). This tendency for diabetes to concentrate in older age groups aligns with findings b (Nurliah *et al.*, 2023). Such a pattern can be explained by the natural decline in physiological function that accompanies aging, which may impair pancreatic endocrine activity and reduce insulin production, thereby heightening susceptibility to diabetes mellitus (Harefa & Lingga, 2023). This study additionally found that women (82%) were more commonly affected by diabetes mellitus than men (18%), a pattern echoed (Garcia *et al.*, 2023). who reported that women in Eloy Alfaro faced a fivefold higher risk of diabetes and obesity compared with men. Conversely, some studies report a slightly higher number of men diagnosed with type 2 diabetes and fasting hyperglycemia (Willer *et al.*, 2023). One possible explanation for women's heightened risk is their generally higher body mass index relative to men, compounded by hormonal fluctuations during the reproductive years and after menopause that influence body fat distribution and, consequently, diabetes risk (Rosita *et al.*, 2022). The length of time a person has lived with diabetes also shapes their complication risk, since prolonged hyperglycemia promotes the formation of advanced glycation end products (AGEs), raises reactive oxygen species (ROS) levels, and induces oxidative stress—processes that ultimately damage nerves and organs (Wirayudha *et al.*, 2025). Interestingly, patients diagnosed with type 2 DM for five years or less tend to show poorer treatment adherence (Wulandari *et al.*, 2020).

Only 9% of participants in this study used insulin, a finding that may reflect limited understanding of and adherence to insulin therapy among DM patients (Feleke *et al.*, 2025). Classic clinical symptoms of DM typically include polydipsia, polyuria, and polyphagia (Dong *et al.*, 2023). However, atypical presentations are also frequently observed among newly diagnosed cases (Joseph, 2025). Notably, none of the respondents in this study presented with

diabetic ulcers. As a complication that does not affect every diabetic patient, diabetic ulcers occur at a prevalence of roughly 4-10%, indicating that they remain relatively uncommon within the broader DM population (Miyan *et al.*, 2024). Smoking is another factor capable of worsening health outcomes in diabetic patients, as the toxic compounds in cigarette smoke heighten oxidative stress and stimulate the release of pro-inflammatory cytokines, including procalcitonin, TNF- α , and IL-6. Such changes can drive procalcitonin levels upward as a marker of inflammation while simultaneously lowering lymphocyte counts due to compromised immune function—effects that, in diabetic patients, may further destabilize an already imbalanced immune system (Elisia *et al.*, 2020).

Regular physical activity plays a vital role in maintaining physical strength, and insufficient activity has been linked to reduced diabetes awareness among affected individuals. Poor dietary habits and obesity are likewise recognized as contributing factors in the onset of diabetes (Bai *et al.*, 2021). Cupping therapy is generally considered safe and may offer additional benefits, whether for relaxation purposes or as a complementary component of diabetes management (Rahman *et al.*, 2020). In this study, the mean procalcitonin level among DM patients undergoing cupping therapy was 0.323 ± 0.0869 ng/mL, ranging from a minimum of 0.3 ng/mL to a maximum of 0.7 ng/mL. As a biomarker, procalcitonin holds prognostic value and offers relatively high specificity for identifying bacteremia, sepsis, bacterial superinfection, and systemic inflammation (Cynthia *et al.*, 2022). It is synthesized by parafollicular cells as well as by the lungs and pancreas; while its levels normally stay low, they rise sharply during bacterial infection and only modestly in viral infections or non-infectious inflammatory states (Omar *et al.*, 2023). Although the association is weak, procalcitonin has been shown to correlate significantly with fasting blood glucose in type 2 diabetes patients, reinforcing its role not only as a marker of bacterial infection but also as an indicator of chronic inflammation (Purwanto *et al.*, 2024).

The mean lymphocyte count observed among cupping-treated DM patients in this study was $32.27 \pm 5.700\%$, ranging between 22% and 40%, which falls within the normal reference range of 20-40% (Kemenkes RI, 2020). This finding contrasts with earlier research reporting a lower total lymphocyte percentage in diabetic patients relative to healthy controls, along with shifts in lymphocyte subtype proportions potentially tied to heightened infection risk and altered immune responses in diabetes (Allahyani *et al.*, 2023). Based on Table 2, there is no statistically significant relationship emerged between procalcitonin levels and lymphocyte counts in diabetic patients following cupping therapy ($p > 0.05$). One possible explanation lies in the differing biological mechanisms governing each parameter: procalcitonin responds rapidly to acute conditions, whereas lymphocyte counts shift more gradually and are shaped by chronic factors and individual patient variation (Schuetz *et al.*, 2018). Variability in how patients individually respond to cupping therapy may also have contributed to this outcome. Although cupping is believed to reduce inflammation and enhance circulation, its effects on procalcitonin and lymphocyte counts do not necessarily manifest in tandem (Wang *et al.*, 2019). This indicates that changes in procalcitonin levels in diabetic patients do not directly affect lymphocyte counts, and vice versa.

Regarded as a relatively safe complementary and alternative treatment (Rahman *et al.*, 2020). Cupping therapy nonetheless appears capable of modulating immune responses, as reflected in reduced inflammatory markers and improved immune cell parameters. The magnitude of this immunomodulatory effect, however, is not uniform and can depend on the patient's clinical status, how often the therapy is performed, and the specific cupping technique applied (Kouser, 2021). Mechanistically, the microtrauma inflicted on skin and superficial tissue during cupping can provoke a mild inflammatory response, releasing inflammatory

mediators that may, under certain circumstances, contribute to a modest rise in procalcitonin—though far less pronounced than what is seen in acute bacterial infection. In diabetic patients free of infectious complications, this PCT elevation typically remains minor and stays within normal limits, since procalcitonin is a biomarker more closely tied to bacterial infection than to non-infectious inflammation (Mucka *et al.*, 2025).

The fact that none of the participants had diabetic ulcers likely accounts for why their procalcitonin levels stayed within the normal range or reflected only mild inflammation, given that procalcitonin is specifically tied to systemic inflammatory responses triggered by bacterial infection. In this study, the median procalcitonin level among cupping-treated DM patients was 0.3 ng/mL, which corresponds to the local infection category according to established reference values (PT Akurat Intan Madya, 2018). This figure is comparable to levels seen in healthy individuals and markedly lower than those reported in patients with diabetic foot ulcers or active infection (Omar *et al.*, 2023). Since procalcitonin responds most strongly to acute bacterial infection, its levels do not typically rise substantially under conditions of mild inflammation or in the absence of infection—such as in this diabetic cohort—which helps explain the lack of correlation with lymphocyte count (Wang *et al.*, 2019). The results of this study have implications for clinicians in understanding cupping therapy as a complementary therapy for patients with diabetes mellitus. The absence of a significant correlation between procalcitonin and lymphocytes does not necessarily indicate the absence of a physiological response, but may involve other immunological mechanisms that were not measured. Monitoring for infection remains important in patients with diabetes. Furthermore, the single-group design without a pretest and a control group limits the interpretation of post-intervention changes and the drawing of causal conclusions (Bierer *et al.*, 2025).

Even though diabetes brings about changes in immune function, lymphocyte counts tend to stay within normal limits as long as acute infection is absent (Torcal *et al.*, 2024). This is largely because lymphocytes, as core components of the adaptive immune system, respond more to chronic metabolic disturbance and prolonged oxidative stress than to acute inflammatory triggers (Moshfegh & Case, 2021). Cupping therapy's immunomodulatory properties may further help keep immune responses balanced, preventing sharp increases or decreases—an effect that could explain why lymphocyte levels remained within normal range in several patients, including those with diabetes, following treatment (Al-Bedah *et al.*, 2019). Taken together, these mechanisms likely account for the absence of a significant relationship between procalcitonin levels and lymphocyte counts among the DM patients who underwent cupping therapy in this study. Several limitations should be acknowledged. First, the sample was restricted to DM patients without diabetic ulcers. Second, the analysis focused solely on the relationship between procalcitonin levels and lymphocyte counts, without accounting for other inflammatory biomarkers such as TNF- α , IL-1, IL-6, and IL-12, or additional hematological parameters like monocytes, platelets, NLR, and PLR. A more comprehensive assessment incorporating these inflammatory biomarkers alongside a complete blood count would likely offer a fuller picture of inflammatory status and immune activity (Minko *et al.*, 2024).

CONCLUSION

This study found no significant correlation between procalcitonin levels and lymphocyte counts in DM patients post-cupping therapy ($p = 0.257$, $r = 0.253$). Future research involving patients with diabetic ulcers is recommended, along with the inclusion of additional inflammatory biomarkers—such as TNF- α , IL-1, IL-6, and IL-12—and hematological parameters, including monocytes, platelets, NLR, and PLR. The authors gratefully acknowledge the Institute for Research and Community Service (LPPM) of Universitas Muhammadiyah



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