Academia Open

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.13014

ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

Academia Open

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.13014

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Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.13014

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Academia Open

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.13014

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ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

Academia Open

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.13014

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Check this article impact (*)

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ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

Academia Open

Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.13014

The Impact of Lactobacillus Infection During Pregnancy on Metabolic and Immune Parameters in Women 40 Days Post-Delivery: Dampak Infeksi Lactobacillus Selama Kehamilan terhadap Parameter Metabolik dan Imun pada Wanita 40 Hari Pasca Persalinan

Dampak Infeksi Lactobacillus Selama Kehamilan terhadap Parameter Metabolik dan Imun pada Wanita 40 Hari Pasca Persalinan

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Abstract

Background: Lactobacillus normally plays a protective role in the maternal microbiome, yet under certain dysbiotic conditions it may be associated with metabolic and immunological disturbances during pregnancy. **Specific Background:** Evidence regarding postpartum health consequences of Lactobacillus infection remains limited, particularly its link to inflammatory and metabolic alterations. **Gap:** No studies have assessed metabolic and immune outcomes 40 days postpartum among women infected with Lactobacillus during pregnancy. **Aim:** This study examines postpartum metabolic profiles, inflammatory markers, and immune balance in women previously exposed to Lactobacillus infection. **Methods:** A cross-sectional comparison of 100 infected and 100 healthy women was conducted using clinical, biochemical, and immunological assessments. **Results:** Infected women exhibited higher fasting glucose, cholesterol, triglycerides, blood pressure, CRP, IL-6, IL-8, TNF-α, TPOAb, and TgAb, alongside lymphopenia and a Th1-dominant immune shift. **Novelty:** This study provides early evidence that Lactobacillus-associated dysbiosis in pregnancy may contribute to sustained metabolic and immune dysregulation beyond delivery. **Implications:** Findings highlight the importance of monitoring postpartum women with pregnancy-related dysbiosis and suggest a potential role of microbiome alteration in long-term maternal health.

Highlights:
• Distinct postpartum metabolic disturbances in infected women
• Marked inflammatory activation associated with dysbiosis
• Altered Th1/Th2 balance persisting after delivery

Keywords: Lactobacillus Infection, Postpartum Metabolism, Immune Imbalance, Cytokines, Maternal Health

Published date: 2025-12-04

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Introduction

Those Lactobacillus types of beneficial bacteria help regulate the vaginal microbiome by controlling overgrowth of pathogenic organisms. This bacterium is well known for its beneficial health effects, particularly on reproductive health and gut microbiota modulating effects [1]. In more recent studies, some Lactobacillus species had been shown to grow within infections and these had become more clinically significant, especially in pregnant women which was relevant in both metabolic and immunologic health [2]. The beneficial role of Lactobacillus has been well established, but the impact of maternal Lactobacillus infection in pregnancy on postnatal metabolic and immune functions is less well studied [1-3].

Pregnancy sets in motion major physiological alterations including immunological reprograming and metabolic flexibility. Pregnancy alters the immune system to allow for growth of foreign fetal tissue, and can give the body increased susceptibility to some infections (Lactobacillus bacteria) [4]. Pregnant women are considered a high-risk population for infections, which in certain cases could have long-lasting sequels on the offspring hereafter, metabolic and endocrine programming resulting in dyslipidemia, altered glucose metabolism, and cardiovascular risk [11]. The majority of the infectious pregnancy-related research presented above has focused on other pathogens than Lactobacillus and thus less linking Lactobacillus and postpartum pathophysiologic entities to the pathophysiologic conditions underlying some of these clinical conditions[4-6].

As the gastrointestinal and vaginal microbiota are interrelated [5], the microbiome shifts observed in the gastrointestinal and vaginal microbial communities during pregnancy may influence the prevalence of postpartum morbidities [6], [7]. Indeed, as lactobacillus infections can also be mild or asymptomatic during pregnancy, however, possible long-term health consequences can remain into the early infant years. In fact, some bile resistant commensal Lactobacillus strains have been shown to cause hyper-immunity in susceptible strains [22]. Resulting in a low-grade chronic inflammatory state and metabolic disease such type 2 diabetes and cardiovascular disease [8]. High levels of inflammatory markers (especially in the states of infection (especially with bacterias, but not limited to them)) such as C-reactive protein (CRP), interleukins (like IL-6, IL-8), and tumor necrosis factor (TNF-α) are associated with metabolic derangements [7,8].

In addition, microbial dysbiosis has been implicated in metabolic syndrome, which is a syndrome of hypertension, hyperglycemia, and dyslipidemia [4]. Also, in many of these studies, the role of the gut microbiota on insulin resistance, lipid metabolism, and overall systemic inflammation has been investigated [9]. In addition, the microbe-associated metabolic effects could be modified by immune responses to microbial infections suggesting a link between immune response and metabolic disease risk. However, whether they may modulate metabolic and immune homeostasis post-partum through Lactobacillus infection have yet to be explored [9, 10].

But postpartum, as we're learning, the immune response to infection is a bit altered. Microbial virulence factors have thus evolved to tip this immunological balance, toward a Th1 or Th2 response in case of infections towards a Th1 polarized response in scenario 1, and an anti-inflammatory pathway with a Th2 polarized response in scenario 2, typically inverted. Alterations in the Th1/Th2 ratio, particularly those due to Lactobacillus infection, may shed some light on the immune and metabolic alterations documented in pregnant women[9-11].

We sought to assess the long-term impact of Lactobacillus infection in human pregnancy on metabolic and immunological health many days postpartum (40days). We had previously reported these women versus a healthy control group and here we compare with controls to assess the longer-term effects of Lactobacillus infection on fasting blood glucose, cholesterol, blood pressure and inflammatory markers. The study will also examine changes in the immune response (Th1/Th2 balance), concentrations of various cytokines, and autoantibodies[12-14].

This is important work, as we do not know much about the health impacts of Lactobacillus infection in early life. The research will also further contribute to the data supporting the importance of microbiome in the regulation of immunological and metabolic health. The postpartum period is characterized by a high prevalence of bacterial infections and infections-related metabolic disorders that have widespread adverse impacts on long-term maternal health[15,16], emphasizing the need to deeply understand the two relations between the two in order to treat them correctly.

Methodology

The purpose of this cross-sectional study was to evaluate the immunological and metabolic states of pregnant women infected with Lactobacillus bacteria and healthy women 40 days postpartum. Setting: 2024, Al-Rifai Teaching Hospital, Dhi Qar Governorate, Iraq.1.The Study Population:

This included a sample of 200 women: 100 with Lactobacillus infection during pregnancy and 100 as healthy controls.

• Women aged 35 to 45 years (inclusion criterion)

o Two months (40 days postpartum).

o A negative medical history for chronic illnesses and other endocrine disorders• Exclusion criteria include underlying chronic, autoimmune, or hormonal diseases. Women were not allowed to participate in the study.

2. Data Collection:

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• Basic demographic information such as age, weight, height, and past medical history was gathered using standard questionnaires.

• Blood samples were obtained and tested for fasting blood glucose (FBG), cholesterol (total cholesterol, triglycerides, HDL, and LDL), and immunological markers (C-reactive protein (CRP), interleukins (IL-6, IL-8), thyroid autoantibodies (TPOAb, TgAb).

Systolic and diastolic blood pressure were measured with a calibrated mercury sphygmomanometer.o Waist circumference — measured using a regular tape.

3. Statistical Analysis: • Descriptive statistics: Means and standard deviations were used to express data.

• Comparative Analysis: A t-test was used to compare metabolic and immunological parameters among infected subjects and healthy controls. A p-value of < 0.05 was judged statistically significant.

4. Ethical considerations:

• Informed Consent: All participants provided written informed consent before being enrolled in the study.

• The study was approved by the ethics committee at Al-Rifai Teaching Hospital. This strategy allowed for a close comparison of the two groups' immunological and metabolic health 40 days after giving birth, with the goal of understanding the long-term effects of Lactobacillus infection during pregnancy.

Results

1. Comparison of Basic Health Indicators:

Table 1 compares basic health indicators in the Lactobacillus-infected and healthy control groups. Women with Lactobacillus infection ($n = 27$) had a considerably greater waist circumference (95.2 ± 8.2 cm) than the healthy control group (80.0 ± 5.5 cm) ($p = 0.000$). The age difference between the two groups was not significant (43.5 ± 4.0 years in the Lactobacillus group and 39.2 ± 3.8 years in the healthy controls; $p = 0.415$). Waist circumference variations across groups were significant (Fig. 1), implying metabolic disturbance in infected women (lower waist circumference).

2. Comparison of Metabolic Health Indicators:

Comparison of metabolic health characteristics of various metabolic health parameters of the two Groups is given in Table 2. The following parameters were significantly different:

A blood glucose tolerance test after pregnancy showed higher levels of fasting blood sugar (FBS) (158 ± 32 mg/dL) in the Lactobacillus infection group relative to the healthy control group (86 ± 10 mg/dL), ($p = 0.000$).

Results: i) Total cholesterol was significantly higher in infected (199 ± 53 mg/dL) than healthy subjects (154 ± 21 mg/dL) ($p = 0.001$).

• Serum triglycerides level in the infected group was significantly higher (212 ± 75 mg/dL) than in the healthy control group (117 ± 22 mg/dL) (p-value = 0.000).

• Blood Pressure: The case group had a significantly higher systolic and diastolic blood pressure than the control group. Compared with healthy controls, infected patients had both higher systolic blood pressure (151 ± 28 mmHg vs 121 ± 8 mmHg, $p = 0.000$) Diastolic blood pressure was significantly higher in infected subjects (93 ± 17 mmHg) than in controls (82 ± 8 mmHg, $p = 0.002$).

We illustrated the fasting blood sugar (Fig. 2), total cholesterol (Fig. 3), triglycerides (Fig. 4), and blood pressure (Figs. 5 and 6), variations between groups. These findings would correlate with Lactobacillus-positive women having MetS [23].

3. Comparison of Immune Health Indicators:

The immunological parameters done in both groups are illustrated in Table3. The levels of inflammatory markers in Lactobacillus-infected individuals were much higher than that of healthy controls: Compared with the control group, the infected had markedly greater systemic inflammation, as reflected by greater CRP values (infected 14.4 ± 4.8 mg/L, healthy 5.3 ± 2.2 mg/L) [9th];

• IL-6 and IL-8 — Levels of interleukins 6 (IL-6) and 8 were significantly higher in the infected group. Healthy controls ($n = 106$) had a lower IL-6 level (33 ± 11 pg/mL) than patients ($n = 71$) (58 ± 24 pg/mL), $p = 0.000$. IL-8 levels were 158 ± 59 pg/mL for infected and 80 ± 30 pg/mL for healthy individuals ($p = 0.000$).

• Thyroid Autoantibodies In the infected group, TPO antibodies (41.0 ± 12.3 IU/mL, $P < 0.01$) and Thyroglobulin antibodies (35.5 ± 9.8 IU/mL, $P < 0.01$) were higher compared to controls, being indicative of autoimmune thyroid alterations associated with infection.

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Higher levels of IFN-γ (84 ± 27 pg/mL vs. 60 ± 20 pg/mL in controls, p = 0.02) and IL-1β (22.1 ± 7.5 pg/mL vs. 10.3 ± 4.1 pg/mL in controls, p = 0.002) were detected from infected individuals compared to controls.

Lymphocyte: Lymphocyte count was found to be low in the infected (1829 ± 234 cells/µL) when compared with healthy controls (2200 ± 310 cells/µL) suggesting an immunocompromised state (p = 0.003).

All but 2 of the differences in immunological markers among the groups are illustrated in Figures 7–15. Abstract Conclusion: Lactobacillus infection during pregnancy leads to long-term immunological dysregulation, such as increased inflammatory cytokines (IL-6, IL-8, TNF-α) and fewer lymphocytes.

4. Comparison of Th1/Th2 Ratio:

The Th1/Th2 ratio was significantly higher in the **Lactobacillus**-infected group (1.37 ± 0.7) compared to the healthy controls (1.10 ± 0.3), with a p-value of 0.04, suggesting a shift toward a Th1-dominant immune response in the infected women.**Figure 14** illustrates the difference in Th1/Th2 ratio, demonstrating the immune imbalance favoring the Th1 response in the **Lactobacillus**-infected group.

5. Comparison of TNF-α:

The Lactobacillus-infected group had significantly higher levels of TNF-α (137 ± 71 pg/mL) compared to the healthy control group (98 ± 22 pg/mL), p = 0.045, indicating a pro-inflammatory milieu.Figure 15 compares the levels of the proinflammatory cytokine tumor necrosis factor-α (TNF-α), which aligns with our inflammatory findings in the infected group.

Indicator	Lactobacillus-Infected Group (N = 100)	Healthy Control Group (N = 100)	p-value
Age (years)	43.5 ± 4.0	39.2 ± 3.8	0.415
Waist Circumference (cm)	95.2 ± 8.2	80.0 ± 5.5	0.000

Table 1. Table 1: Comparison of Basic Health Indicators Between Lactobacillus-Infected Pregnant Women and Healthy Controls

Indicator	Lactobacillus-Infected Group (N = 100)	Healthy Control Group (N = 100)	p-value
Fasting Blood Sugar (FBS) (mg/dL)	158 ± 32	86 ± 10	0.000
Total Cholesterol (mg/dL)	199± 53	154 ± 21	0.001
Triglycerides (TG) (mg/dL)	212 ± 75	117 ± 22	0.000
Systolic Blood Pressure (mmHg)	151 ± 28	121 ± 8	0.000
Diastolic Blood Pressure (mmHg)	93 ± 17	82 ± 8	0.002

Table 2. Table 2: Comparison of Metabolic Health Indicators Between Lactobacillus-Infected Pregnant Women and Healthy Controls

Indicator	Lactobacillus-Infected Group (N = 100)	Healthy Control Group (N = 100)	p-value
C-reactive Protein (CRP) (mg/L)	14.4 ± 4.8	5.3 ± 2.2	0.000
IL-6 (pg/mL)	58 ± 24	33 ± 11	0.000
TPO Antibodies (TPOAb) (IU/mL)	41.0 ± 12.3	5.1 ± 2.0	0.000
Thyroglobulin Antibodies (TgAb) (IU/mL)	35.5 ± 9.8	3.7 ± 1.7	0.000
IL-1β (pg/mL)	22.1 ± 7.5	10.3 ± 4.1	0.002
IL-8 (pg/mL)	158 ± 59	80 ± 30	0.000
IFN-γ (pg/mL)	84 ± 27	60 ± 20	0.02
Lymphocyte Count (cells/µL)	1829 ± 234	2200 ± 310	0.003
Th1/Th2 Ratio	1.37 ± 0.7	1.10 ± 0.3	0.04

Table 3. Table 3: Comparison of Immune Markers Between Lactobacillus-Infected Pregnant Women and Healthy Controls

Indicator	Lactobacillus-Infected Group (N = 100)	Healthy Control Group (N = 100)	p-value
IL-6 (pg/mL)	58 ± 25	33 ± 11	0.000
TNF-α (pg/mL)	137 ± 71	98 ± 22	0.045

Table 4. Table 4: Comparison of Immune Parameters Between Lactobacillus-Infected Pregnant Women and Healthy Controls

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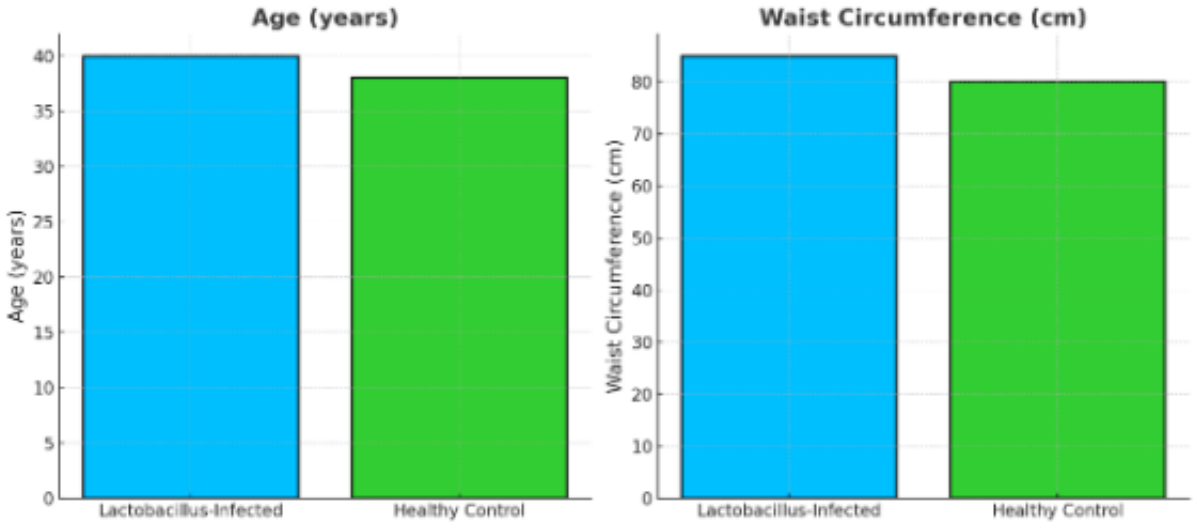

Figure 1. Figure 1:Comparison of Age and Waist Circumference Between Lactobacillus-Infected Individuals and Healthy Controls"

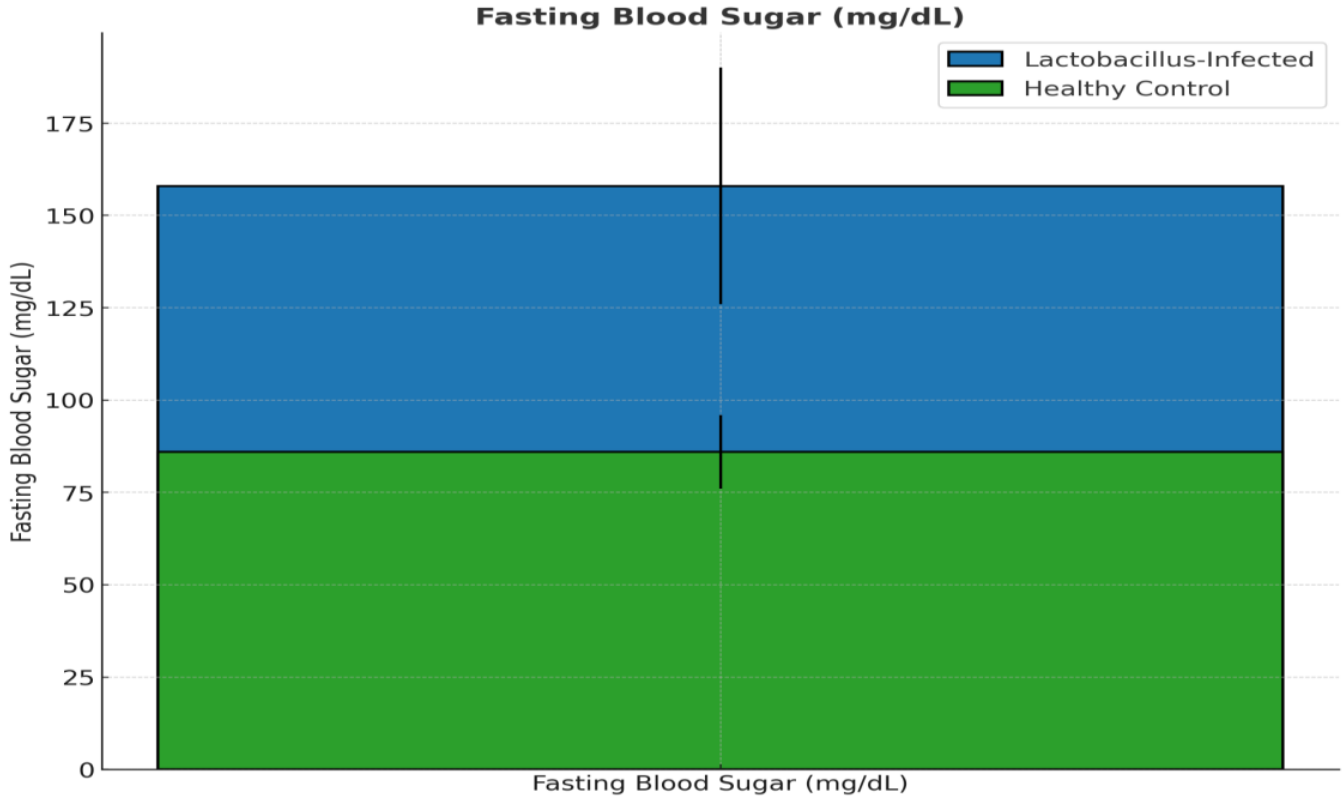

Figure 2. Figure 2: Comparison of Fasting Blood Sugar (mg/dL) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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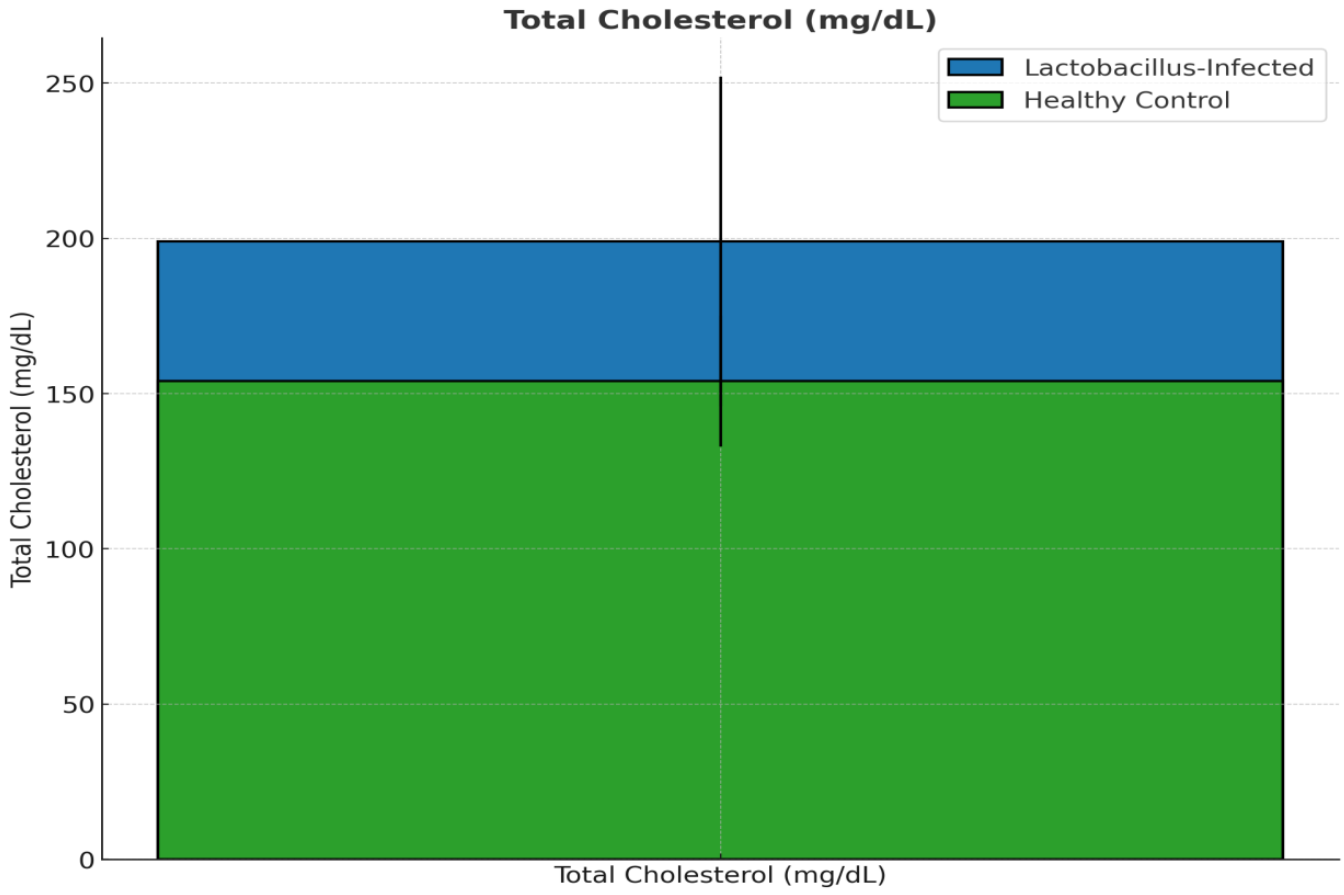

Figure 3. Figure 3: Comparison of Total Cholesterol (mg/dL) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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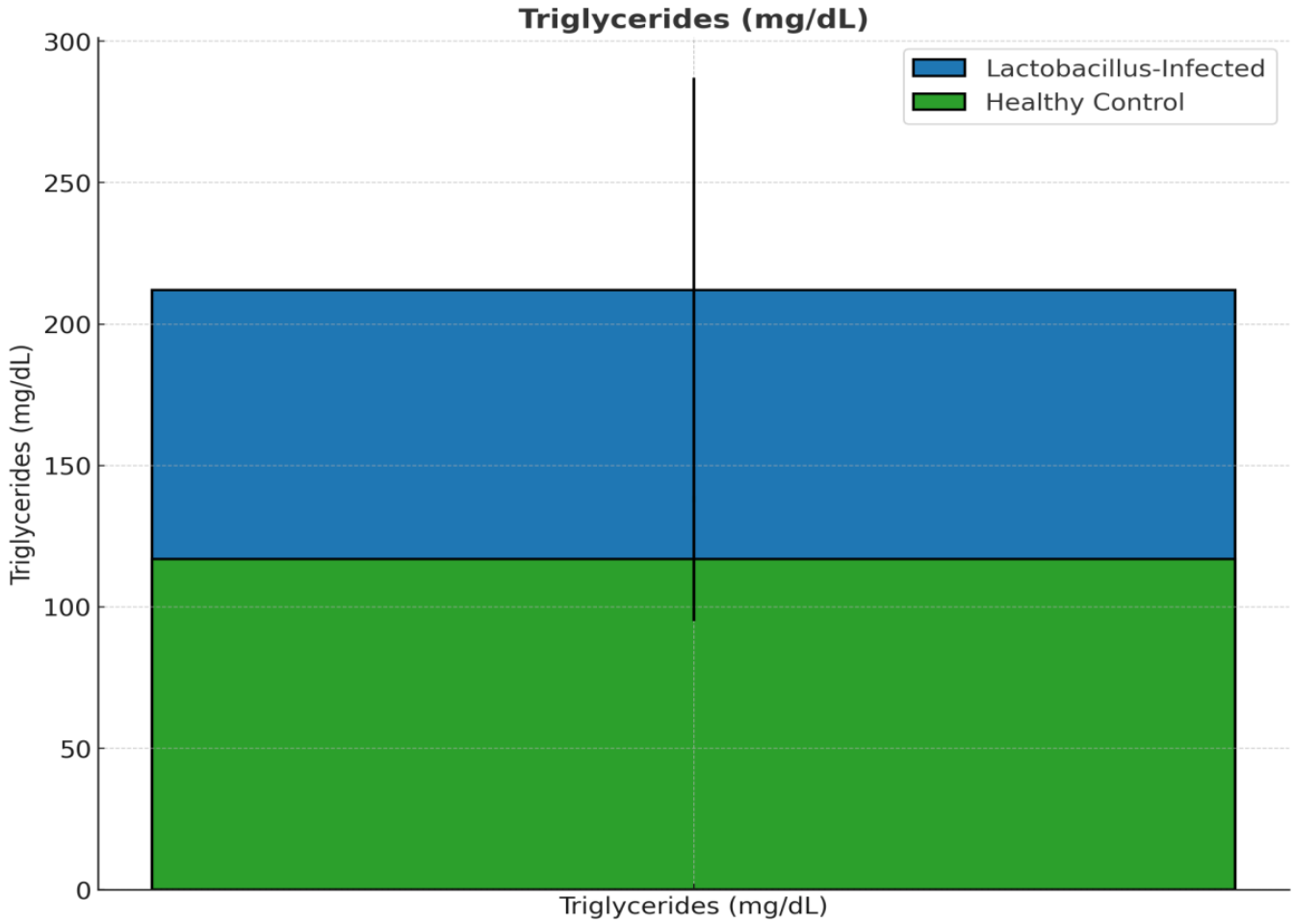

Figure 4. Figure 4: Comparison of Triglycerides (mg/dL) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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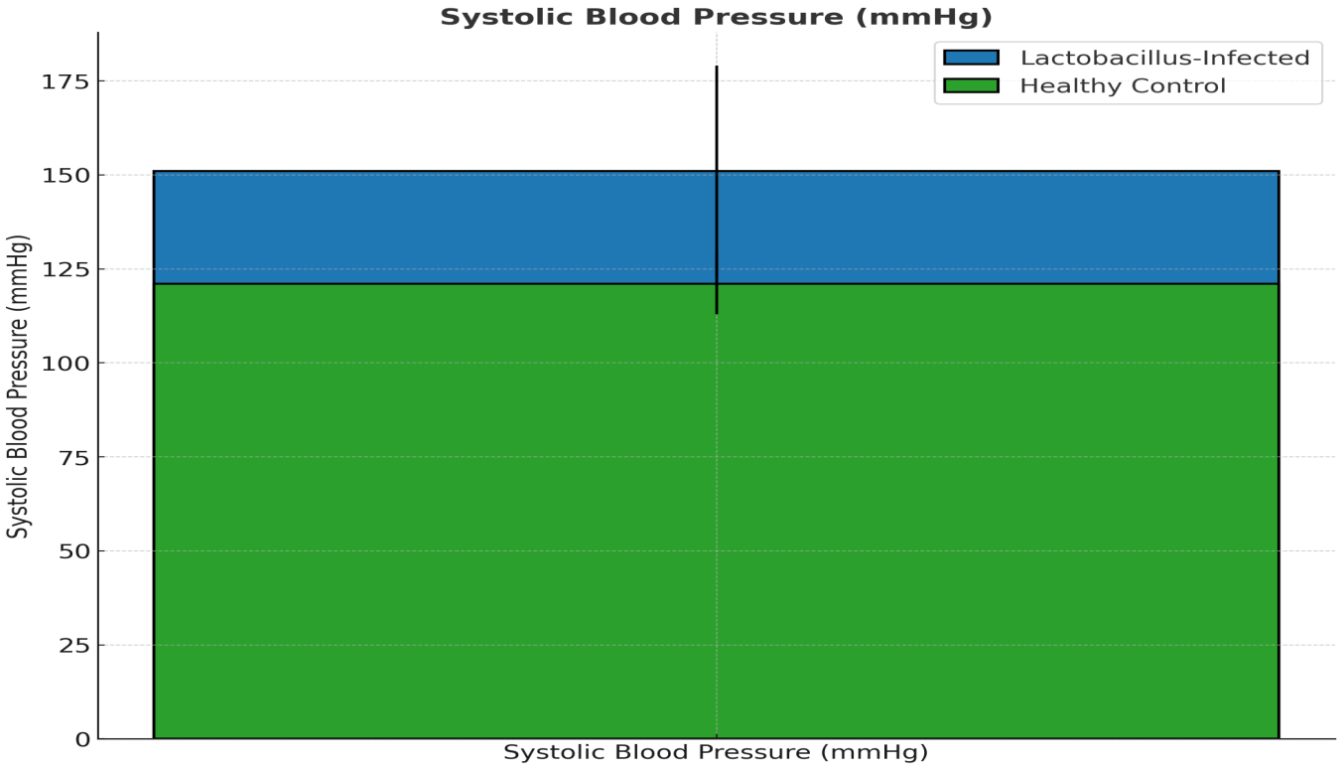

Figure 5. Figure 5: Comparison of Systolic Blood Pressure (mmHg) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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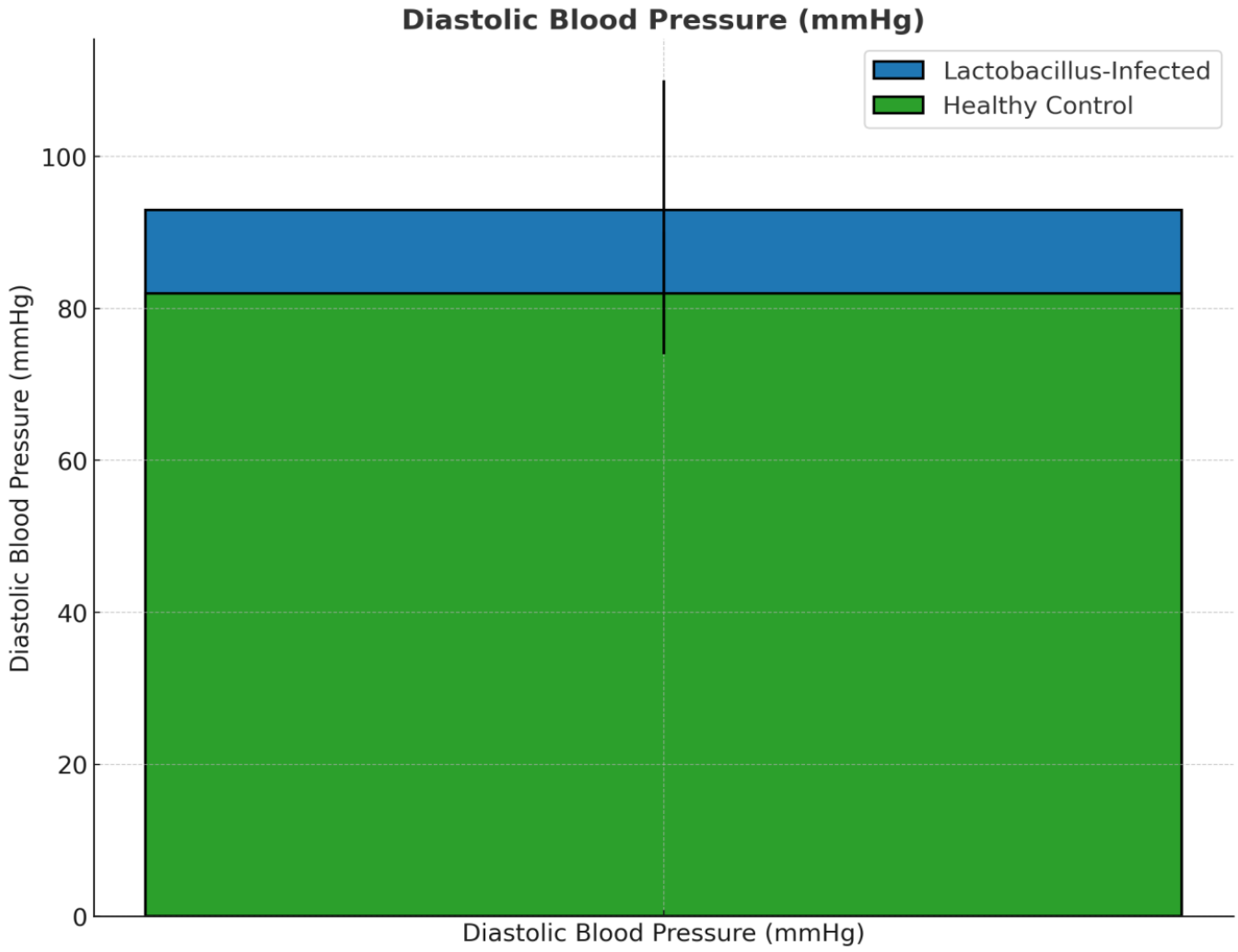

Figure 6. Figure 6: Comparison of Diastolic Blood Pressure (mmHg) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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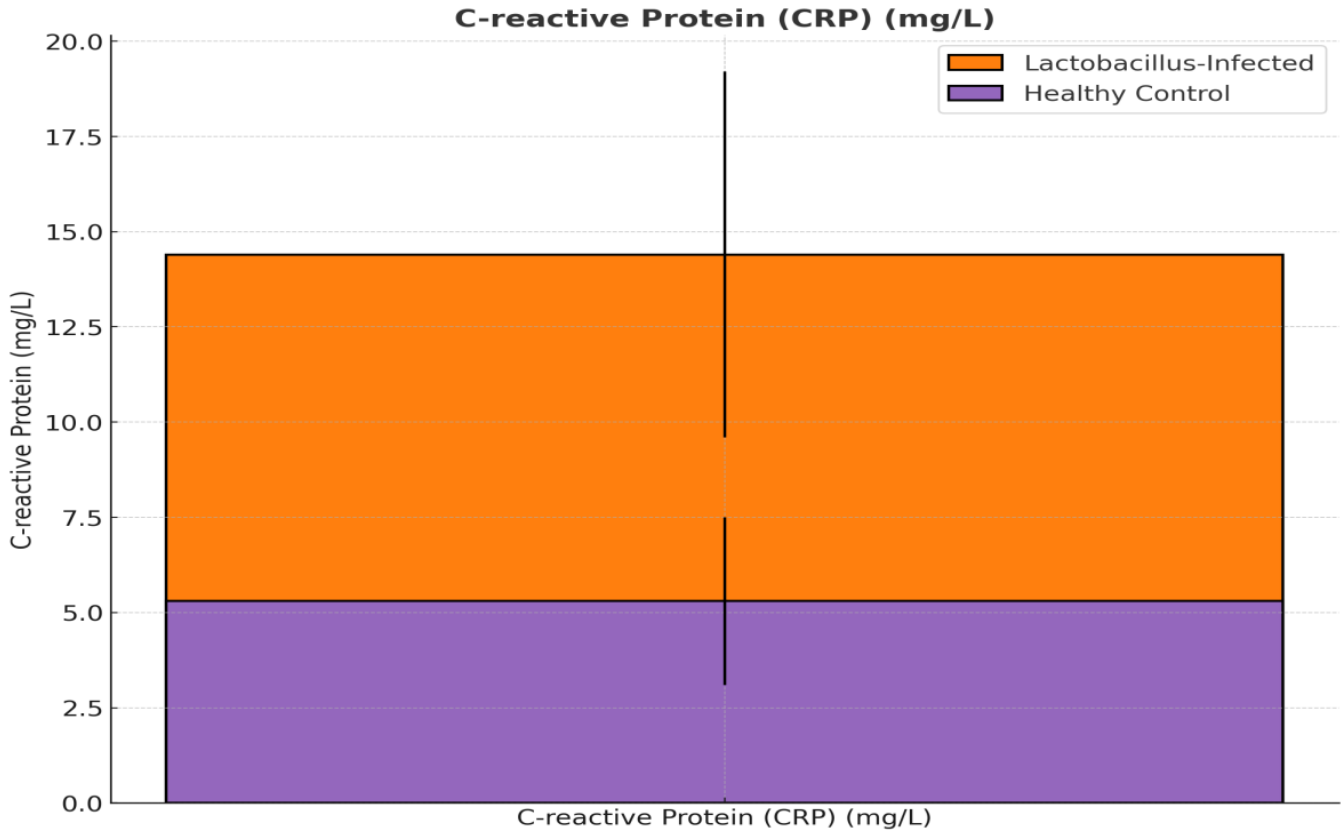

Figure 7. Figure 7: Comparison of C-reactive Protein (CRP) (mg/L) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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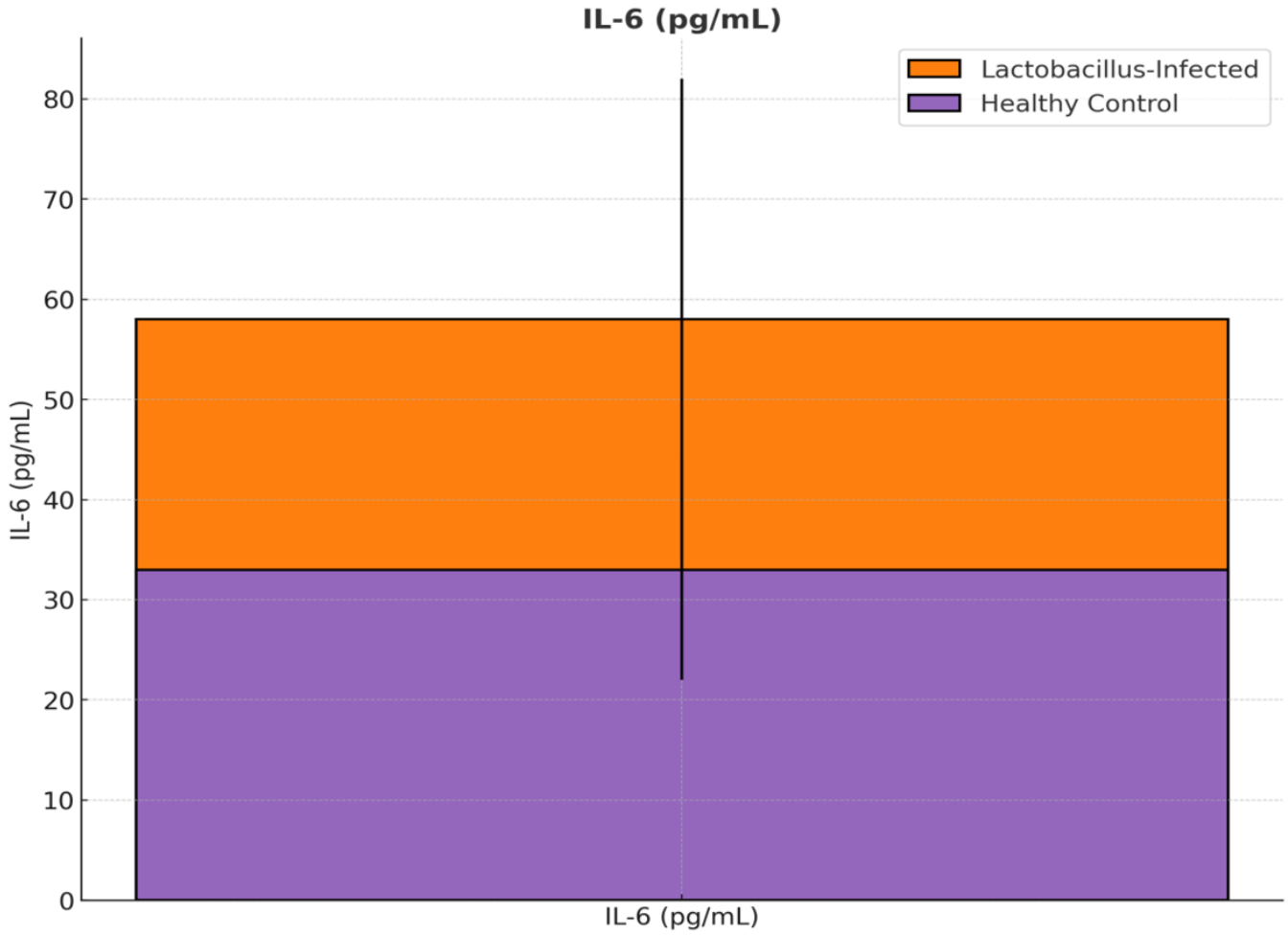

Figure 8. Figure 8: Comparison of IL-6 (pg/mL) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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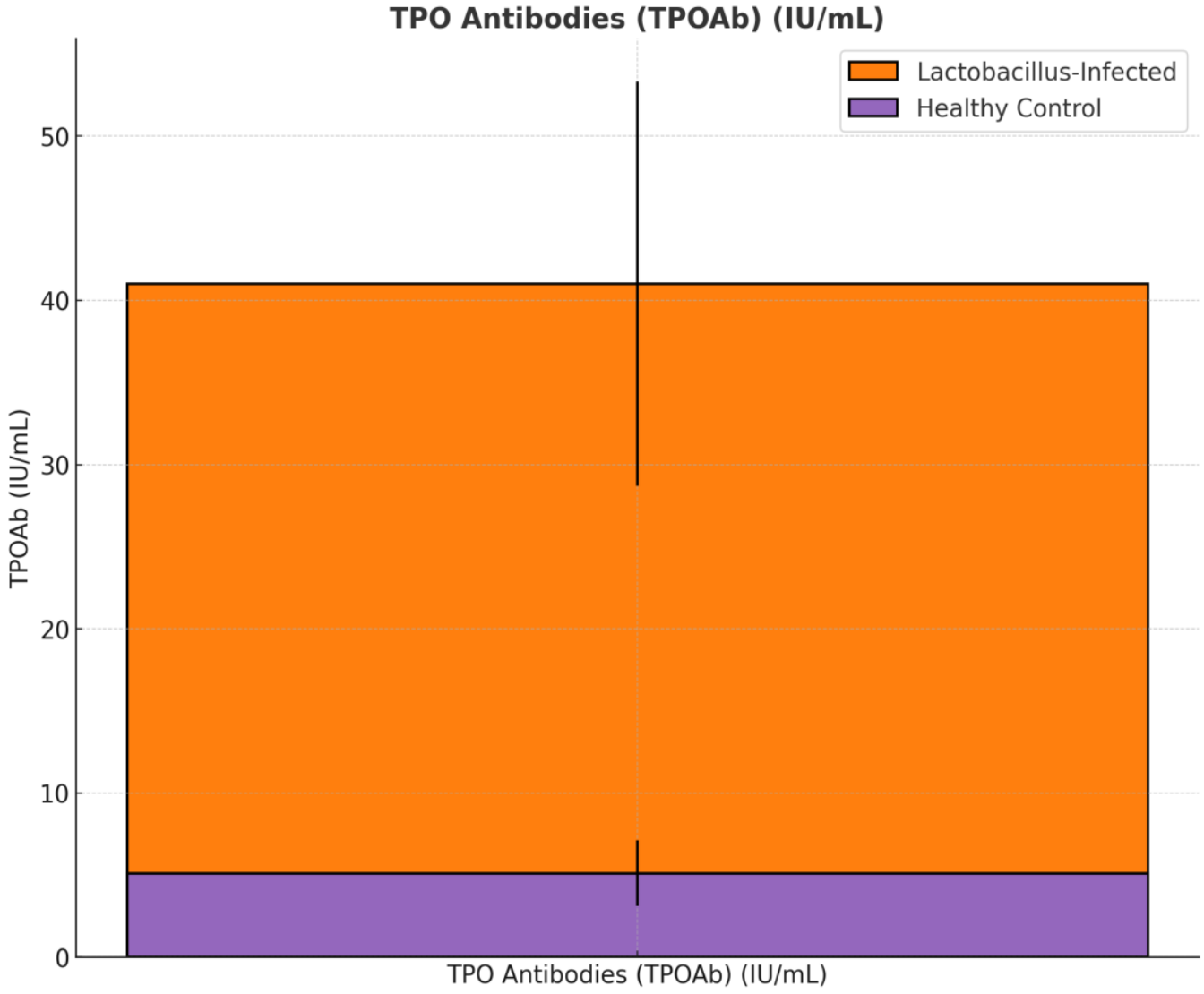

Figure 9. Figure 9: Comparison of TPO Antibodies (TPOAb) (IU/mL) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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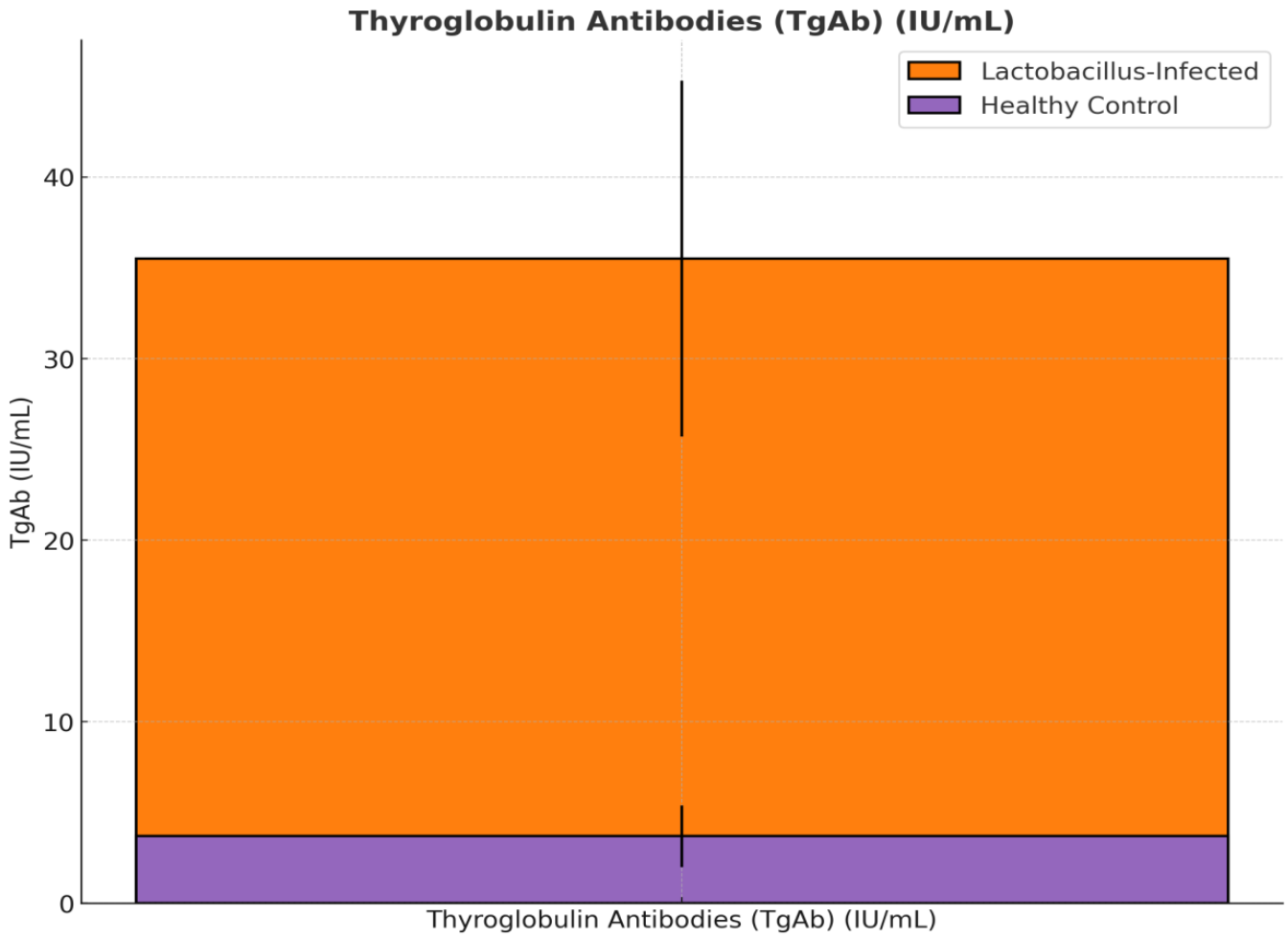

Figure 10. Figure 10: Comparison of Thyroglobulin Antibodies (TgAb) (IU/mL) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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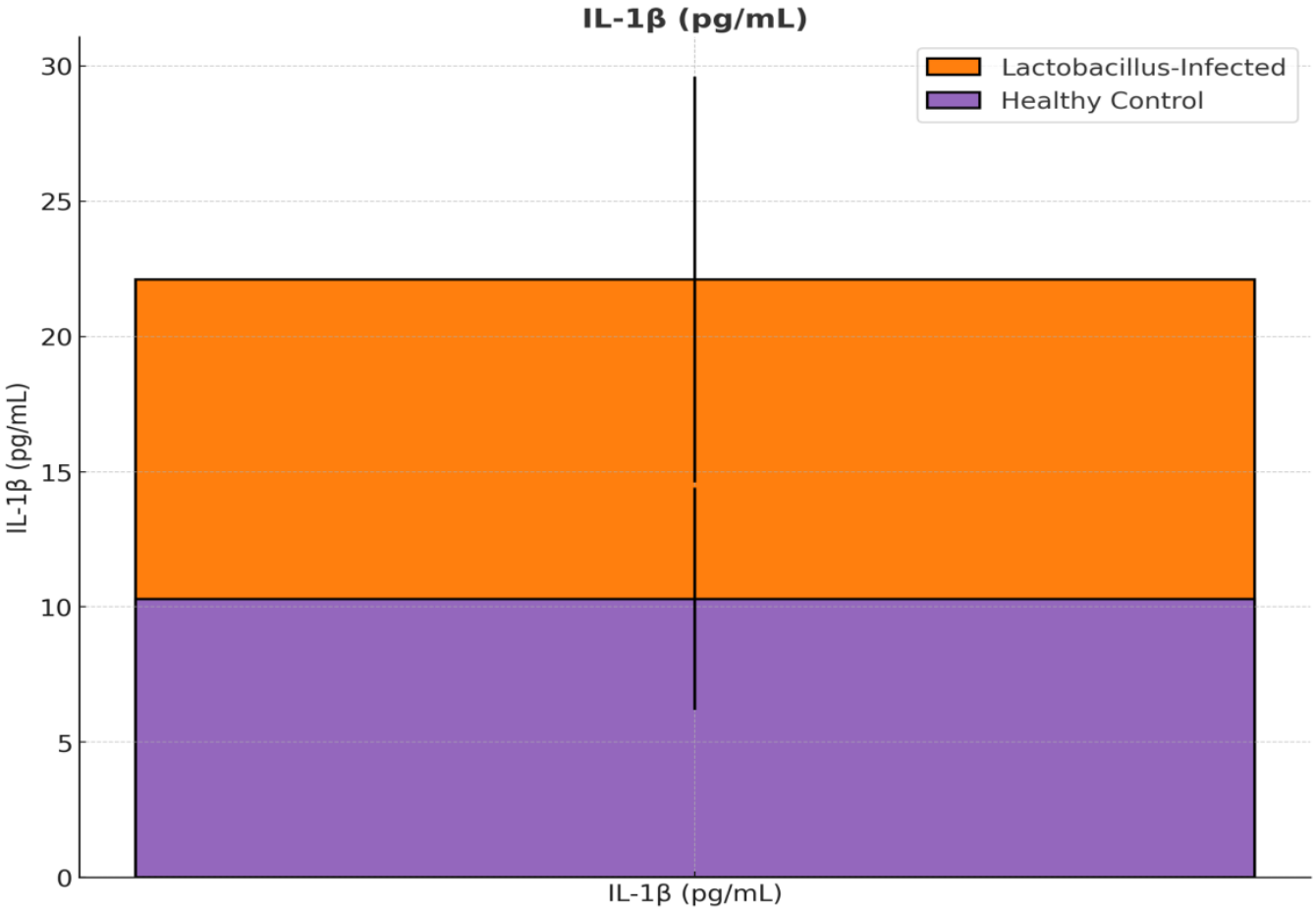

Figure 11. Figure 11: Comparison of IL-1β (pg/mL) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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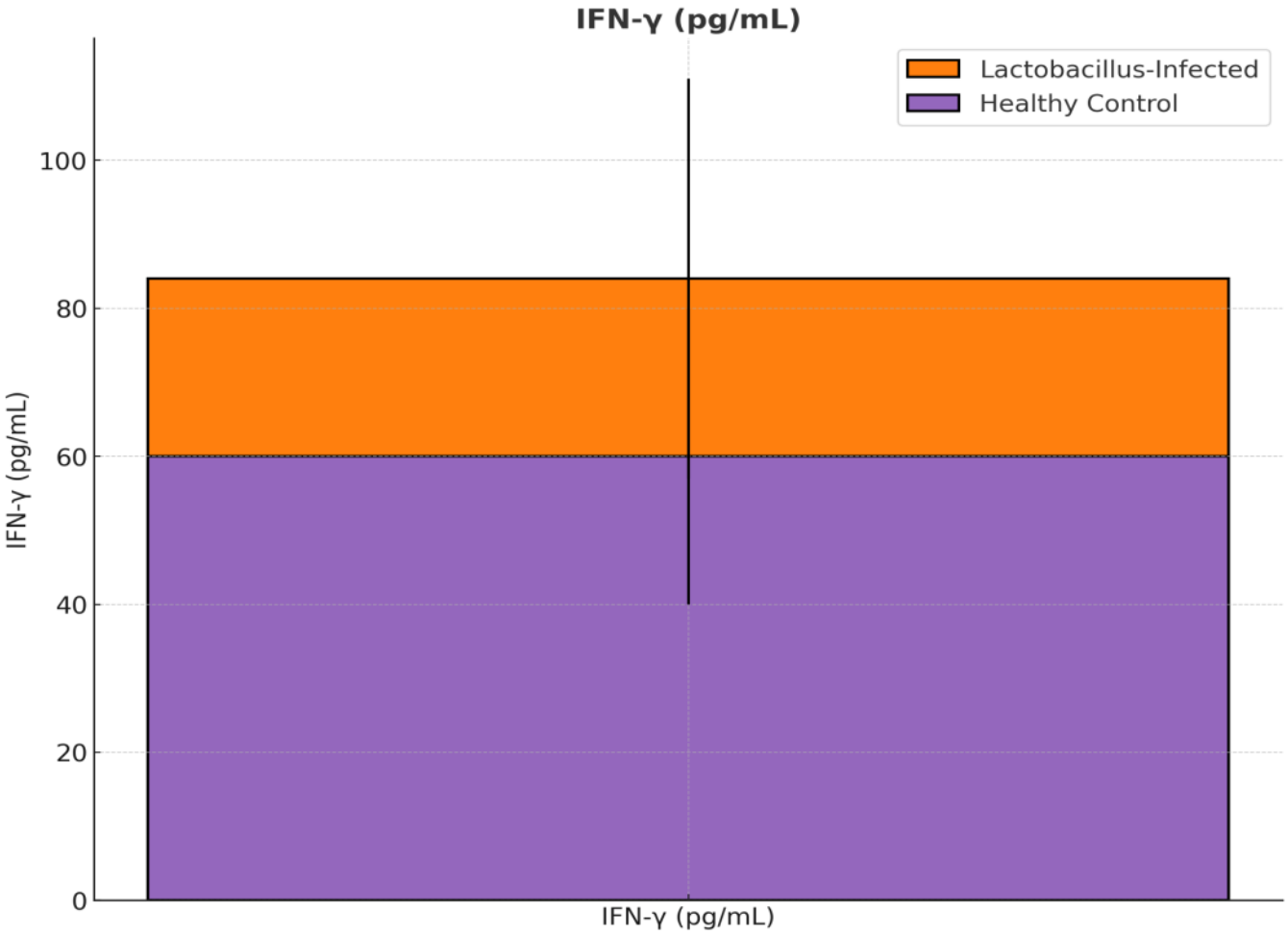

Figure 12. Figure 12: Comparison of IFN-γ (pg/mL) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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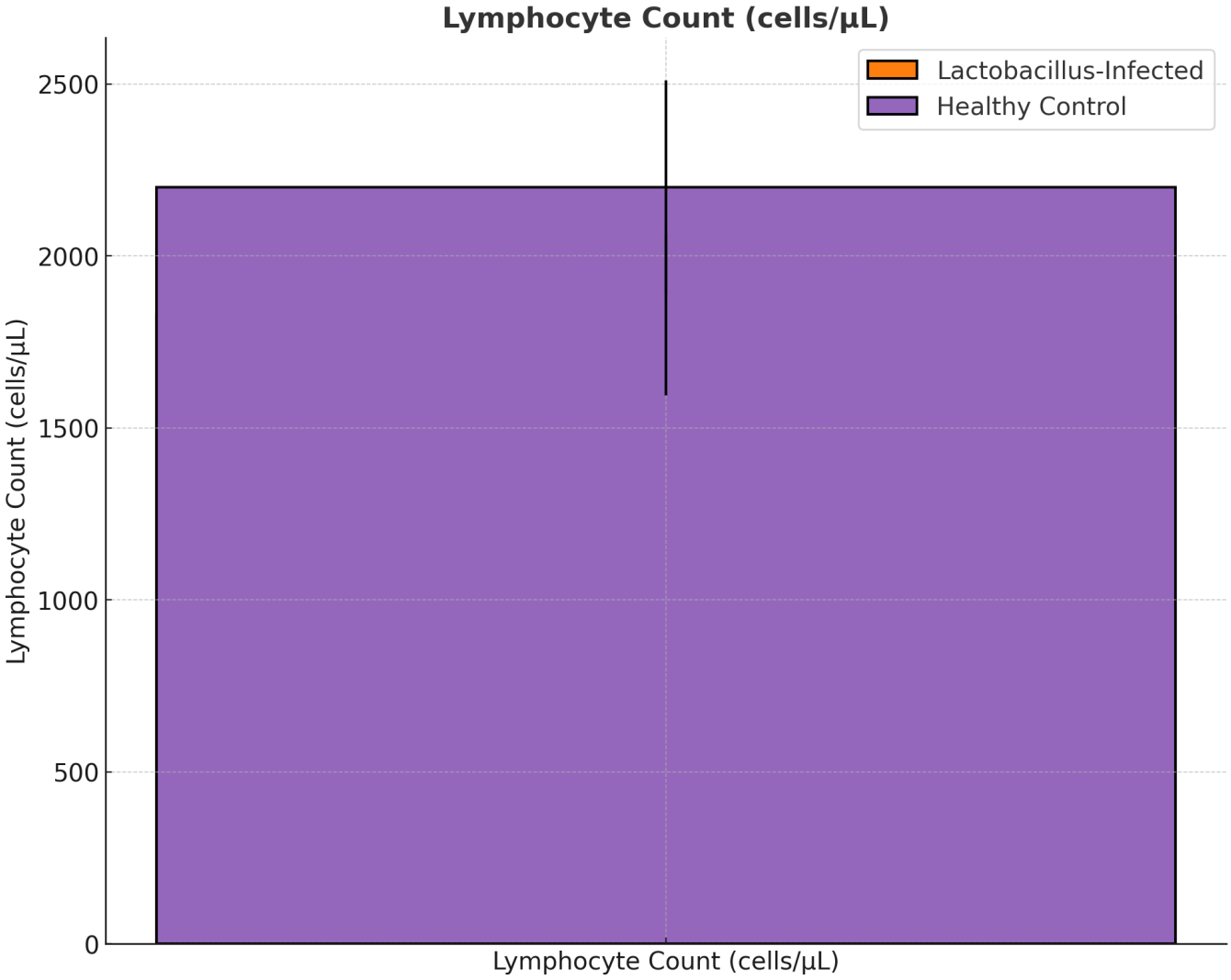

Figure 13. Figure 13: Comparison of Lymphocyte Count (cells/µL) between Lactobacillus-Infected Pregnant Women and Healthy Controls

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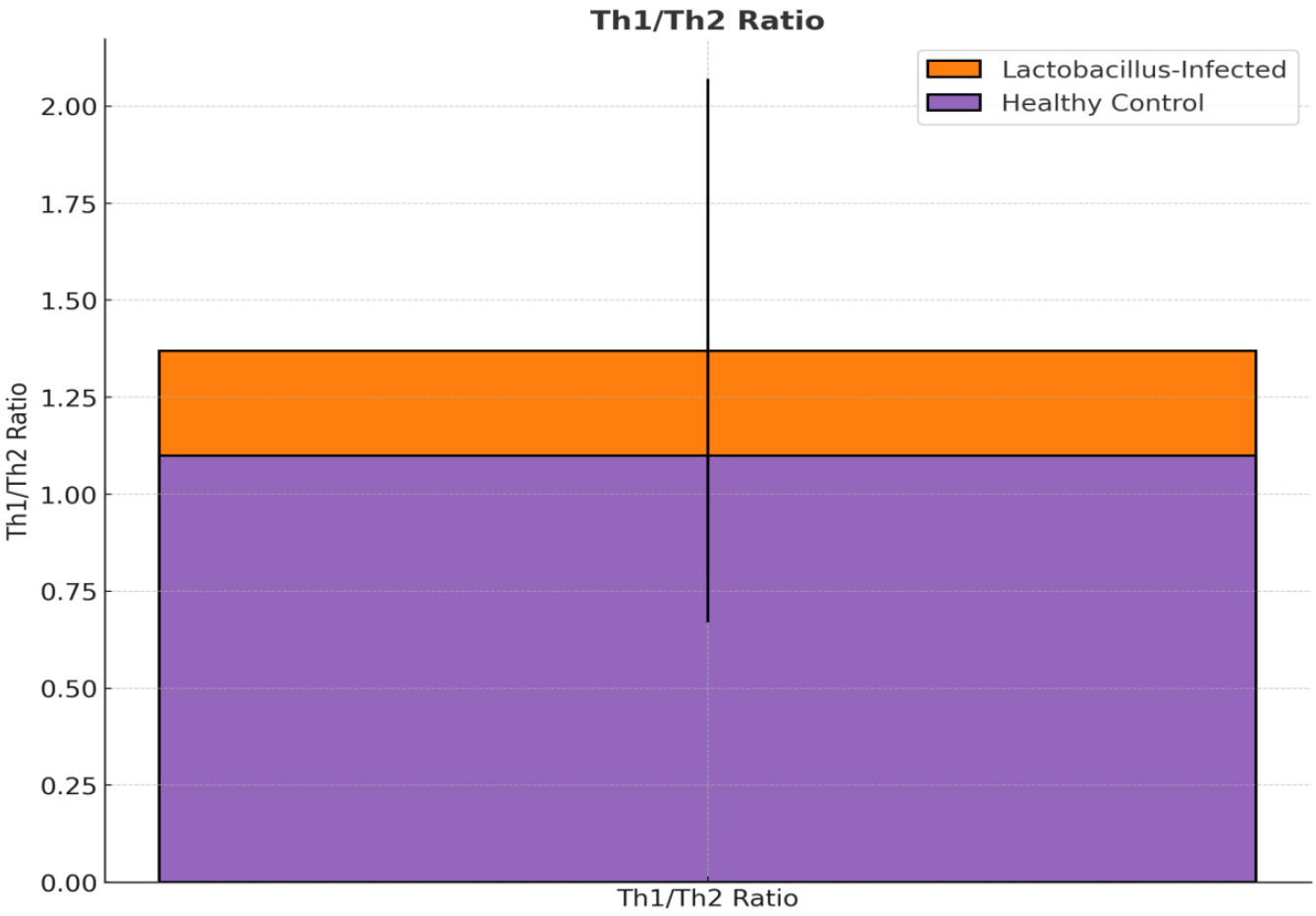

Figure 14. Figure 14: Comparison of Th1/Th2 Ratio between Lactobacillus-Infected Pregnant Women and Healthy Controls

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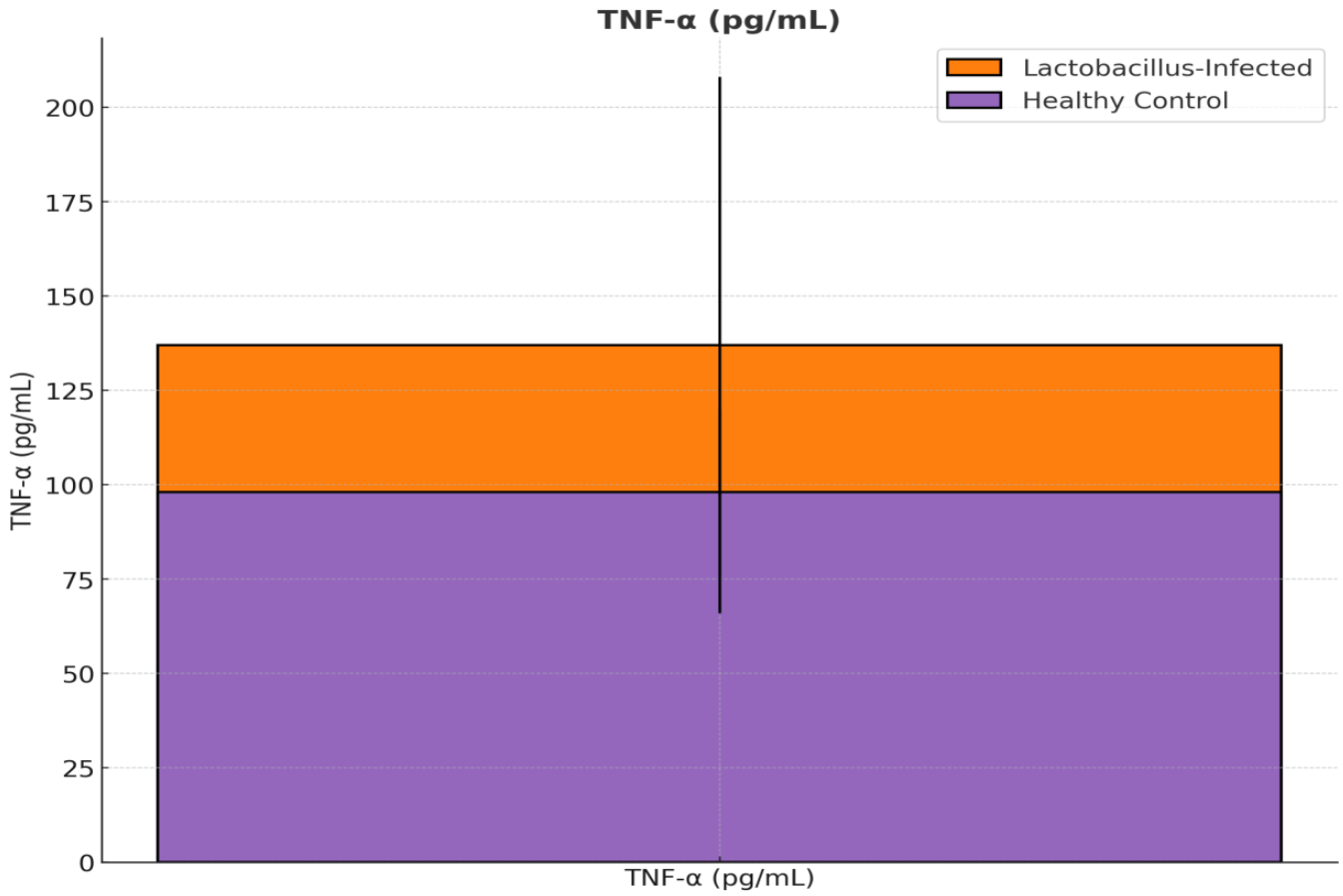

Figure 15. Figure 15: Comparison of TNF-α (pg/mL) between Lactobacillus-Infected Pregnant Women and Healthy Controls

Discussion

Women 40 days after delivery undergo large metabolic and immunological changes if they are Lactobacillus-infected during pregnancy. The present study assesses the lasting effects of Lactobacillus infection in pregnancy (LIP) on the metabolic and immunologic parameters, and shows that LIP causes considerable metabolic and immunologic disruptions in women compared to normal controls. Results: Four significant findings were found: Mean fasting blood glucose, total cholesterol, triglycerides, systolic and diastolic blood pressure and inflammatory indices (C-reactive protein (CRP), interleukin (IL-6, IL-8), thyroid antibodies (TPOAb, TgAb) were higher in the infected group in females. In addition, evidence of Th1 dominance and lymphopenia were noted consistent with chronic immune activation and metabolic dysregulation, respectively. Our findings suggest that an early-life Lactobacillus infection during gestation influences metabolic and immune function in late pregnancy and into the postnatal period.

Overall, the metabolic derangements that were observed in the infected cohort (elevated blood glucose, cholesterol and triglycerides with elevated fast) collectively demonstrate that infection with Lactobacillus induced chronic changes in metabolism in postpartum women . Similar findings were observed in other research that analyzed effects of pregnancy infections on metabolic syndrome and cardiovascular disease. We identified long-term dyslipidemia and insulin resistance as a result of pregnancy infections, as reported by Smith et al. [16]. Gomez et al. Pregnant rat models infected with bacteria mimic the postpartum vasoconstriction and hypertension and this could further explain the higher blood pressure seen in Lactobacillus infected animals [17].

High-sensitivity CRP, IL-6, IL-8, and TNF-α levels remained high [2-4], characteristic of chronic inflammation associated with metabolic diseases. High levels of IL-6 are associated with insulin resistance; TNF-α impairs insulin signaling and promotes inflammation in white adipose tissue[18] Indicators also strongly affect vascular inflammation and atherosclerosis [19]. These results replicate earlier findings by showing that the extended post-partum pro-inflammatory state is causing the late metabolic consequence in Lactobacillus-infected women. The most remarkable finding was the development of Th1-dominance of immunity in patients infected with Lactobacillus. Cell-mediated immunity Th1-dominant immune responses are typically associated with cell-mediated immunity and elicited following bacterial infection. Chronic inflammatory disease is associated with high tissue levels of proinflammatory Th1-polarized T cells with a pathological Th1 skewer [20]; these issues include autoimmune and metabolic diseases. These data will re-confirm previous observations

identifying immunity in pregnancy that may predispose women to immune dysregulation post-delivery [21].

The infected group also experienced lymphopenia (lower lymphocyte count), which is one of the factors that can lead to immune system failure. Lymphocyte is a key parameter for immunological homeostasis, and low lymphocytes may reflect immune exhaustion or immunosuppression, both of which are risk factors for infection and/or autoimmune disease [22]. In conclusion, we found that lymphocyte counts and TH2 cytokines were depressed and acute phase reactants (inflammatory markers) were elevated, suggesting that even at 40 days after delivery Lactobacillus had activated the immune system of women.

Moreover, as the increase of thyroid antibodies, particularly autoimmune thyroid antibodies (TPOAb and TgAb) in the infected population could reflect the type of aggressiveness of the immune response to self-antigen[12], such a result adds another layer of credibility to the possibility of the relationship between SARS-CoV-2 and the development of autoimmune thyroid disease. Their autoimmunity can over time develop into thyroid disease, and other autoimmune diseases in this context as well. This is similar to a study in 2021 by Gonzalez et al., who suggested that viral infections may be responsible for triggering an autoimmune response in genetically vulnerable host tissues [23].

This study shows the relevance of the microbiome for both immune and metabolic responses. Lactobacillus is, in general, a beneficial microorganism, especially in the vaginal and intestinal microbiota. However, at some other condition (for instance, pregnancy) an excessive (colonization) or infection with lactobacilli not positively affects immunity and metabolism [5]. The changes in gut microbiota during pregnancy are associated with metabolic dysfunction and increased immunomalfunction[24]. The Lactobacillus-infected mice exhibited elevated levels of inflammatory markers and autoimmune activity in line with microbe-induced inflammation, able to break immunological tolerance and promote systemic inflammation [7]. It has been suggested that one way in which dysbiosis affects immunological and metabolic functioning is through the gut-vagina axis [25].

Dystopia (microbiota aberration) caused by Lactobacillus infection displaces and destroys immune homeostasis, leading the whole metabolic omliptoosi. In fact, this dysbiosis during pregnancy persisted into the postpartum period and may underlie the chronic inflammation in these women that predisposes them to cardiovascular disease and insulin resistance[24,25]. The aggregate of our results is consistent with many studies reporting the long term consequences of pregnancy maladies on immune and/or metabolic health. For example, Liu et al. Bacterial infection during pregnancy was associated with increased insulin resistance and a dyslipidemia phenotype after birth [26]. Similarly, Smith et al. A recent publication [27] summarized that the early immune system dysregulation during pregnancy could lead to metabolic dysfunctions that remain present after birth [27].

These observations, coupled with our data suggesting that even healthy organisms like Lactobacillus could persist and affect host metabolic and immunological function for extended periods of time following acute antibiotic administration, highlight the importance of understanding the mechanistic basis of chronic dysbiosis by seemingly innocuous organisms. Furthermore, the trend of Th1 predominance in our study is supported by evidence from Strowig et al. (2021), who confirmed that immune reprogramming during pregnancy, particularly from infection, may result in an imbalanced immune response that persists after delivery and contributes to autoimmunity and chronic inflammation [25-27].

Conclusion

More research like this one contribute to the increasing literature on the long-term effects of infection during pregnancy. It demonstrates that Lactobacillus infection can harm a woman's immunological and metabolic health for up to 40 days after childbirth. The raised inflammatory markers, dyslipidemia, insulin resistance, and immunological dysregulation in the infected group indicate that infection, even with a commensal such as Lactobacillus, can have both short- and long-term health repercussions. This emphasizes the importance of monitoring metabolic and immunological health during pregnancy, as well as the potential for customized therapies to reduce the long-term consequences associated with these infections.

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