

REVIEW

Maternal microbiota: changes and consequences during pregnancy. A narrative review

Microbiota materna: cambios y consecuencias durante el embarazo. Una revisión narrativa

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ABSTRACT

Objective: this study aims to review the changes in microbiota during pregnancy, characterized by natural and associative aspects.

Design: a literature review based on a narrative synthesis.

Data Sources: the study was conducted using databases such as PubMed, Science Direct, Web of Science (WOS), Scielo, and Google Scholar.

Study Selection: documents were selected and analyzed through an exhaustive literature review, applying specific inclusion and exclusion criteria.

Results: for the results analysis, 15 articles were selected, including 3 observational studies, 4 clinical trials, 7 statistical analyses, 2 systematic reviews, and 1 narrative review. The research population consisted of both healthy pregnant women and those with pre-existing conditions. Some studies were conducted in Europe, the United States, Australia, China, and South America.

Conclusions: changes in microbiota during pregnancy influence body mass index (BMI) and are associated with hypertensive disorders, gestational diabetes, the use of prebiotic supplements, and periodontitis. Moreover, microbiota is naturally linked to vaginal function changes, contributes to the infant's immune system development, and provides beneficial bacteria through breast milk.

Keywords: Microbiota; Pregnant Women; Associated Changes; Natural Changes.

RESUMEN

Objetivo: este estudio pretende revisar los cambios en la microbiota durante el embarazo, caracterizados por aspectos naturales y asociativos.

Diseño: revisión bibliográfica basada en una síntesis narrativa.

Fuentes de datos: el estudio se realizó utilizando bases de datos como PubMed, Science Direct, Web of Science (WOS), Scielo y Google Scholar.

Selección de estudios: los documentos fueron seleccionados y analizados a través de una revisión exhaustiva de la literatura, aplicando criterios específicos de inclusión y exclusión.

Resultados: para el análisis de resultados, se seleccionaron 15 artículos, incluyendo 3 estudios observacionales, 4 ensayos clínicos, 7 análisis estadísticos, 2 revisiones sistemáticas y 1 revisión narrativa. La población investigada estaba formada tanto por mujeres embarazadas sanas como por mujeres con enfermedades

preexistentes. Algunos estudios se realizaron en Europa, Estados Unidos, Australia, China y Sudamérica. **Conclusiones:** los cambios en la microbiota durante el embarazo influyen en el índice de masa corporal (IMC) y se asocian a trastornos hipertensivos, diabetes gestacional, uso de suplementos prebióticos y periodontitis. Además, la microbiota está vinculada de forma natural a cambios en la función vaginal, contribuye al desarrollo del sistema inmunitario del lactante y aporta bacterias beneficiosas a través de la leche materna.

Palabras clave: Microbiota; Embarazadas; Cambios Asociados; Cambios Naturales.

INTRODUCTION

Maternal microbiota during pregnancy influences both the infant's microbiota and immunity (Custers et al., 2024). It affects fetal and neonatal development (Ibarra et al., 2023) and plays a crucial role in overall health, highlighting the symbiotic relationship between microorganisms and the human body (Nyangahu & Jaspan, 2021). The placenta may expose the fetus to microorganisms different from those in the vaginal microbiota (Ibarra et al., 2023). Compared to the gastrointestinal and oral microbiomes, the vaginal microbiome has relatively low biodiversity (Fox & Eichelberger, 2019). An increase in pathogenic microorganisms in the vagina has been linked to pregnancy complications, including spontaneous abortion and preterm birth (Ibarra et al., 2023). The vaginal microbiota varies throughout a woman's life (Ibarra et al., 2023), becoming less diverse and more stable during pregnancy, which significantly impacts infant immunity (Nyangahu & Jaspan, 2021). It fluctuates over time due to age, hormonal changes, infections, and sexual activity (Fox & Eichelberger, 2019). Antibiotics and other factors alter microbiota composition, affecting metabolism and overall health (Nyangahu & Jaspan, 2021). Lactobacilli imbalances can lead to dysbiosis and bacterial vaginosis (Fox & Eichelberger, 2019). Deviations in microbiota composition increase the risk of atopic diseases, diarrheal infections, and obesity (Collado et al., 2020). Excessive weight gain during pregnancy is linked to gestational diabetes (Collado et al., 2020) and is associated with disorders such as type 1 diabetes and inflammatory bowel disease (Nyangahu & Jaspan, 2021), leading to complications for both mother and child at birth (Collado et al., 2020).

Recent studies have examined microbiota in pregnant women in tissues previously believed to be sterile, revealing potential benefits for both mother and baby (Ibarra et al., 2023). Additionally, microbiota research shows promise in enhancing fertility, reducing pregnancy complications, and optimizing reproductive health (Rodríguez-Purata & Mendieta, 2022). The vaginal microbiota also plays a protective role against infections in women's health, and probiotics may help treat infections, benefiting both mother and child (Álvarez-Calatayud et al., 2020). Furthermore, micronutrient treatments have been found to promote a more diverse and stable microbiome during pregnancy, increasing its resistance to fluctuations (Stevens et al., 2024).

This study aims to review the changes in microbiota during pregnancy, focusing on its natural variations and associative factors.

METHOD

A comprehensive narrative review was conducted to explore the existing scientific literature on microbiota changes in pregnant women, consulting the following databases: Scopus, Web of Science, Science Direct, Scielo, and Google Scholar. To refine the search, the following terms were used: "Microbiota changes during pregnancy", "Microbiota changes during completed pregnancy", and "Changes in maternal microbiota or microbiome and fetal health". Additionally, Boolean operators ("AND") and quotation marks were employed to refine and broaden the search scope. The search period extended from August to November 2024, considering articles published between 2017 and 2024. This search included texts written in Spanish, English, and Portuguese, explicitly excluding case reports, interviews, letters to the editor, theses, and books due to their less empirical nature or specific focus. Within the aforementioned databases, an initial 19 965 articles were identified using the designed search string. Of these, 908 were from Scopus, 3 from Web of Science, 45 from Science Direct, 9 from Scielo, and 19 000 from Google Scholar. Subsequently, 19 918 articles were excluded for not aligning with the study's objective, while an additional 30 articles did not meet the inclusion criteria. As a result of this filtering and selection process, a final corpus of 17 relevant articles was obtained for review.

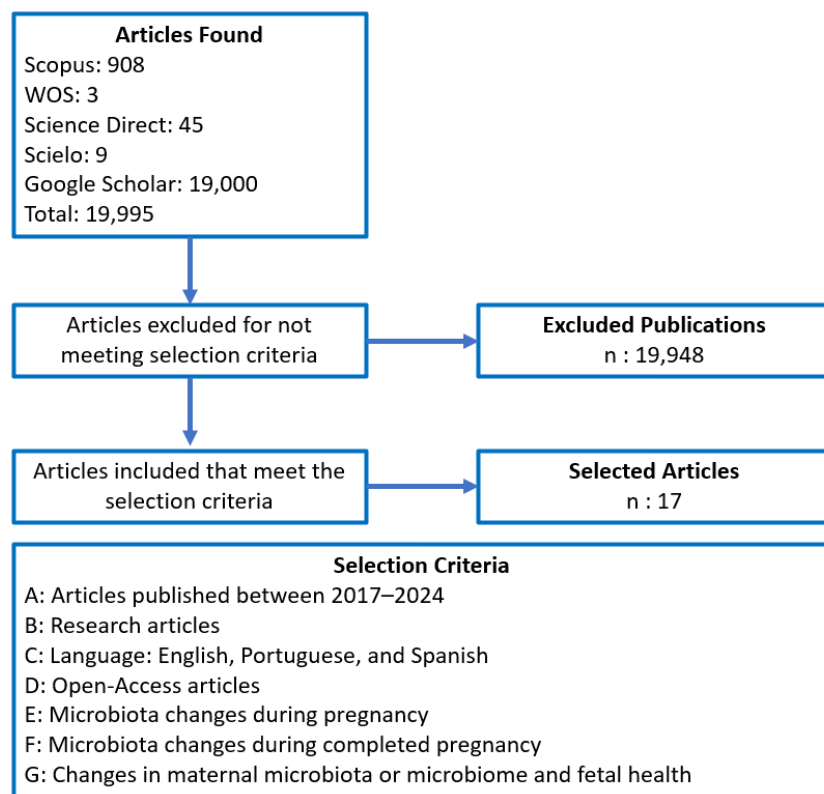


Figure 1. Search strategy

RESULTS

For the analysis, 15 articles were selected, including 3 observational studies, 4 clinical trials, 7 statistical analyses, 2 systematic reviews, and 1 narrative review. The study populations consisted of both healthy pregnant women and those with pre-existing conditions. Some studies were conducted in Europe, the United States, Australia, China, and South America.

Table 1. Analyzed articles

Study Title	Methodology	Objective / Sample	Key Findings
Microbiome Changes in Pregnancy Disorders (Giannella et al., 2023)	Literature Review	Provide a broad overview of microbiota changes during pregnancy.	Microbiota changes are associated with hypertensive disorders, gestational diabetes mellitus, preterm birth, and recurrent spontaneous abortions. (Associated changes)
Women Skin Microbiota Modifications during Pregnancy (Radocchia et al., 2024)	Descriptive Study	Characterize modifications in skin microbiota during pregnancy. Sample: Skin samples from 52 pregnant women (1st and 2nd trimester) with no complications and 17 age- and sex-matched healthy controls.	Changes in skin microbiota composition from the 1st to the 3rd trimester create more favorable conditions for fetal growth. (Associated changes and benefits)
Microbiota During Pregnancy: Findings from a Cohort of Pregnant Women (Chi et al., 2024)	Descriptive Study	Explore the association between anxiety, depression, and gut microbiota in pregnant women. Sample: Analysis of 87 subjects at 225 time points throughout early, mid, and late pregnancy.	Mental health can influence gut microbial diversity, potentially impacting overall health.
Multi-omic Analysis Reveals the Associations Between Altered Intestinal Microbiota, Metabolites, and Cytokines During Pregnancy (Huang et al., 2024)	Experimental Study	Examine how altered gut microbiota and metabolites interact with the host during pregnancy. Sample: 30 healthy pregnant women and 15 non-pregnant healthy women as controls, considering age.	Significant increase in Actinobacteria (Gram-positive bacteria found in soil, plants, and animals that decompose organic matter). Differences in bile acid secretion. Marked reduction in pro-inflammatory cytokine levels. (Natural change) Changes are related to vaginal functions.

Maternal Supplementation During Pregnancy and Lactation Modifies the Microbiome and Short-Chain Fatty Acid Profile of Both Mother and Infant (Jones et al., 2024)	Prebiotic During Study	Experimental Study	Evaluate the impact of a prebiotic supplement (galacto-oligosaccharides and fructo-oligosaccharides) on maternal gut health during pregnancy and lactation. Sample: 74 mother-infant pairs in a double-blind, randomized, controlled trial.	Significant differences in maternal microbiota profiles between the start and 28 weeks of pregnancy. (Associated changes) Prebiotic supplementation (start-28-36 weeks of gestation) was linked to an increase in commensal bacteria and a decrease in Gram-negative bacteria in both mothers and infants (12 months).
Distinct Composition of Gut Microbiota During Pregnancy in Overweight and Normal-Weight Women (Collado et al., 2020)		Prospective Longitudinal Study	Evaluate gut microbiota concerning BMI, weight gain during pregnancy, and microbiota composition before delivery.	Third-trimester microbiota is linked to weight gain. - Bacteroides increase with higher weight and BMI. Bifidobacterium is more abundant in women with lower weight gain. Deviations in gut microbiota composition may predispose individuals to excessive energy consumption.
Maternal Microbiome and Pregnancy Outcomes (Fox & Eichelberger, 2019)		Descriptive Study	Compare microbiota in non-pregnant and pregnant women, assessing its role in preterm birth.	Lactobacillus during pregnancy influences neonatal microbiota and protects against infections that cause preterm birth. The placental microbiome mainly contains Firmicutes, Tenericutes, Proteobacteria, Bacteroides, and non-pathogenic Fusobacteria. - Decreased Lactobacillus is associated with dysbiosis and bacterial vaginosis.
Changes in the Microbiota During Pregnancy: A Narrative Review (Ibarra et al., 2023)		Systematic Review	Assess scientific evidence on microbiota changes during pregnancy.	Intestinal dysbiosis increases the risk of obesity and diabetes in mothers and infants. Pregnancy-related microbiota changes indicate a risk for diabetes. Children of overweight mothers or those with gestational diabetes have higher levels of Firmicutes, Lachnospiraceae, Proteobacteria, and Actinobacteria. Babies born via C-section have Staphylococcus and Klebsiella, increasing asthma, obesity, and diabetes risk in early months. Antibiotics, C-section delivery, and formula feeding alter microbiota. Oral microbiota dysbiosis is linked to dental caries, periodontitis, and oral mucosal diseases.
Influence of Maternal Microbiota During Pregnancy on Infant Immunity (Nyangahu & Jaspan, 2019)		Descriptive Study	Review current literature on maternal microbiota's impact on infant immunity.	Early fetal exposure to microbial antigens influences immunity. Maternal exposure contributes to the critical window of immune development. Altering maternal gut microbiota during pregnancy indirectly affects breast milk and, to a lesser extent, vaginal microbiota. Unhealthy diet and excessive antibiotic use weaken infant immune systems, increasing allergy, asthma, and obesity risk.
Synbiotics in Patients at Risk for Spontaneous Preterm Birth: Multi-Center, Double-Blind, Randomized, Placebo-Controlled Trial (PRIORI) (Nulens et al., 2024)		Clinical Trial	Assess the effect of oral synbiotics on vaginal microbiota in high-risk pregnancies and correlate microbial changes with gestational age and pregnancy outcomes. Sample: Pregnant women aged 18+ with a singleton pregnancy. Exclusion: Multiple pregnancy, cervical conization, inflammatory bowel disease, uterine anomalies, use of pro-/pre-/synbiotics.	Low diversity and reduced beneficial bacteria (Lactobacilli) are associated with preterm birth. Participants take synbiotics or placebo until delivery. Primary outcome: Gestational age at birth. Secondary outcomes: premature membrane rupture, antibiotic use, prenatal care, neonatal outcomes.

The Evolving Microbiome From Pregnancy to Early Infancy: A Comprehensive Review (Mesa et al., 2020)	Narrative Review	Summarize current knowledge on maternal, fetal, and neonatal microbiota changes and their influence on newborn development and specific pathologies.	Maternal and fetal microbiota changes during pregnancy impact newborn and infant development. Further studies are needed to confirm findings and their relevance in healthy and complicated births. These changes affect maternal microbiota at various sites, including the gut, vagina, and oral cavity.
Temporal and Spatial Variation of the Human Microbiota During Pregnancy (DiGiulio et al., 2020)	Observational Study	Analyze microbiota composition based on prospective weekly sampling of four body sites: vagina, distal gut (feces), saliva, and gums/teeth, as well as postpartum changes.	Pregnant women's vaginal communities were dominated by <i>Lactobacillus</i> species. Preterm birth is associated with bacterial vaginosis, a disruption of vaginal microbiota affecting the entire community. Postpartum, vaginal microbiota changes persist for up to a year.
Shifting Pattern of Gut Microbiota in Pregnant Women Two Decades Apart—An Observational Study (Rautava et al., 2023)	Observational Study	Investigate gut microbiota composition and function in pregnant women over 20 years (1997, 2007, 2017). Sample: 124 pregnant women (41 overweight, 83 normal weight).	Significant differences in gut microbiota composition between overweight and normal-weight women in 1997, but not in 2007 or 2017. Pre-pregnancy overweight was present in 41 subjects, while 83 had normal weight.
Affective Symptoms in Pregnancy Are Associated With the Vaginal Microbiome (Scheible et al., 2024)	Prospective Longitudinal Study	Establish plausible biological pathways in the maternal vaginal microbiome, with affective symptoms and associated biomarkers as primary variables in a cohort of pregnant women at normative and healthy risk. Sample: 275 medically healthy mother-child pairs.	Research findings linking the vaginal microbiome, affective symptoms, and possible biological pathways are rare. Some of the limited available evidence comes from preclinical animal model studies, suggesting that experimentally induced stress reduces vaginal microbiome diversity.
Maternal Immune Cell Gene Expression Associates With Maternal Gut Microbiome, Milk Composition, and Infant Gut Microbiome (Gurung et al., 2024)		Analyze how gene expression changes are associated with maternal diet, gut microbiota, breast milk composition, and infant gut microbiota.	Pre-pregnancy overweight alters the expression of 453 inflammation-related immune genes. A healthy diet at 36 weeks positively regulates DTD1 and GALNT8 genes. Overweight women exhibit upregulation of inflammatory genes during pregnancy. Correlations were found between maternal PBMC gene expression, gut microbiome, and breast milk composition. Genes in maternal PBMCs and oligosaccharides in breast milk show a significant correlation, emphasizing the influence of maternal health and nutrition on breast milk quality and infant health.
Randomized Control Trial Indicates Micronutrient Supplementation May Support a More Robust Maternal Microbiome for Women With Antenatal Depression During Pregnancy (Stevens et al., 2024)		Investigate the effects of high-dose micronutrient supplementation on the human gut microbiome in pregnant women experiencing moderate prenatal depression. Sample: 33 pregnant women between 12 and 24 weeks of gestation.	The microbiome community structure became more heterogeneous, and diversity decreased. Significant changes were observed in alpha and beta diversity. Elevated presence of <i>Coprococcus</i> was associated with symptoms of depression and anxiety.
Effects of Probiotics on Preterm Infant Gut Microbiota Across Populations: A Systematic Review and Meta-Analysis (He et al., 2024)		Characterize gut microbiota in women based on body mass index (BMI) and assess the effect of weight gain during pregnancy on gut microbiota composition before birth.	Experimental studies suggest that deviations in gut microbiota composition predispose individuals to excessive energy consumption.

DISCUSSION

The purpose of this literature review is to report on microbiota changes during pregnancy, considering natural aspects and their association with certain diseases, complications, and clinical trials.

Microbiota-Associated Changes

Microbiota changes during pregnancy are associated with hypertensive disorders, gestational diabetes mellitus, preterm birth, and recurrent spontaneous abortions (Giannella et al., 2023), as well as body mass index (BMI) (Collado et al., 2020) and prebiotic supplementation (Jones et al., 2024). Additionally, these changes have been linked to dental caries, periodontitis, and oral mucosal diseases (Jang et al., 2021).

Microbiota changes are related to hypertensive disorders (Collado et al., 2020). The gut microbiota can affect the production of pro-inflammatory cytokines and other mediators that influence blood pressure and cardiovascular health (Giannella et al., 2023). Gut bacteria produce short-chain fatty acids (SCFAs), which have beneficial effects on cardiovascular health, but alterations in microbiota composition can disrupt SCFA production, affecting blood pressure regulation (Mora-Janiszewska et al., 2022).

It was identified that gut microbiota can contribute to metabolic complications in both mother and child by increasing insulin levels, thereby leading to gestational diabetes mellitus (Mora-Janiszewska et al., 2022). Pregnant women with gestational diabetes experience microbiota changes during the third trimester, characterized by a decrease in Actinobacteria, which serves as a biomarker for gestational diabetes mellitus (Mesa et al., 2020).

Microbiota changes are also related to preterm birth and spontaneous abortions (Giannella et al., 2023) due to the predominance of *Lactobacillus iners* along with Clostridiales, Bacteroidales, and Actinomycetales, leading to dysbiosis, which is a triggering factor for preterm labor (Wang et al., 2019). In cases of in vitro fertilization (IVF), endometrial microbiota patterns tend to show lower implantation rates and higher risks of spontaneous abortions (Grewal et al., 2021). Additionally, Bacteroides, Lactobacillus, Delftia, and Pseudomonas have been found to be increased in women with preterm birth (Valentine et al., 2018), as well as Staphylococcus aureus, which is associated with a higher risk of preterm delivery (Farooqi et al., 2022).

When microbiota changes are associated with BMI, obesity predisposes individuals to higher energy intake, leading to greater weight gain in pregnant women (Collado et al., 2020). Women with obesity tend to have higher levels of Staphylococcus in the second and third trimesters, and their babies may be colonized after birth (Ratsika et al., 2021). However, during pregnancy, they exhibit lower bacterial diversity, particularly Bacteroides in infant fecal microbiota (RR 0,83, 95 % CI 0,71-0,96, $p < 0,01$) (Robinson et al., 2017). Bacteria such as Firmicutes, Lachnospiraceae, Proteobacteria, and Actinobacteria have been found to increase the risk of overweight in the first and third years of life (Wang et al., 2019). According to multivariable models, pre-pregnancy BMI and prenatal factors influence gut microbiota (Nel et al., 2024).

Changes in gut microbiota during pregnancy are also influenced by prebiotic supplementation, which increases commensal bacteria and reduces Gram-negative bacteria (Jones et al., 2024). According to macrobiotic principles, the consumption of probiotic supplements one month before birth may help reduce allergies in newborns (Moreno, 2023). The World Allergy Organization recommends probiotics for pregnant women, lactating mothers with allergic babies, and neonates at risk of allergies (Baldassare et al., 2018). Additionally, while probiotics are used for the prevention of gestational diabetes, they may also increase the risk of preeclampsia (Davidson et al., 2021).

Microbiota changes are also related to dental caries, periodontitis, and oral mucosal diseases (Jang et al., 2021). The microbial composition of the placenta can impact pregnancy outcomes through the oral cavity (Zakis et al., 2022). Porphyromonas gingivalis, Streptococcus spp., and Fusobacterium nucleatum have been detected in oral and amniotic fluid samples, and are associated with preterm birth (Dunlop et al., 2019). A 16S rRNA sequencing analysis of oral microbiota in 20 full-term newborns delivered vaginally showed a distinct oral microbiota profile in infants born to mothers with gestational diabetes mellitus, compared to those born to non-diabetic mothers (He et al., 2019).

Natural Changes

Microbiota in pregnant women is naturally associated with vaginal function changes (Huang et al., 2024), which are crucial for the development of the infant's immune system (Agostinis et al., 2019). Additionally, changes in breast milk microbiota contribute beneficial bacteria that promote newborn health (Méndez-León et al., 2022).

Microbiota is linked to natural vaginal function changes (Huang et al., 2024), showing fluctuations during different stages of a woman's life. During the reproductive stage, Lactobacillus species predominate, producing acid that inhibits opportunistic infections through protective effects such as lactic acid and bacteriocin production (Ganal-Vonarburg et al., 2017). During pregnancy, an increase in Lactobacillus and a decrease in anaerobic bacteria are observed. However, after childbirth, the opposite occurs, regardless of ethnicity (Al-

Nasiry et al., 2020). Additionally, maternal diet is essential for microbiota health, which in turn influences the newborn's microbiota and early development.

Natural changes are also linked to breast milk, which contains beneficial bacteria for the newborn, while pre-pregnancy BMI and weight gain influence breast milk microbiota (Duttaroy & Basak, 2022). This has been associated with lower incidence rates of gastrointestinal infections, allergies, and chronic diseases throughout life (Navarro-Cáceres, 2017). Additionally, women from urban areas have been found to have higher levels of Proteobacteria, whereas those from rural areas have a higher prevalence of Firmicutes, suggesting that breast milk microbiota varies based on geographic location, diet, and cultural practices. Studies conducted in China have also found regional differences in microbial composition (Barrantes-Juan, 2021).

This study presents some limitations that should be considered when interpreting the results. First, the search was limited to articles in Spanish, Portuguese, and English, possibly excluding relevant literature published in other languages. Although multiple databases were used, this study did not include specialized health databases. Additionally, selection criteria may have been subjective, potentially excluding relevant studies that did not perfectly align with the review's objectives. Since this is a narrative review, the synthesis of results is more qualitative, which limits the ability to derive generalizable and quantifiable conclusions.

CONCLUSIONS

Microbiota changes during pregnancy are associated with various complications, including hypertensive disorders, gestational diabetes mellitus, preterm births, and spontaneous abortions. Alterations in gut microbiota composition influence the production of metabolites that affect cardiovascular health and glucose control, while dysbiosis can trigger complications such as preterm birth and increase the risk of spontaneous abortions.

BMI and prebiotic supplementation have a significant impact on microbiota health, which in turn influences the newborn's microbial composition. Maternal oral health also plays a crucial role, as oral microorganisms have been identified in association with preterm births and neonatal oral microbiota changes.

Finally, pregnancy-related microbiota changes influence vaginal functions and breast milk composition. Lactobacillus species predominate during pregnancy, inhibiting infections, while postpartum microbiota changes occur. Maternal diet and BMI affect breast milk microbiota, influencing disease risk in infants. Additionally, geographical and cultural factors play a role in shaping microbiota composition and its long-term health effects.

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CONFLICT OF INTEREST

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