



## ORIGINALS

### Fatty liver associated with metabolic dysfunction as a risk factor for preeclampsia in pregnant women

Hígado graso asociado a disfunción metabólica como factor de riesgo para preeclampsia en gestantes

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#### ABSTRACT:

**Introduction:** Fatty liver disease associated with metabolic dysfunction is an obstetric emergency that can lead to maternal and foetal complications, including death.

**Objective:** The present investigation aimed to analyze whether fatty liver associated with metabolic dysfunction is a risk factor for preeclampsia in pregnant women in a level III hospital in Trujillo - Peru.

**Method:** Descriptive study type, quantitative approach and non-experimental, observational, analytical, retrospective, case-control design. Using a data collection form, data related to the variables analyzed in 404 pregnant women were collected. They were then analyzed with the software spss version 26, the OR and confidence intervals were calculated.

**Results:** The results show that pregnant women with preeclampsia and MAFLD come from urban areas, higher education level, marital status cohabiting/married, multi-pregnancy, do not have the minimum number of prenatal check-ups, are obese, do not have type II diabetes mellitus or dyslipidemia. The prevalence of MAFLD in this population of pregnant women is low.

**Conclusions:** Fatty liver associated with metabolic dysfunction is a risk factor for preeclampsia in pregnant women.

**Keywords:** Pregnant women; Pre-eclampsia; Fatty liver; Risk factor; Obesity.

#### RESUMEN:

**Introducción:** La enfermedad del Hígado graso asociado a disfunción metabólica es una emergencia obstétrica que puede provocar complicaciones maternas y fetales, incluida la muerte.

**Objetivo:** La presente investigación tuvo como objetivo analizar si el hígado graso asociado a disfunción metabólica es factor de riesgo para preeclampsia en gestantes en un hospital nivel III de Trujillo - Perú.

**Método:** Tipo de estudio descriptivo, enfoque cuantitativo y diseño no experimental, observacional,

analítico, retrospectivo, de casos y controles. Mediante una ficha de recolección de datos se tomaron datos relacionados con las variables analizadas en 404 gestantes. Luego fueron analizados con el software spss versión 26, se calculó el OR e intervalos de confianza. **Resultados:** Los resultados muestran que las gestantes con preeclampsia e MAFLD provienen de zona urbana, grado de instrucción superior, estado civil conviviente/casada, multigesta, no cuentan con el mínimo número de controles prenatales, si presentaron obesidad, no tienen diabetes mellitus tipo II ni dislipidemias. La prevalencia de MAFLD en esta población de gestantes es baja.

**Conclusiones:** El hígado graso asociado a disfunción metabólica si constituye un factor de riesgo para preeclampsia en gestantes.

**Palabras clave:** Gestantes; Preeclampsia; Hígado graso; Factor de riesgo; Obesidad.

## INTRODUCTION

Metabolic dysfunction-associated fatty liver disease (MAFLD), formerly known as non-alcoholic fatty liver disease (NAFLD), constitutes a clinically relevant entity in the obstetric context, characterized by maternal hepatic functional impairment and/or insufficiency secondary to the accumulation of fatty acids in the hepatic parenchyma. This lipid infiltration leads to progressive liver damage and is associated with potentially life-threatening maternal and fetal complications<sup>(1)</sup>.

During pregnancy, MAFLD represents a serious obstetric complication that usually manifests predominantly in the third trimester. Despite its clinical importance, the pathophysiology of this disease is not yet fully understood. However, both maternal and fetal genetic alterations have been identified that affect mitochondrial beta-oxidation of long-chain fatty acids, a fundamental process for lipid metabolism and cellular energy production. Disruption of this metabolic pathway promotes the accumulation of toxic lipid metabolites, triggering hepatic fat infiltration, inflammation, oxidative stress, and ultimately acute liver failure, a distinctive feature of MAFLD<sup>(2,3)</sup>.

From an epidemiological perspective, MAFLD affects approximately one-third of the adult population worldwide. Although pregnancy-related liver diseases are rare, affecting about 3% of pregnant women, MAFLD stands out for its rarity and high lethality. Despite its low incidence, this condition is associated with multiple systemic complications, such as hepatic encephalopathy, ascites, hypoglycemia, fever, gastrointestinal bleeding, renal failure, and pancreatitis. A high coexistence with preeclampsia has also been documented, present in 50% to 70% of cases, along with an increased risk of postpartum hemorrhage and infections. Clinically, MAFLD often presents with nonspecific symptoms such as malaise, persistent fatigue, anorexia, nausea, and vomiting, affecting more than 75% of diagnosed women<sup>(4,5)</sup>.

Regarding diagnosis, hepatic transaminases may show mild elevations, particularly alanine aminotransferase (ALT), although its isolated value is unreliable, as it may remain within normal ranges. However, an aspartate aminotransferase/alanine aminotransferase (AST/ALT) ratio greater than one may suggest advanced stages of the disease. Imaging techniques such as abdominal ultrasound and computed tomography are useful complementary tools for assessing hepatic structure, showing increased echogenicity or changes in tissue density compatible with steatosis. Although liver biopsy remains the diagnostic gold standard, its use is limited due to its invasive nature. In this context, non-invasive methods such as magnetic resonance elastography or vibration-controlled elastography have proven useful for estimating the degree of hepatic fibrosis<sup>(5)</sup>.

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A meta-analysis study found that the highest prevalence of fatty liver was recorded in Latin America (44.37%), followed by North Africa, the Middle East, South Asia, North America, Southeast Asia, East Asia, and finally Western Europe (25.10%)<sup>(6)</sup>. In South America, the prevalence by country was distributed as follows: Brazil (35.2%), Ecuador (27.7%), Colombia (26.6%), Chile (23%), Peru (18%), and Argentina (Buenos Aires) (17%)<sup>(7)</sup>.

Preeclampsia is a progressive condition involving multiple organs, characterized by the sudden onset of hypertension and proteinuria, or hypertension accompanied by end-organ dysfunction, with or without associated proteinuria, and typically manifests after 20 weeks of pregnancy or postpartum. Its etiology is multifactorial and involves abnormal placentation, maternal systemic vascular dysfunction, immunological alterations, oxidative stress, and possible genetic and environmental factors, which significantly increase the risk of complications and perinatal maternal mortality<sup>(8)</sup>.

It is a serious complication of pregnancy that can have repercussions on the health of both the mother and the fetus. Some of the associated complications can result in premature birth, intrauterine growth retardation, HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count, and protein loss), eclampsia, stroke, renal dysfunction, disseminated intravascular coagulation, liver failure, renal failure, coma, and even maternal and fetal death<sup>(9,10)</sup>.

Preeclampsia is a cause of maternal death, with 14% of all maternal deaths worldwide caused by hypertensive disorders<sup>(7)</sup>. In Peru, preeclampsia is the second leading cause of maternal mortality, accounting for 43.33%. It occurs in 5% to 7% of all pregnancies and is more common on the coast of the country.<sup>(11)</sup>

The maternal liver undergoes physiological adaptations during pregnancy, increasing plasma protein synthesis, lipid metabolism, and free fatty acid mobilization, as well as increasing insulin resistance, particularly in the second and third trimesters. This ensures the supply of nutrients to the fetus; however, when MAFLD is present, these responses are altered. Insulin resistance is exacerbated by the accumulation of hepatic fat, leading to systemic inflammation and oxidative stress, which compromises vascular and endothelial homeostasis. This promotes endothelial dysfunction, a central mechanism in the pathophysiology of preeclampsia<sup>(12,13)</sup>.

A retrospective cohort study was conducted in Thailand on adult women with single pregnancies. Clinical records were used to obtain aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels collected 12 months before pregnancy or

during pregnancy. Over a period of 40 months, 1,192 women were included, with 1,885 selected for liver enzyme testing and ultrasound diagnosis of hepatic steatosis. In this subgroup, the prevalence of preeclampsia was 11% in women with hepatic steatosis compared to 3% in those without this condition ( $p < 0.05$ ), concluding that MAFLD is indeed a risk factor for preeclampsia<sup>(12)</sup>.

In China, a study was conducted to explore the relationship between maternal MAFLD and adverse pregnancy outcomes, considering different groups and body mass index (BMI) according to Chinese criteria (normal weight: 18.5-23.9 kg/m<sup>2</sup>). A database of prenatal care and childbirth was used, and MAFLD was confirmed by ultrasound at the beginning of pregnancy. The statistical analysis was a logistic regression model, adjusted for confounding variables. A total of 14,708 pregnant women were included, of whom 554 (3.8%) had MAFLD. Potential confounding factors were evaluated, leading to the conclusion that MAFLD significantly increased the risk of developing gestational diabetes mellitus, gestational hypertension, preeclampsia/eclampsia, and the need for a cesarean section. These findings suggest that women with MAFLD and normal weight are at increased risk of experiencing preeclampsia and adverse pregnancy outcomes<sup>(14)</sup>.

In 2021, in South Africa, the association between preeclampsia and HELLP syndrome, as well as the role of the liver in this relationship, was evaluated through a review of various electronic data sources including PubMed, Embase, Medline, and a review of the reference lists of selected articles. The findings revealed that elevated levels of total cholesterol, non-HDL cholesterol, triglycerides (TG), and liver enzymes AST and ALT were identified as useful predictors for the development of preeclampsia. It was highlighted that these biomarkers were closely related to increased liver fibrosis, resulting from an imbalance in lipid metabolism, suggesting a possible underlying mechanism in the interaction between preeclampsia and liver function. One conclusion was that elevated liver enzymes in the context of preeclampsia could be linked to prior liver damage, particularly MAFLD. This connection raises additional concerns about the severity and complexity of preeclampsia, as well as the importance of comprehensively addressing liver health during pregnancy to prevent significant complications for both the mother and the fetus<sup>(15)</sup>.

In Korea, the association between elevated ALT in early pregnancy and the subsequent development of preeclampsia were evaluated in a retrospective cohort study of a total of 2,322 women who met the inclusion criteria. Cases with early elevated ALT levels (>95th percentile) had a higher risk of subsequent preeclampsia ( $p < 0.01$ ; preeclampsia, 1.0% in normal ALT vs. 4.1% in elevated ALT,  $p < 0.05$ ). This relationship between elevated ALT and increased risk of preeclampsia remained significant after adjusting for maternal age and pre-pregnancy body mass index, concluding that ALT is commonly associated with MAFLD and its unexplained elevation at the beginning of pregnancy is associated with the risk of subsequent development of preeclampsia at the end of pregnancy. This result also highlights the importance of considering other risk factors and variables in future studies on this topic, in order to obtain a more accurate and comprehensive picture of the relationship between MAFLD and preeclampsia. <sup>(16)</sup>

In Saudi Arabia, they evaluated temporal trends in MAFLD in pregnancies after 20 weeks of gestation, comparing the results with pregnancies with or without MAFLD; a linear regression study was performed; the results were analyzed by age, race, multiple gestation, and diabetes, obesity, dyslipidemia, and hypertension before pregnancy;

5,640 had MAFLD. Likewise, the group of pregnant women with MAFLD had a higher prevalence of gestational diabetes (23% vs. 7–8%) and preeclampsia (16% vs. 4%) ( $p < 0.01$ ) compared to the group without MAFLD. In the adjusted analysis, it was associated with hypertensive complications (OR 3.1, 95% CI 2.6–3.8,  $p < 0.001$ ), but not with fetal death ( $p = 0.90$ ); concluding that MAFLD should be considered a high-risk obstetric condition due to its association with preeclampsia during pregnancy. Furthermore, it highlights the importance of future research to better understand the mechanisms of this association and develop prevention and treatment strategies to improve maternal and neonatal outcomes in this high-risk population<sup>(17)</sup>.

Preeclampsia is characterized by proteinuria and de novo hypertension, or a new onset of hypertension and significant end-organ dysfunction with or without proteinuria after 20 weeks of pregnancy or postpartum in women without previous hypertension. It consists of several hypertensive disorders during pregnancy that can be extremely dangerous to both the mother and her developing fetus. <sup>(18,19)</sup> It is determined by the presence of significant proteinuria (0.3 g or  $> 30$  mg/mmol) in a 24-hour urine sample, accompanied by systolic blood pressure equal to or higher than 140 mmHg and/or diastolic blood pressure equal to or higher than 90 mmHg in two separate measurements taken within a four-hour interval. In previously normotensive women, creatinine excretion increases significantly after 20 weeks of pregnancy and then returns to normal levels approximately six weeks (42 days) after delivery<sup>(20)</sup>.

Despite the high incidence of preeclampsia, currently available preventive medications only slightly reduce the risk of developing this condition. Furthermore, to date, the predominant variables identified to predict its onset are insufficient to provide an accurate risk assessment for all pregnant women. This lack of robust predictors underlines the complexity of preeclampsia and the urgent need for a better understanding of its underlying mechanisms and risk factors. The potential outcomes of preeclampsia can be devastating for both the mother and the fetus. These include intrauterine growth restriction (IUGR), as well as an increased risk of preterm delivery, coupled with all the complications associated with preterm birth, placental abruption, and intrauterine fetal death.<sup>(16)</sup> Not only does preeclampsia pose a significant threat to the health and well-being of the mother and fetus during pregnancy, but it has also become a leading cause of morbidity and mortality in pregnancy worldwide<sup>(2)</sup>.

MAFLD represents a growing challenge to global public health and can advance to nonalcoholic steatohepatitis, cirrhosis, and end-stage liver failure. The predominant variables are advanced age, Hispanic ethnicity, obesity, genetic predisposition, and type 2 diabetes mellitus (T2DM)<sup>(21)</sup>. The frequency of MAFLD in women of reproductive age is around 10%, which is lower than that observed in the general adult population, probably due to the youth of this demographic group. On the other hand, the incidence of MAFLD in pregnant women varies widely, ranging from 1% to 55%, suggesting differences in the demographic characteristics of the populations studied, especially with regard to the proportion of overweight or obese women included in these studies.<sup>(22)</sup> MAFLD in pregnancy is associated with multiple maternal and perinatal complications, including gestational diabetes mellitus, with a bidirectional relationship; women diagnosed with MAFLD early in pregnancy have a higher risk of developing comorbidities<sup>(23)</sup>.

The causes and development of MAFLD are not yet fully understood and remain active areas of research worldwide. Although certain characteristics, such as obesity, are well-



known risk factors, it is important to note that a significant proportion of obese individuals do not develop MAFLD, while some individuals of normal weight do develop it, suggesting the involvement of additional pathogenic factors<sup>(24)</sup>. Excessive food intake and an unbalanced diet can lead to obesity and excessive fat accumulation in the liver in non-pregnant individuals, which can develop or accelerate the progression of MAFLD. In animal studies, it has been shown that a fructose-based, low-protein diet induces glucose intolerance and fatty acid deposition in hepatocytes in pregnant rats. However, the evidence available from human studies is insufficient to draw definitive conclusions, and there is a lack of research on the dietary habits of pregnant women or women of reproductive age with MAFLD<sup>(25)</sup>.

## MATERIAL AND METHOD

A quantitative study was conducted with a non-experimental, observational, analytical, and retrospective design, under the case-control modality. The case group consisted of pregnant women diagnosed with preeclampsia, regardless of exposure to the study factor, while the control group comprised pregnant women without a diagnosis of preeclampsia, equally exposed or not to the factor. A paired sampling was used, selecting one control for each case included in the study.

The independent variable considered was metabolic dysfunction-associated fatty liver (MAFLD), and the dependent variable corresponded to preeclampsia. The study population consisted of pregnant women treated at a level III hospital in the city of Trujillo during the period between 2019 and 2023. Pregnant women aged 18 to 35 years, with a single pregnancy and complete medical records, were included. Those with a diagnosis of hepatitis, chronic liver disease, hepatocellular carcinoma, or choledocholithiasis were excluded.

The sample size was determined using the formula corresponding to case-control studies, establishing a total of 202 cases with MAFLD and 202 controls without MAFLD, resulting in a total sample of 404 pregnant women<sup>(27)</sup>.

For data collection, the documentary analysis technique was used, based on the systematic review of medical records. The instrument employed was a data collection form designed by the researcher, in which the study variables were recorded. This instrument underwent a validation process through expert judgment, consisting of two gynecologists, one obstetrician, and one internist, who provided observations aimed at optimizing its content. The statistical analysis of the instrument's validity showed an Aiken's V of 100%, confirming its adequacy for application in the study.

Once the research project was approved, authorization was requested from the hospital administration for its execution. After obtaining institutional permission, access was granted to the database containing the medical records of pregnant women treated between 2019 and 2023, verifying compliance with the previously established inclusion and exclusion criteria<sup>(28)</sup>.

Subsequently, a visit was made to the hospital facilities, where, according to the required number of cases and controls, the sample was randomly selected for the review of medical records. The information was recorded in the data collection form, including the review of abdominal ultrasound reports for the characterization of fatty liver, as well as

blood pressure and proteinuria records for the identification of preeclampsia, in addition to intervening variables. Once data collection was completed, the information was systematized and analyzed according to the established schedule.

Statistical analysis was performed using SPSS software version 26. Descriptive statistics were applied for the preparation of frequency tables and summary measures, while inferential statistics included the chi-square test and odds ratio calculation with a 95% confidence level, in order to evaluate the association and estimate the risk between the studied variables<sup>(29)</sup>.

Regarding ethical aspects, the research was carried out after the protocol was approved by the Ethics Committee of the Faculty of Health Sciences of César Vallejo University. The study was conducted in accordance with the ethical principles established in the Declaration of Helsinki<sup>(30)</sup>, ensuring the anonymity of pregnant women, the confidential use of information, and respect for the integrity of the individuals involved.

## RESULTS

Table 1 shows that most pregnant women come from urban areas (11.4%), have a higher education level (9.4%), are cohabiting/married (9.4%), are multiparous (10.9%), do not have the minimum number of prenatal check-ups (8.4%), are obese (9.9%), do not have type II diabetes mellitus (8.9%), and do not have dyslipidemia (7.9%).

**Table 1.** Characteristics of pregnant women with preeclampsia according to the prevalence of fatty liver associated with metabolic dysfunction.

Characteristics		MAFLD						Sig.
		No	%	Yes	%	Total	%	
Origin	Rural	12	5.9	4	2.0	16	7.9	0.297
	Urban	163	80.7	23	11.4	186	92.1	
Level of education	Basic	53	26.2	8	4.0	61	30.2	0.945
	Higher	122	60.4	19	9.4	141	69.8	
Marital status	Single/Other	62	30.7	8	4.0	70	34.7	0.556
	Cohabiting/Married	113	55.9	19	9.4	132	65.3	
Pregnancies	Primiparous	50	24.8	5	2.5	55	27.2	0.275
	Multiparous	125	61.9	22	10.9	147	72.8	
Prenatal check-ups	Not controlled	47	23.3	17	8.4	64	31.7	0.000
	Controlled	128	63.4	10	5.0	138	68.3	
Obesity	No	108	53.5	20	9.9	128	63.4	0.215
	Yes	67	33.2	7	3.5	74	36.6	
Type II diabetes mellitus	No	154	76.2	18	8.9	172	85.1	0.004
	Yes	21	10.4	9	4.5	30	14.9	
Dyslipidemia	No	107	53.0	16	7.9	123	60.9	0.852
	Yes	68	33.7	11	5.4	79	39.1	
Total		175	86.6	27	13.4	202	100.0	

**Source:** Trujillo Level III Hospital - Data collection records: 2019-2023.

Likewise, among the characteristics analyzed, there is a significant association ( $p < 0.005$ ) between prenatal checkups and type II diabetes mellitus with MAFLD, unlike the other variables, which have no significant association.

Table 2 shows pregnant women without preeclampsia in relation to MAFLD. Among the characteristics analyzed, no association was found among the variables studied.

It should also be noted that most pregnant women with MAFLD come from urban areas (5.9%), have a higher level of education (4.0%), are cohabiting/married (5.0%), have multiple pregnancies (5.4%), have the minimum number of prenatal checkups (3.5%), are not obese (4.0%), do not have type II diabetes mellitus (5.4%), and do not have dyslipidemia (4.0%).

**Table 2.** Characteristics of pregnant women without preeclampsia according to the prevalence of fatty liver associated with metabolic dysfunction

Characteristics		MAFLD						Sig.
		No	%	Yes	%	Total	%	
Origin	Rural	10	5.0	0	0.0	10	5.0	0.897
	Urban	180	89.1	12	5.9	192	95.0	
Level of education	Basic	55	27.2	4	2.0	59	29.2	1.000
	Higher	135	66.8	8	4.0	143	70.8	
Marital status	Single/Other	63	31.2	2	1.0	65	32.2	0.386
	Cohabiting/Married	127	62.9	10	5.0	137	67.8	
Pregnancies	Primiparous	45	22.3	1	0.5	46	22.8	0.382
	Multiparous	145	71.8	11	5.4	156	77.2	
Prenatal check-ups	Not controlled	72	35.6	5	2.5	77	38.1	1.000
	Controlled	118	58.4	7	3.5	125	61.9	
Obesity	No	150	74.3	8	4.0	158	78.2	0.523
	Yes	40	19.8	4	2.0	44	21.8	
Type II diabetes mellitus	No	179	88.6	11	5.4	190	94.1	1.000
	Yes	11	5.4	1	0.5	12	5.9	
Dyslipidemia	No	145	71.8	8	4.0	153	75.7	0.682
	Yes	45	22.3	4	2.0	49	24.3	
Total		190	94.1	12	5.9	202	100.0	

Source: Trujillo Level III Hospital - Data collection records: 2019-2023.

Table 3 shows the relationship between MAFLD and preeclampsia in pregnant women. Of the group of pregnant women who had MAFLD, 12 women (3.0%) did not develop preeclampsia, while 27 women (6.7%) did develop preeclampsia. A statistically significant association was found among the variables analyzed ( $p < 0.05$ ), with an OR of 2.44 (95% CI: 1.201–4.970), meaning that women with MAFLD are 2.44 times more likely to develop preeclampsia compared to those without this condition.

**Table 3.** Relationship between fatty liver associated with metabolic dysfunction and preeclampsia

MAFLD	Preeclampsia						OR	C.I.
	No	%	Yes	%	Total	%		
No	190	47.0	175	43.3	365	90.3	2.44	1.201-4.970
Yes	12	3.0	27	6.7	39	9.7		
TOTAL	202	50.0	202	50.0	404	100.0		

Note: Chi-square: 6.39,  $p < .05$

Source: Trujillo Level III Hospital - Data collection records: 2019–2023.



## DISCUSSION

The investigation of MAFLD as a possible risk factor for the development of preeclampsia in pregnant women is relevant due to the negative impact that both conditions exert on maternal and fetal health. Considering that preeclampsia is one of the leading causes of maternal morbidity and mortality worldwide, the identification of additional associated factors, such as MAFLD, could significantly contribute to improving strategies for early detection, prevention, and timely clinical management of this pathology<sup>(1,10-11)</sup>.

The results obtained show that pregnant women with concomitant diagnoses of preeclampsia and MAFLD present sociodemographic characteristics similar to those reported by Seung M. et al.<sup>(31)</sup> in China and Mousa N. et al.<sup>(19)</sup> in the United Kingdom. In those studies, participants were mostly from urban areas, lived with a partner or were married, were multigravida, and had no history of diabetes, hypertensive diseases, or dyslipidemia. These similarities may be explained by lifestyle patterns typical of urban environments, characterized by high-calorie diets, increased consumption of ultra-processed foods, reduced physical activity, and greater exposure to stress. In this context, a systematic review reported that dietary patterns based on high vegetable intake and low consumption of processed meats are associated with a lower risk of hypertensive disorders during pregnancy<sup>(32)</sup>.

Regarding pregnant women without a diagnosis of preeclampsia, the characteristics observed according to MAFLD prevalence were comparable to those of women with preeclampsia in aspects such as urban residence, higher education level, marital status (cohabiting or married), and multiparity. However, unlike the preeclampsia group, these women did not present obesity, diabetes mellitus, or dyslipidemia. Similar findings were reported by Chai T. et al. in Thailand<sup>(12)</sup>, who observed that women without preeclampsia were more likely to be multiparous, reside in urban areas, and be married. Likewise, Seung M. et al. in China identified similar characteristics in pregnant women without preeclampsia, such as urban residence, multiparity, and absence of diabetes or dyslipidemia<sup>(31)</sup>.

The results of the present study show a low prevalence of MAFLD in the population of pregnant women evaluated, consistent with findings reported by Chai T. et al. in Thailand<sup>(12)</sup>, who identified MAFLD in 625 of 1,885 pregnant women included. Similarly, Mousa N. et al. in the United Kingdom found that only one-fourth of pregnant women with MAFLD developed preeclampsia, suggesting a low frequency of this condition in that population<sup>(19)</sup>. In contrast, a study conducted in Saudi Arabia evaluating pregnancies beyond 20 weeks found that only 4.6% of women presented MAFLD, while the majority had other unrelated conditions, such as HELLP syndrome, lupus, fetal demise, and various neonatal complications, including respiratory distress syndrome, neonatal jaundice, necrotizing enterocolitis, sepsis, and hypoglycemia<sup>(17)</sup>.

The bivariate analysis performed between MAFLD and preeclampsia supports the hypothesis that MAFLD constitutes a risk factor for the development of preeclampsia. From a pathophysiological standpoint, this association can be explained by several mechanisms, one of the most accepted being related to maternal and/or fetal genetic alterations affecting mitochondrial beta-oxidation of long-chain fatty acids. This metabolic dysfunction promotes the accumulation of lipid metabolites and leads to

hepatic fat infiltration, causing significant liver damage<sup>(3)</sup>. The findings of the present study are consistent with those reported by Seung M. et al. in China, who demonstrated a higher prevalence of preeclampsia in pregnant women with MAFLD<sup>(31)</sup>. Similarly, Mousa N. et al. in the United Kingdom observed a higher frequency of preeclampsia and hypertensive disorders<sup>(19)</sup> in pregnant women with MAFLD, while Sarkar et al. in Saudi Arabia reported a greater risk of preeclampsia in women with this condition compared to those without MAFLD<sup>(17)</sup>.

Among the limitations of the study is the absence of multivariate analysis, such as logistic regression, which would have allowed control of possible confounding factors such as maternal age, body mass index, or the presence of comorbidities. However, this methodological decision was based on the study objectives, specifically focused on evaluating the relationship between MAFLD and preeclampsia. Likewise, the low prevalence of MAFLD observed may limit the generalizability of the results, so future research is recommended to incorporate other possible risk factors, such as alterations of the immune system.

Among the main strengths of the study is the availability of a robust database, which allowed a detailed and comprehensive analysis of the information, as well as the application of quality controls during the data collection process. The sample size was adequate, and the data came from a level III hospital, which adds reliability to the results. In addition, the use of a data collection form previously validated by experts increases the study's reliability. Finally, the findings provide relevant information for monitoring hepatic metabolic status in pregnant women, which could contribute to the design of preventive strategies and educational programs aimed at improving maternal-perinatal health.

## CONCLUSIONS

Metabolic dysfunction-associated fatty liver disease is identified as a risk factor significantly associated with the development of preeclampsia in pregnant women ( $p < 0.05$ ), with an odds ratio of 2.44 (95% CI: 1.201–4.970).

In the population of pregnant women evaluated, the frequency of metabolic dysfunction-associated fatty liver disease was low.

Pregnant women diagnosed with both preeclampsia and MAFLD were mainly characterized by urban residence, higher education level, cohabiting or married marital status, multiparity, failure to meet the minimum number of prenatal visits, and obesity; moreover, most did not present type II diabetes mellitus or dyslipidemia.

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