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Original article

Clinical and epidemiological characterization of hepatobiliary diseases in pregnant women

Caracterización clínica y epidemiológica de las enfermedades hepatobiliares en embarazadas

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SUMMARY

Introduction: Liver disease occurs in approximately 3 % of pregnant women and ranges from minor biochemical abnormalities to severe liver failure.

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Objective: To describe the clinical and epidemiological characteristics of hepatobiliary diseases in a group of pregnant patients.

Methods: A descriptive and retrospective study was conducted in 46 pregnant women who met the inclusion criteria (diagnosis of liver disease concomitant with pregnancy, chronic liver disease concomitant with pregnancy and liver disease specific to pregnancy); cases with individual clinical history with insufficient data were excluded. The variables analyzed were: age groups, personal pathological history, liver diseases and laboratory tests. The results were expressed in absolute numbers and percentages.

Results: Hyperemesis gravidarum occurred in 26 (56,5 %) patients, followed by intrahepatic cholestasis of pregnancy (12; 26 %) and biliary lithiasis (10; 32,6 %) pregnant women. There were 18 (39,1 %) pregnant women between 31-35 years old. The four patients with preeclampsia had elevated hypertransaminasemia (15,4 %), GGT (8,7 %) and total bilirubin (15,4 %). In the case of acute fatty liver of pregnancy, the two patients with this diagnosis showed alterations in all parameters (transaminases, GGT, ALP and bilirubin).

Conclusions: Hyperemesis gravidarum and biliary lithiasis were the most frequent pregnancy-specific liver disease and concomitant hepatobiliary disease with pregnancy, respectively. There was a predominance of patients aged between 31 and 35 years. Transaminases were the laboratory parameter with the most affectations in these diseases.

Keywords: hepatobiliary diseases; pregnant women; transaminases.

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RESUMEN

Introducción: Las hepatopatías se presentan en alrededor del 3 % de las embarazadas; incluyen desde alteraciones bioquímicas insignificantes, hasta la insuficiencia hepática grave.

Objetivo: Describir las características clínicas y epidemiológicas de las enfermedades hepatobiliares en un grupo de pacientes embarazadas.

Métodos: Se realizó un estudio descriptivo y retrospectivo en 46 embarazadas, que cumplieron con los criterios de inclusión (diagnóstico de enfermedad hepática concomitante con el embarazo, enfermedad hepática crónica que concomita con el embarazo y enfermedad hepática específica del embarazo); se excluyeron los casos con historia clínica individual con datos insuficientes. Las variables analizadas fueron: grupos de edad, antecedentes patológicos personales, enfermedades hepáticas y exámenes de laboratorio. Los resultados se expresaron en números absolutos y porcientos.

Resultados: La hiperémesis gravídica se presentó en 26 (56,5 %) pacientes, seguida por la colestasis intrahepática del embarazo (12; 26 %) y la litiasis biliar (10; 32,6 %) gestantes. Hubo 18 (39,1 %) embarazadas entre 31-35 años. Las cuatro pacientes con preeclampsia presentaron hipertransaminasemia (15,4 %), GGT (8,7 %) y bilirrubina total elevadas (15,4 %). En el caso del hígado graso agudo del embarazo las dos pacientes con este diagnóstico mostraron alteraciones de todos los parámetros (transaminasas, GGT, FA y bilirrubina).

Conclusiones: La hiperémesis gravídica y la litiasis biliar fueron la enfermedad hepática específica del embarazo y hepatobiliar concomitante con el embarazo más frecuentes, respectivamente. Hubo predominio de las pacientes con edades comprendidas entre 31-35 años. Las

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transaminasas fueron el parámetro de laboratorio con más afectaciones en estas enfermedades.

Palabras claves: enfermedades hepatobiliares; gestantes; transaminasas.

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INTRODUCTION

Liver disease, as a complication of pregnancy, occurs in approximately 3 % of pregnant women; it ranges from insignificant biochemical alterations to severe liver failure. The trimester of pregnancy is important in its management. [1]

There are three categories of liver diseases during pregnancy:

1. Pregnancy-specific liver diseases.
2. Acute liver diseases concomitant with pregnancy.
3. Chronic liver diseases that can complicate pregnancy, such as cirrhosis of the liver.

Pregnancy-specific liver diseases are divided into two categories (depending on whether or not they are associated with preeclampsia). Preeclampsia-related diseases are: [2-4]

1. Preeclampsia itself.
2. HELLP syndrome
3. Acute fatty liver of pregnancy (AFP).

The other two diseases that are not related to preeclampsia are hyperemesis gravidarum and intrahepatic cholestasis of pregnancy. [2-4]

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When we talk about hepatobiliary diseases concomitant with pregnancy, we are referring to acute hepatitis, tumorshepatic, the sBudd Chiari syndrome, gallstones and cholecystitis. The most common chronic liver diseases (pre-pregnancy) are: chronic hepatitis and cirrhosis of the liver of various etiologies. Patients with liver transplants may also be found. [3]

One of the most common conditions affecting pregnant women, with some degree of liver involvement, is hyperemesis gravidarum. Nausea and vomiting typical of pregnancy do not usually occur with liver disorders. [4]

Intrahepatic cholestasis of pregnancy is the most common liver disease in pregnancy, in which there is a disturbance in the homeostasis of bile acids at the level of the maternal hepatocyte, which determines their accumulation and elevation in the blood. [5]

Pregnant women with elevated aminotransferases and no symptoms or signs of liver disease have been observed. [6] In relation to the causes, when elevated alanine aminotransferase (ALT) predominates, these include chronic hepatitis B and C viruses, drug use, metabolic liver disease, hereditary hemochromatosis, autoimmune hepatitis, Wilson's disease, and alpha-1 antitrypsin deficiency. [7]

Causes of elevated aminotransferases less than five times the maximum normal value and when the elevation of aspartate aminotransferase (AST) predominates include: alcohol abuse, liver metastases, congestive liver and non-hepatic causes (hemolytic states and myopathies). Patients who present these enzymes greater than 15 times the maximum normal values are limited: they include acute hepatitis due to hepatotropic and non-hepatotropic viruses, as well as drugs. [8-11]

Liver diseases concomitant with pregnancy and chronic diseases are a medical problem that explains a high proportion of complications, where the diagnostic and therapeutic decisions must

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take into account the health of the mother and the fetus. This makes the clinical management of these patients difficult. [12]

This study was carried out with the aim of describing the clinical and epidemiological characteristics of hepatobiliary diseases in a group of pregnant patients.

METHODS

Study classification and context

A descriptive and retrospective study was carried out in a group of pregnant women diagnosed with hepatobiliary diseases associated or concomitant with pregnancy, treated at the "Mariana Grajales" Gynecological-Obstetric Hospital in the period from December 2016 to June 2018.

Study population

A population of 46 patients was studied, delimited by the selection criteria specified below:

Inclusion criteria

Diagnosis of hepatobiliary disease concomitant or associated with pregnancy.

Exclusion criteria

Individual medical history with insufficient data, which makes it impossible to collect information of interest for the study.

Variables

- Age groups: up to 19 years, 20-25, 26-30, 31-35 and > 35 years.

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- Personal medical history: obesity, arterial hypertension, diabetes mellitus, peripheral venous insufficiency, gestational diabetes and bronchial asthma.
- Hepatobiliary diseases concomitant or associated with pregnancy.
- Laboratory tests: ALT and AST, alkaline phosphatase (AP), total bilirubin (TB), gamma-glutamyltranspeptidase (GGT), and abdominal ultrasound.

Aminotransferases were evaluated as follows:

- Normal: there are no alterations inALT, nor AST (value up to 49 mmol/L).
- Mild: increase in aminotransferases less than 5 times their normal value.
- Moderate: aminotransferases greater than 5 to 10 times their normal value.
- Severe: aminotransferases above 10 times their normal value.

Data collection and analysis

The information required for the study was obtained by reviewing medical records and recorded in data collection forms. Descriptive statistics techniques were used to analyze the results:

Summary measures for the variables were as follows:

• For quantitative data, measures of central tendency (mean) and dispersion (standard deviation, maximum and minimum) were used.

• For qualitative data, absolute frequencies and relative frequencies such as percentages were used.

Ethical considerations

This research was conducted under the principles established in the Declaration of Helsinki. [13] It was approved by the research ethics committee and the scientific council of the institution.

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RESULTS

Table 1 shows the behavior of hepatobiliary diseases concomitant or associated with pregnancy. Hyperemesis gravidarum occurred in 26 (56,5 %) patients, followed by intrahepatic cholestasis of pregnancy (12; 26 %). Gallstones were the most frequent liver disease concomitant with pregnancy (10; 32,6 %). No patients with chronic liver disease that can complicate pregnancy were found.

Table 1. Distribution of patients according to hepatobiliary diseases concomitant or associated with pregnancy

Pregnancy-specific liver diseases		
Related to preeclampsia	**n**	**%**
Preeclampsia	4	8.6
HELLP syndrome	2	4.3
Acute fatty liver of pregnancy	2	4.3
Not related to preeclampsia		
Hyperemesis gravidarum	23	56.5
Intrahepatic cholestasis of pregnancy	12	26
Hepatobiliary disease concomitant with pregnancy	**n**	**%**
Biliary lithiasis	10	32.6
Cholecystitis	5	10.8
Acute viral hepatitis	3	6.5

The distribution of patients according to age groups is shown in Table 2. There was a predominance of patients aged between 31-35 years (18; 39.1 %).

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Table 2. Distribution of patients according to age groups

Age groups	n	%
Up to 19 years old	2	4.3
20-25 years	10	21.7
26-30 years	9	19.5
31-35 years	18	39.1
> 35 years	7	15.2
Total	46	100

Figure 1 shows the distribution of patients according to personal history. Obese patients were the most frequent (16; 34,8 %), followed by hypertensive patients (10; 21,7 %) and diabetics (8; 17,4 %).

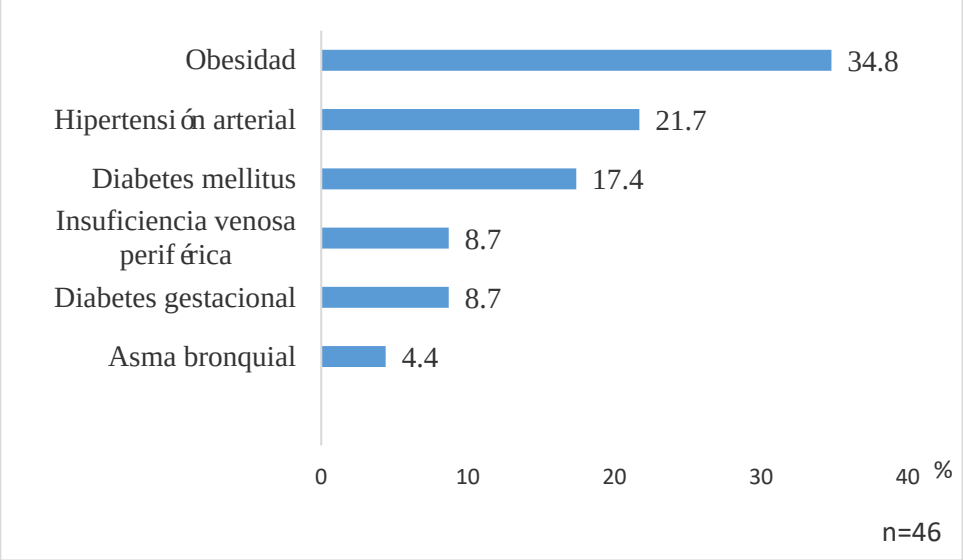

Figure 1. Distribution of patients according to personal pathological history

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Table 3 shows the distribution of pregnancy-specific liver diseases according to laboratory test abnormalities. The four patients with preeclampsia had elevated aminotransferases, GGT and total bilirubin, only one (2,2 %) had normal ALP. In the case of acute fatty liver of pregnancy, the two patients with this diagnosis showed alterations in all parameters (aminotransferases, GGT, ALP and bilirubin).

Table 3. Distribution of pregnancy-specific liver diseases according to laboratory test abnormalities

Pregnancy-specific liver diseases	Elevated aminotransferases		Elevated GGT		Elevated AF		Elevated bilirubin	
	n	%	n	%	n	%	n	%
Related to preeclampsia								
Preeclampsia	4	15.4	4	8.7	3	6.5	4	15.4
HELLP syndrome	2	4.3	2	4.3	2	4.3	2	4.3
Acute fatty liver of pregnancy	2	4.3	2	4.3	2	4.3	2	4.3
Not related to preeclampsia								
Hyperemesis gravidarum	21	45.7	4	15.4	12	26.1	6	13.0
Intrahepatic cholestasis of pregnancy	12	26.1	10	21.7	9	19.6	9	19.6

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DISCUSSION

The prevalence of hepatobiliary diseases in pregnant women ranges from 3-5 %. The causes are diverse and include: pre-existing liver disease (primary biliary cholangitis, primary sclerosing cholangitis, autoimmune hepatitis, Wilson's disease, chronic viral hepatitis, liver cirrhosis of any etiology and history of liver transplantation); liver disease acquired during pregnancy (viral hepatitis, drug-induced toxicity and hepatolithiasis); pregnancy-related liver disease (hyperemesis gravidarum, intrahepatic cholestasis of pregnancy, preeclampsia, HELLP syndrome and fatty liver of pregnancy). [14]

In this investigation, hyperemesis gravidarum was the most prevalent pregnancy-specific liver disease, followed by intrahepatic cholestasis; while biliary lithiasis behaved as the most frequent concomitant disease with pregnancy. These results differ from a study carried out at the "Comandante Faustino Pérez Hernández" University Hospital in Matanzas, in which intrahepatic cholestasis was the second most frequent cause, preceded by chronic hepatitis B virus. [15]

An association has been found between the onset of liver disorders with age, personal and family history of liver disease, and skin color. Advanced maternal age is associated with the risk of obstetric and non-obstetric complications during pregnancy, both for the mother and the fetus. All women, regardless of age, may be at risk for some type of liver disease. [16]

Obesity was found in more than half of the patients studied. The relationship between this history and the diagnosis of diseases such as: arterial hypertension, diabetes mellitus, ischemic heart disease, peripheral vascular disorders and possible complications that may occur at the time of delivery and the immediate postpartum period is recognized. [17, 18]

The evaluation of the increase in aminotransferases is the main analytical factor to consider for the diagnosis of gestational liver disease and constitutes an effective biochemical marker for the

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evolutionary follow-up and for defining the clinical and obstetric management. The increase in aminotransferases in the pregnant women studied was an analytical expression of the liver disease and, in some cases, the only alteration found in the liver function tests. [19]

In a study that analyzed the predictive factors of adverse perinatal effects in pregnant women with intrahepatic cholestasis of pregnancy, it was determined that, of the different variables studied, ALAT was statistically significant as a predictor of perinatal complications with 76,5 % sensitivity and 78,4 % specificity. [4]

The most common cause of jaundice and hyperbilirubinemia during pregnancy in the United States is still attributed to viral hepatitis, despite the decrease in its incidence in that country. One publication reveals that of all pregnant women who gave birth to a baby between 2005 and 2011 in a single hospital in Dallas, only 0,5 % had elevated bilirubin levels, much less than those in this study, and their third cause was preeclampsia or eclampsia. [20]

It should be noted that Elevated AST may be caused by disorders of other organs, most often striated muscle. If striated muscle disease is suspected, creatine phosphokinase and aldolase levels should be determined. [2]

CONCLUSIONS

Hyperemesis gravidarum and biliary lithiasis were the most frequent pregnancy-specific liver disease and concomitant hepatobiliary disease with pregnancy, respectively. There was a predominance of patients aged between 31 and 35 years. Transaminases were the laboratory parameter with the most effects in these diseases.

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Conflicts of interest

The authors report no conflicts of interest.

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