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Screening for chronic hepatitis C and chronic hepatitis B infections among pregnant females: a cross-sectional study

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Abstract

Background: In Egypt, an endemic country for both viral hepatitis C and B infections, infection could be more prevalent in pregnant females. This study aimed to assess the prevalence of chronic HCV and HBV in a cohort of pregnant Egyptian females, highlighting the disease burden for better preventive measures and better disease outcome. In this cross-sectional prospective study, 399 pregnant women attending antenatal clinic in a tertiary care center in Egypt were screened for HCV and HBV infection using ELISA testing. Clinical and biochemical characteristics were compared between positive and negative cases.

Results: Mean age was 26.78 years. Prevalence rates of HCV-Ab and HBsAg positivity were 7.02% and 7.52%. Isolated HBcAb positivity was found in only 2 patients (0.5%). All cases were negative for HBsAb. No combined HBV/HCV infection was detected. All positive cases for either HBV or HCV infections did not show any signs of hepatic decompensation. ALT was significantly higher among HBV positive versus negative patients (mean ± SD of 14.2 ± 5.77 IU/L versus 11.95 ± 5.21 IU/L, $p = 0.02$, reference range: 7-56 IU/L), while no significant difference was found between HCV positive and negative cases as regards liver enzymes.

Conclusion: In Egypt, HBV prevalence in pregnant females seems to be higher than general population. This was not evident for HCV infection; however, it is still higher than pooled prevalence rates worldwide. This higher prevalence for both viral infections warrants strict screening programs to prevent vertical transmission and to provide better maternal and fetal outcome.

Keywords: HCV, HBV, Pregnancy, Prevalence rate

Background

Pregnant females represent a vulnerable cohort where infection with either HBV or HCV or both has been linked to adverse pregnancy and birth outcomes, including mother to child transmission (MTCT) [1].

Egypt represents one of the countries with the highest HCV prevalence [2]. Ten percent and 7.0% of the population aged 15-59 years had positive HCV antibody and HCV RNA according to the 2015 Egyptian Health Issues Survey (HIS) [3]. Chronic HCV is the leading cause for end-stage liver disease, hepatocellular carcinoma (HCC), and liver-related mortality in Egypt [4]. Despite shifting to low endemicity area of hepatitis B (HBsAg prevalence < 2%) with the rapid expansion of the coverage of hepatitis B vaccinations following their addition to the national immunization program in the 1990s, HBV still represents disease burden in Egypt [5].

Females represented 55.2% of HCV-infected population in the 2015 HIS. Females aged 15-59 years had HCV antibody and HCV-RNA prevalence of 8.1% and 5.5% respectively and HBcAb, HBsAg prevalence of

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13.2% and 1.2% [3]. This infection rate may reflect more prevalent infection among pregnant females.

Women in the child-bearing period can transmit the infection through vertical transmission to their babies. Vertical transmission was a major problem with HBV infection prior to the era of postexposure prophylaxis. Approximately, 85% of infants born to HBsAg and HBeAg positive women acquire HBV infection and about 30% of those born to HBeAg-negative mothers [6]. Vertical transmission is also documented in HCV infection. A meta-analysis revealed a risk of 5.8% for children of HCV antibody, RNA–positive, HIV-negative women, and 10.8% for children of HCV antibody, RNA–positive HIV-positive mothers. This means that more than 1 in every 20 children born to chronically infected mother are HCV infected which is the primary transmission route among children [1]. In Egypt, an endemic country for both viral hepatitis infections, vertical transmission risk may be more prevalent than other regions.

Although females in the reproductive age have a slower rate of disease progression in chronic HCV or HBV than men [7], liver fibrosis rates increase after menopause and become comparable to men [8]. This is principally because postmenopausal women have higher incidence of insulin resistance and metabolic syndrome, and due to loss of protective effects of estrogen [9].

In the current study, we screened a cohort of pregnant Egyptian females for HCV and HBV infections and assessed their liver disease status, clinical and laboratory characteristics with the objective of highlighting the disease burden, and, hence, need for development of guided policies for access to early preventive and therapeutic measures prior to childbearing targeting elimination and better outcomes for both mothers and their children.

Methods

This is a cross-sectional prospective study that included 399 pregnant women attending to obstetric outpatients' clinic, Faculty of Medicine, Cairo University, Cairo, Egypt, in the period from January 2018 till September 2018.

All pregnant women in the first and second trimester of pregnancy who had no history of prior diagnoses or treatment of HCV or HBV were included.

Patients who were included in this study underwent the following:

1. Informed consent: All patients enrolled had signed informed consent including the study procedures. The study was conducted according to Helsinki Declaration [10].
2. Full history taking: including age, sex, residence, presence of hypertension or diabetes, possible risk factors for viral hepatitis acquisition as previous operation or blood transfusion, possible past maternal or fetal complications as history of previous miscarriage, previous preterm labor, still birth or dead fetus, and history of complications during previous pregnancy as postpartum hemorrhage. Past history of chronic liver disease and family history of liver disease.
3. Clinical assessment: with special emphasis on manifestations suggestive of chronic liver disease.
4. Laboratory investigations including: Liver biochemical profile in the form of aspartate aminotransferase (AST), alanine aminotransferase (ALT)
5. Viral hepatitis markers (HBsAg, HBcTotal, HBsAb, HCV Ab) were tested using ELISA technique.

– Prevalence rate of HCV and HBV infections was assessed in the study population with analysis of their demographic and laboratory data.

– Positive cases for HCV and/or HBV infection were counseled. Patients with hepatitis B were managed according to guidelines either during or after pregnancy and were counseled to give their babies hepatitis B immune-globulins at birth and the routine hepatitis B vaccine schedule. Although treatment for hepatitis C was deferred after pregnancy for fear of teratogenicity or adverse pregnancy outcome. They were also counseled to defer treatment after lactation for those who were willing to lactate as direct acting antivirals for HCV treatment are not well studied during lactation.

Statistical analysis

Descriptive statistics were done; categorical variables were presented as frequency (%) and numerical ones as mean (SD) or median (IQR).

Comparison between two groups was done using the Chi-square test or Fischer's exact for categorical variables and the independent samples t test or Mann-Whitney's test as appropriate for numerical variables.

P values <0.05 were deemed significant. STATA 15 was used for the analysis.

Results

Mean age was 26.78 years. Thirty-nine patients (9.77%) were diabetic, 28 patients (7.02%) were hypertensive. In total, 84.96% of participants were in the second trimester. Other demographic and clinical data are shown in Table 1.

Prevalence rates of HCV-Ab and HBsAg positivity were 7.02% and 7.52%. Isolated HBcAb positivity was found in only 2 patients (0.5%). All cases were negative

Table 1 Demographic, risk factors, and clinical data of the study population (number = 399)

		(Number = 399)
Age/years		
Median (IQR)		28 (22-30)
Range		18-37
Residence		
Rural/urban (number %)		219 (54.89%)/180 (45.11%)
DM (number %)		39 (9.77%)
Hypertension (number %)		28 (7.02%)
Trimester of pregnancy (number %)	1st trimester	60 (15.04%)
	2nd trimester	339 (84.96%)
Family history of liver disease (number %)		36 (9.02%)
Blood transfusion (number %)		30 (7.52%)
Previous operations (number %)		47 (11.78%)
History of abortion (number %)		54 (13.53%)
History of preterm labor (number %)		26 (6.52%)
History of stillbirth (number %)		30 (7.52%)
History of newborn congenital anomalies (number %)		33 (8.27%)
Complicated previous pregnancies (number %)		23 (5.76%)

for HBsAb. No combined HBV/HCV infection was detected (Table 2).

No significant difference was found between HBV or HCV positive cases and those with negative markers as regards demographic or clinical data apart from hypertension that was detected in a significantly higher ratio in HBV positive cases versus those with negative markers or HCV positive cases (16.67% versus 6.78% and 0%) (Table 3).

All positive cases for either HBV or HCV infections did not show any signs of hepatic decompensation. ALT was significantly higher among HBV positive versus negative patients (median (IQR) 13 (10-19) versus 12 (8-15), $p = 0.03$), while no significant difference was found between HCV positive and negative cases as regards liver enzymes (Tables 4 and 5).

Discussion

Although Egypt is an endemic country to both viral hepatitis C (HCV) and B (HBV) infections, there is limited data on their related burden among pregnant women. In the current study, we aimed to assess the prevalence of chronic HCV and HBV in a cohort of pregnant Egyptian females highlighting the disease burden for better preventive measures.

Table 2 Prevalence of HCV and HBV among the study population (number = 399)

	Number (%)
HCV Ab positivity	28 (7.02%)
HBsAg positive	30 (7.52%)
HBcAb positive	32 (8.02%)
Positive HBcAb and HBsAg	30 (7.52%)
Positive HBcAb and HBsAb	0 (0.0%)
Isolated HBcAb positive	2 (0.50%)

Results of the current study revealed prevalence rates of HCV-Ab and HBsAg positivity of 7.02% and 7.52% respectively. Isolated HBcAb positivity was found in only 2 patients (0.5%). All cases were negative for HBsAb. No combined HBV/HCV infection was detected.

HCV Ab prevalence among pregnant females in the current study (7.02%) matches with the general prevalence of HCV in 2015 Egyptian Health Issues Survey (HIS) for females aged 15-59 years who had HCV antibody and HCV-RNA prevalence rates of 8.1% and 5.5% respectively [3]. On the other side, it is higher than the rate of HCV Ab positivity found in the systematic review and meta-analysis conducted by Binga and collaegues in 2019 to determine the magnitude of HCV and HBV infections among pregnant women living in 30 countries in Africa; they reported a pooled prevalence rate of 3.4% for HCV Ab positivity and 6.8% for HBsAg positivity [11]. High prevalence rate in our study may be explained by the findings that 42.8% of HCV Ab positive females had rural residence, and 46.41% of them had previous pregnancy-related complications including miscarriage and still birth, also 7.14% of them had history of previous operations. In such situations (miscarriage, stillbirth, previous operations), poor implementation of infection control measures in the

Table 3 Demographic, risk factors, and clinical data of females with positive versus negative hepatitis markers

	HCV positive (*n* = 28)	HBV positive (*n* = 30)	Negative hepatitis markers (*n* = 339)	*P*
Age Median (IQR)	28 (23-29.5)	24.5 (21-29)	28 (22-30)	0.5
Residence Rural/urban	12/16	16/14	190/149	0.4
DM*	4 (14.28%)	4 (13.33%)	31 (9.14%)	0.5
Hypertension*	0	5 (16.67%)	23 (6.78%)	**0.04**
Blood transfusion*	1 (3.57%)	3 (10%)	26 (7.67%)	0.6
Previous operations*	2 (7.14%)	5 (16.67%)	40 (11.80%)	0.6
Family history of liver disease*	2 (7.14%)	1 (3.33%)	33 (9.73%)	0.6
History of abortion*	6 (21.43%)	4 (13.33%)	43 (12.68%)	0.4
History of preterm labor*	2 (7.14%)	0	24 (7.08%)	0.4
History of stillbirth*	2 (7.14%)	3 (10%)	25 (7.37%)	0.8
Complicated previous pregnancies*	3 (10.7%)	0	20 (5.90%)	0.2

*Data are given as number (%)

hospital and especially in the operation rooms and lack of awareness about transmission of these blood born viral infections may contribute to the higher transmission and prevalence rates. This finding necessitates application of strong awareness and screening programs for females in childbearing period prior to marriage or conception to offer treatment with direct acting antiviral therapy with high efficacy and tolerability to avoid risk of vertical transmission and for better maternal outcomes.

In the current study, HBsAg positivity rate (7.52%) is much higher than that detected in 2015 Egyptian Health Issues Survey (HIS) for females aged 15-59 years who had prevalence rate of 1.2% for HBsAg [3]. It is also much higher than the pooled prevalence found in a systematic review and meta-analysis conducted on the frequency of HBsAg in pregnant women from Eastern Mediterranean and Middle Eastern countries by Malekifar and colleagues in 2018, where pooled prevalence in pregnant Egyptian females was 3.2% [12]. This higher rate may reflect lack of awareness and poor compliance of these females to the compulsory HBV vaccination in their childhood especially that 54.89% of them were from rural areas with poor socioeconomic conditions. It also gives insight on the mandatory screening for HBV in pregnant females even with the nationwide application of vaccination programs to save the newborns from getting HBV infected via vertical transmission with application of proper preventive measures including immunoglobulin administration and HBV vaccination of the newborn in the first few hours of his life according to the most recent guidelines [13].

It appears that women in child-bearing period (CBP) have a slower rate of disease progression in viral hepatitis than men and postmenopausal females [7]. This may be attributed to the protective effect of estrogen in females of the CBP. Estrogen in the liver seems to protect the hepatocytes from inflammatory injury, oxidative stress, and cell death [14]. In the current study, no significant difference was found between HCV positive and negative cases as regards liver enzymes. And although ALT was significantly higher among HBV positive versus negative patients, all values were within normal ranges. However, risk of disease progression increases after menopause with loss of hormonal protective effects [8].

Main limitations of our study are being in one center; however, being in a tertiary hospital, it represents a referral center for different destinations, next is the absence of confirmatory PCR results, although all positive patients were referred to specialized clinics for further follow-up for both mothers and neonates.

Table 4 Liver enzymes in HCV positive versus negative cases and HBV positive versus negative cases

	HCV positive	Non-HCV	*p* value	HBV positive	Non-HBV	*p* value
ALT (IU/L)	10.5 (7.5-15)	12 (9-15)	0.4	13 (10-19)	12 (8-15)	**0.03**
AST (IU/L)	12 (7-14)	12 (9-17)	0.4	11.5 (9-16)	12 (9-16)	0.8

Table 5 Liver enzymes in HCV positive versus HBV positive versus cases with negative hepatitis cases

	HCV positive (*n* = 28)	HBV positive (*n* = 30)	Negative hepatitis markers (*n* = 339)	*P*
ALT	10.5 (7.5-15)	13 (10-19)	12 (8-15)	**0.07**
AST	12 (7-14)	11.5 (9-16)	12 (9-17)	0.7

Conclusion

Based on the results of the current study, we can conclude that chronic HCV and HBV infections are prevalent in pregnant Egyptian females, and even more prevalent than general population in HBV infection which highlights the need for national screening programs with clear referral pathways and joint hepatology/obstetrician clinics with applying proper preventive measures and performing further research to prevent vertical transmission and to provide better maternal and fetal outcome.

Abbreviations

HCV: Hepatitis C virus; HBV: Hepatitis B virus; ELISA: Enzyme-linked immunesorbent assay; MTCT: Mother to child transmission

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Not applicable.

Authors' contributions

The authors read and approved the final manuscript. All authors contributed to the work. AF: Idea of the study, revision of the thesis, and manuscript. M abd EL: Supervising the gynecology and obstetrics clinic for the included subjects. RE: Revising the thesis, drafting the manuscript, and the corresponding author. MN: Performing the laboratory studies of ELISA testing for viral markers. M B: Performing the clinical work and data collection for included subjects. NZ: Idea of the study as part of the scientific work of clinic of pregnant females with liver disease activities in Kasr Alainy, revising the manuscript. AY: Idea of the study as part of the scientific work of clinic of pregnant females with liver disease activities in Kasr Alainy. ZA: Doing the statistical tests for the study.

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Availability of data and materials

Data are available.

Declarations

Ethics approval and consent to participate

All patients signed informed consent. The study was carried out following the Helsinki Declaration, and was approved by the ethical committee of endemic medicine department, Kasr Alainy Hospital, Cairo University, as a master thesis; hence, it did not have an ethics committee's reference number.

Consent for publication

Patients had signed informed consent for use of their data in research and publication without the appearance of their names.

Competing interests

No competing interests

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