

## Summary

Hepatitis C virus (HCV) infection is a worldwide health problem and Egypt, in particular, suffers from its resulting cirrhosis and HCC.

Among the groups less often discussed when considering the burden of HCV infection are pregnant women and their infants. Much remains unknown about HCV dynamics during and after pregnancy, as well as in the neonatal period. It is clear that pregnancy induces tremendous physiological changes leading to a modified course of chronic hepatitis C in infected mothers.

High interferon (IFN) levels were reported in pregnant women that could be due to the placental production. During pregnancy, human trophoblasts produce different types of IFN that can be detected in both maternal and fetal blood.

Worldwide, the seroprevalence of HCV in pregnant women is around 0.15% to 2.4% and much higher in countries like Egypt where it is estimated to be as high as 8.6%. The overall rate of mother-to-child transmission for HCV from HCV-infected, HIV-negative, mothers has been estimated around 5% or less. This relatively low rate has attracted the attention towards studying the immunological changes occurring during pregnancy in women with chronic hepatitis C that might protect the foetus.

The presence of maternal neutralizing antibodies was found to have no role in promoting or protecting against HCV- vertical transmission (VT), while placental NK cells and endogenous interferon- $\alpha$  (IFN- $\alpha$ ) were claimed to be protective and may explain the relatively low rate of HCV-VT. Moreover, the endogenous production of IFN- $\alpha$  was also suggested to explain the reduction in transaminases serum levels that commonly occurs in patients with chronic hepatitis C during pregnancy.

For all these considerations, the present study was planned to monitor the changes in serum levels of endogenous IFN- $\alpha$  and transaminases (namely AST and ALT) in pregnant women with chronic hepatitis C.

It involved 56 Egyptian women. The **Cases group** comprised 26 pregnant women proved to have chronic hepatitis C (positive for anti HCV and HCV- RNA- PCR) whose mean age was  $27.9 \pm 3.8$  years. Three **Control groups** were taken and each one comprised 10 women, namely:

- Pregnant women with negative HCV-Ab (mean age  $29.8 \pm 3.9$  y).
- Non pregnant, HCV-Ab -positive women (mean age  $26 \pm 5.2$  y).
- Non pregnant, HCV-Ab -negative women (mean age  $32.6 \pm 6.2$  y).

All were attending Benha University Hospitals, at the Hepatology, Gastroenterology and Infectious Diseases Department, in collaboration with the Obstetrics and Gynecology, Clinical Pathology as well as the Medical Biochemistry Departments, within the period between June 2010 and August 2011. The study protocol was approved by the Ethical Committee of Benha Faculty of Medicine and its University Hospitals.

**In the present study**, the cases group comprised 14 primi- and 12 multi- gravida patients, of whom 15 patients (57.7 %) underwent normal vaginal delivery (NVD) while the remaining 11 (42.3 %) got caesarian section (CS). While in the HCV-Ab negative pregnant group, 60% got NVD and 40% got CS. The mean gestational age was similar ( $38.2 \pm 2.2$  Ws) between both groups. Hence, HCV had non significant impact on either gestational age or mode of delivery in infected mothers.

As regards CBC findings, haemoglobin level as well as platelet- and WBCs- count showed no statistically significant difference ( $P > 0.05$ ) between the cases group and the 3 control groups.

The current study presented a statistically highly significant negative correlation ( $P < 0.001$ ) between serum transaminases, namely AST and ALT, levels and pregnancy duration. Both were similarly decreasing as pregnancy was progressing. They showed a statistically highly significant progressive decrease ( $P < 0.001$ ) when assessed in the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> trimesters in the studied cases with chronic hepatitis C. Moreover, in the 3<sup>rd</sup> trimester, pregnant women with chronic hepatitis C had serum transaminases levels comparable to those of the studied healthy pregnant and non pregnant women without hepatitis C with no statistically significant ( $P > 0.05$ ) difference. Our studied non pregnant women who were HCV- Ab +ve showed the highest transaminases level and this rise was highly significant ( $P < 0.001$ ) when compared to that of the cases group in the 3<sup>rd</sup> trimester and statistically significant ( $P < 0.05$ ) when compared with that measured in the 1<sup>st</sup> and 2<sup>nd</sup> trimesters in the cases group.

In the present study, there was a statistically non significant ( $P > 0.05$ ) increase in HCV-RNA-viral load assessed in early 2<sup>nd</sup> and late 3<sup>rd</sup> trimesters in the cases group. This rise may be seen because of the role of oestrogen and the relative suppression of immunity as pregnancy proceeds.

The present study showed a statistically significant ( $P < 0.05$ ) positive correlation between serum endogenous INF- $\alpha$  level and pregnancy duration in the cases group. The serum endogenous IFN- $\alpha$  level was significantly increased ( $P < 0.05$ ) when measured in late 3<sup>rd</sup> trimester ( $39.1 \pm 30.0$  pg/ml) compared to that in early 2<sup>nd</sup> ( $22.1 \pm 15.3$  pg/ml) trimester. This high level in the 3<sup>rd</sup> trimester was highly significant ( $P < 0.001$ ) when compared to that in pregnant women without HCV, and statistically significant ( $P < 0.05$ ) when compared to its level in the studied non pregnant groups. On the other hand, the IFN- $\alpha$  level measured in the cases group in early 2<sup>nd</sup> trimester showed no significant difference when compared to the studied 3 control groups.

In the current study, age has no statistically significant impact ( $P > 0.05$ ) on serum endogenous IFN- $\alpha$  level in the studied pregnant women with chronic hepatitis C (despite negative correlation). The study also showed a statistically highly significant negative correlation ( $P < 0.001$ ) between serum endogenous IFN- $\alpha$  levels and ALT in the studied cases group and a statistically significant one with AST ( $P < 0.05$ ) which augments the hypothesis that the endogenous IFN- $\alpha$  may be the direct cause of such reduction in transaminases levels in HCV- infected mothers.