

***Role of Chronic Hepatitis C Virus (cHCV) Infection in  
Liver Fibrogenesis: Relationship to Transforming  
Growth Factor- Beta 1 (TGF- $\beta$ 1) and Collagen I (Col I)  
Expression***

A thesis Submitted to Zoology Department  
Faculty of Science, Ain Shams University

**For the Master Degree of Science**

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**2010**

دور الإصابة المزمنة بفيروس الألتهاب الكبدى سى فى تليف الكبد :  
علاقتها بتعبير عامل النمو المحول بيتا- ١ والكولاجين- ١

رسالة مقدمة تمهيدا للحصول علي درجة الماجستير في قسم الحيوان

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## ***List of Abbreviation***

<b><math>\alpha</math>CP2</b>	: Alpha globins transcription factor.
<b>`3H</b>	: Thymidine.
<b>AAIR</b>	: Age-adjusted incidence rate.
<b>ADAM</b>	: A disintegrin and metalloprotease domain.
<b>ADAMTS2</b>	: ADAM metalloproteinase with thrombospondin type 1 motif, 2.
<b>ADAMTS 3</b>	: A disintegrin and metalloprotease with thrombospondin motifs 3.
<b>ADAMTS14</b>	: A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 14.
<b>ADH2</b>	: Alcohol Dehydrogenase 2.
<b>ALDH2</b>	: Aldhyde Dehydrogenase 2.
<b>AFP</b>	: Alpha Feto Protein.
<b>AFU</b>	: Alpha-L-Fucosidase.
<b>ALB</b>	: Albumin.
<b>ALP</b>	: Alkaline phosphotase.
<b>ALT</b>	: Alanine Amino Transferase.
<b>ARFP</b>	: Alternate Reading Frame Protein.
<b>AST</b>	: Aspartate Amino Transferase.
<b>Bcl-2</b>	: B cell lymphoma leukemia 2.
<b>Bcl-xs</b>	: Small protein of Bclx Gene.
<b>b-DNA</b>	: Branched DNA Technology.
<b>BMI</b>	: Body mass index.

<b>BMPs</b>	: Bone morphogenic proteins.
<b>BMPs</b>	: Bone morphogenic proteins.
<b>CD</b>	: Cluster of differentiation.
<b>c-DNA</b>	: Complementary Deoxy Ribo Nucleic Acid .
<b>CHC</b>	: Chronic Hepatitis C.
<b>CLD</b>	: Chronic Liver Disease.
<b>CICP</b>	: C-terminal of type 1 collagen.
<b>COL 1</b>	: Collagen type 1.
<b>CT</b>	: Computed tomography.
<b>DCP</b>	: Des-Gamma-Carboxy-Prothrombin.
<b>DPC</b>	: Deleted in Pancreatic Cancer.
<b>E1</b>	: Envelope region 1.
<b>E2</b>	: Envelope region 2.
<b>ECM</b>	: Extra Cellular Matrix.
<b>ELISA-3</b>	: Third generation Enzyme Linked Immuno Sorbent Assay.
<b>FACITs</b>	: Fibril-Associated Collagens with interrupted Triple Helices.
<b>FACS</b>	: Flow cytometric analysis
<b>G1</b>	: Gap 1.
<b>G2</b>	: Gap 2.
<b>GbE</b>	: Ginkgo biloba extract.
<b>GPC</b>	: Glypican.
<b>GPC3</b>	: Glypican 3.
<b>HBsAg</b>	: Hepatitis B Surface Antigen.
<b>HBV</b>	: Hepatitis B Virus.

<b>HCC</b>	: Hepatocellular Carcinoma.
<b>HCCSMC</b>	: Human corpus cavernosum smooth muscle cells.
<b>HCOL1A1</b>	: Human collagen type I $\alpha 1$ gene.
<b>HCV</b>	: Hepatitis C Virus.
<b>HCV-Ab</b>	: Hepatitis C Virus Antibody.
<b>HDV</b>	: Hepatitis D Virus.
<b>HRP</b>	: Horseradish peroxidase
<b>HSC</b>	: Hepatic Stellate Cells.
<b>HSCs</b>	: Hepatic stellate cells.
<b>HSPGs</b>	: Heparan sulfate proteoglycans.
<b>IBD</b>	: Inflammatory Bowel Diseases.
<b>IgG</b>	: Immunoglobulin G.
<b>IMx</b>	: Full automated immuno analyzer system.
<b>KDA</b>	: Killodalton.
<b>LAP</b>	: Latency associated Peptide.
<b>LC</b>	: Liver cirrhosis.
<b>LD</b>	: Lactate dehydrogenase.
<b>LFT</b>	: Liver function test.
<b>MEIA</b>	: Microparticle enzyme Immunoassay.
<b>MMP-2</b>	: Matrix metalloproteinase 2.
<b>MMP-9</b>	: Matrix metalloproteinase 9.
<b>MMPs</b>	: Matrix MetalloProteinases.
<b>MRI</b>	: Magnetic Resonance Imaging.
<b>MRNA</b>	: Messenger RNA.
<b>mRNA</b>	: Messenger Ribonucleic Acid.
<b>MU</b>	: Methyl umbelliferone.

<b>MUP</b>	: Methyl umbelliferyl phosphate.
<b>NAD<sup>+</sup></b>	: oxidizing agent of Nicotinamide adenine dinucleotide
<b>NASH</b>	: Non-alcoholic steatohepatitis.
<b>NC</b>	: Non Collagenous.
<b>NK</b>	: Natural Killer cells.
<b>NS2</b>	: Non structural protein 2.
<b>NS-3</b>	: Non structural protein 3.
<b>NS-5</b>	: Non structural protein 5.
<b>NS3-4A</b>	: Serine protease.
<b>OD</b>	: Optical Density.
<b>P53</b>	: Protein 53.
<b>PCR</b>	: Polymerase Chain Reaction.
<b>PDGF</b>	: Platelet-derived growth factor.
<b>PEPCK</b>	: Phospho-Enolpyrovate Carboxykinase.
<b>PGCP</b>	: Plasma Glutamate Carboxypeptidase.
<b>PIVA-II</b>	: protein Induced by Vitamin K Absence II.
<b>PLA2G13</b>	: Phospholipase A2 Gene 13.
<b>PLA2G7</b>	: Phospholipase A2 Gene 7.
<b>PNPP</b>	: para-Nitro phenyl phosphate.
<b>PTEN</b>	: Phosphatase and tensin homolog.
<b>Ras</b>	: Reactive oxygen species.
<b>RGD</b>	: Arg-Gly-Asp sequence.
<b>RIBA</b>	: Recombinant immunoblot Assay.

<b>RIBA-3</b>	: Third generation Recombinant-Immuno Blot Assay.
<b>RNA</b>	: Ribonucleic Acid.
<b>ROC</b>	: Receiver Operating Characteristic.
<b>RT-PCR</b>	: Reverse Transcription Polymerase Chain Reaction.
<b>SA</b>	: Sialic Acid.
<b>S Alb</b>	: Serum Albumin.
<b>SGOT</b>	: Serum glutamic oxaloacetic transaminase.
<b>SGPT</b>	: Serum glutamic pyruvic transaminase.
<b>Smad</b>	: proteins involved in cell signaling.
<b>SR-B1</b>	: Scavenger Receptor Class B 1.
<b>SR-B1</b>	: Scavenger receptor class.
<b>STK 15</b>	: Serine/Threonine kinase 15.
<b>TGF-b1</b>	: Transforming growth factor beta 1.
<b>TGF-β</b>	: Transforming Growth Factor β.
<b>TMA</b>	: Transcription Mediated Amplification.
<b>TMB</b>	: Tetra methyl Benzidine.
<b>Tp53</b>	: Tumor suppressor gene.
<b>UL</b>	: Ultrasound.
<b>U/L</b>	: Unit per liter.
<b>WHO</b>	: World Health Organization.

## *Abstract*

The prognosis of chronic liver disease is closely related to the development of hepatic fibrosis. Fibrosis is characterized by excessive deposition of collagen and other components of the extracellular matrix, which leads to a disturbed function of the organs involved, while TGF- $\beta$  was involved in the development of fibrosis by modulating myofibroblast proliferation and collagen secretion. This study aimed to investigate the contributing effects of Transforming Growth Factor beta1 (TGF-  $\beta$ 1) and Collagen type 1 (COL -1) as the inducers of liver fibrosis and/or cirrhotic changes among HCV infected patients with HCC development. In this study, 89 patients were selected and subjected to symptom questionnaire, clinical evaluation, abdominal ultrasonography and laboratory investigations including liver profile, hepatitis markers, assay of TGF- $\beta$ 1 (by ELISA), COL -1 (by ELISA) and AFP assay.

The mean of AFP was significantly higher in HCC group (mean;  $360.0 \pm 253.4$ ) than cirrhotic group (mean;  $137.2 \pm 82.9$ ), CHC group (mean;  $23.9 \pm 15.3$ ) and control group (mean;  $2.2 \pm 1.2$ ), ( $p$ ; 0.001). The mean of TGF- $\beta$ 1 and collagen 1 were significantly higher in cirrhotic group (mean  $246.48 \pm 51.5$ ) than HCC group (mean  $87.66 \pm 11.07$ ), CHC group (mean  $62 \pm 14.9$ ) and control group (mean  $43.05 \pm 12.00$ ), ( $p$ ; 0.001). By using ROC curve the best cutoff of TGF- $\beta$ 1 was specially selected at 58.0 which give sensitivity 83% and specificity 100% and the best cutoff of COL -1 was 126.5 which give sensitivity 88% and specificity 100%.

**Conclusion:** The circulating TGF- $\beta$ 1 and COL -1 could be used as sensitive biomarkers for diagnosis of any abnormal disorder in liver at an early stage.



## **Acknowledgement**

No words could express my sincere appreciation and deepest gratitude to **Prof. Dr. Nahed Hussein Ahmed Riad**, Professor of Histology and Histochemistry, Faculty of Science, Ain Shams University for her guidance, valuable criticism and continuous encouragement. The words will never be enough to express my thanks to her continual support during the whole work.

I wish to express my deepest gratitude and sincere appreciation to **Prof. Dr. Mahmoud I. Hassan**, Professor of Medical Biochemistry and Molecular Biology Faculty of Medicine, Ain Shams University, for supporting me throughout the course of this study. I would like to thank him for step by step guidance and assistance to complete this work. The words cannot express my thanks to his kind supervision.

I would like to express my deepest thanks to **Prof. Dr. Fathy M. Tash**, Professor of Medical Biochemistry, Faculty of Medicine, Ain Shams University, for his expertise supervision, generous guidance and encouragement to fulfill this work. The words cannot express my thanks to his kind supervision.

I have the greatest pleasure in acknowledging **Dr. Naglaa Samir Ahmed**, Assistant Professor of Pathology, Faculty of Medicine, Ain Shams University, for her willing assistance, guidance and encouragement during this work.

Finally, I would like to express my deepest gratitude to all friends of the **Oncology Diagnostic Unit**, Faculty of Medicine, Ain Shams University for kind help and support, which facilitated the performance of this work.

## ***Aim of the work***

The aim of the present study is to investigate the contributing effects of Transforming Growth Factor beta1 (TGF- $\beta$ 1) and Collagen type 1 (COL -1) as the inducers of liver fibrosis and/or cirrhotic changes among HCV infected patients. Furthermore, the impact of clinicopathological factors on liver fibrogenesis and HCC will be addressed.

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