# SERUM BIOMARKERS AND TRANSIENT ELASTOGRAPHY VERSUS HISTOPATHOLOGY FOR ASSESSMENT OF POST LIVING DONOR LIVER TRANSPLANTATION (LDLT) HCV RECURRENCE

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# بسم الله الرحمن الرحيم

"يُؤْتِي الْحِكْمَةَ مَنْ يَشَاءُ وَمَنْ يُؤْتَ
الْحِكْمَةَ فَقَدْ أُوتِيَ خَيْراً كَثِيراً وَمَا يَذَّكَّرُ
إِلاَّ أُولُو الْأَلْبَابِ"

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# Abstract

This is a retrospective and prospective study that aimed to predict fibrosis in HCV infected liver transplant recipients (25 recipients) with serum markers and TE( Fibroscan )and to validate the diagnostic accuracy of these noninvasive methods in comparison with liver biopsy.

In our series none of the recipients who developed clinical HCV recurrence developed allograft cirrhosis over mean follow up period of 16.8 months and 92% of our patients developed only mild fibrosis (F1).

Non invasive indices showed variable accuracy in prediction of fibrosis; Fib4 was not accurate in prediction of fibrosis while AST/ALT ratio and Age/Plt indices showed rough correlation with fibrosis stages assessed by Metavir score with no adequate results to conclude its ability to predict precisely each stage.

APRI and Hyaluronic (HA) were able to predict fibrosis adequately in comparison with liver biopsy.

Tissue elasticity was moderately able to predict fibrosis. Howevere large sample volume could help in proper validation as well as variability of stages of fibrosis among studied population.



## Key Words

-Fibscan

-Liver Biopsy

-Serum Biomarkers

-HCV Recurrence

-Liver Transplantation

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# INTRODUCTION

Chronic hepatitis C virus (HCV) infection leading to liver cirrhosis and hepatocellular carcinoma is the main indication for liver transplantation (LT) in Western countries and Japan **(Adam et al., 2012).** In Egypt hepatitis C virus (HCV) is considered the most common etiology of chronic liver disease (CLD), where prevalence of antibodies to HCV (anti-HCV) is 10-fold greater than in the United States and Europe with a large underlying reservoir of HCV- caused liver disease **(Thomas Strickland et al., 2015)**.

Those patients are the potential candidates for liver transplantation; Living Donor Liver Transplantation (LDLT) has provided the only option for those patients with end stage liver disease (ESLD). HCV infection recurs universally and persists after LT and has become the most relevant problem of transplant programs **(Garcia et al., 2015).** In fact, in liver transplant recipients chronic HCV infection leads to cirrhosis in around 30% of individuals only 5 years after LT. Once liver cirrhosis is established, the cumulative probability of developing clinical decompensation is close to 50% 1 year after diagnosis and, more importantly, survival after decompensation is extremely short **(Berenguer et al., 2015).**

In Egypt more than 500 HCV infected patients have been transplanted since 2001 in different centres **(Ibrahim, 2015)** prospective study on 113 HCV infected recipients in single center showed that the incidence of pathological recurrence is 33.7% and a protocol liver biopsy on regular intervals were mandatory to follow up the progression of fibrosis which was found to be accelerated more than in non transplanted

cases, it was 0.6 points annually on Ishak score **(Yosri et al., 2008)**. As a result of this accelerated course, long-term graft and patient survival are significantly reduced in patients undergoing LT for HCV-related cirrhosis compared with other groups(recipients undergoing LT for other causes) Currently, severity of HCV disease recurrence after LT is assessed by frequent liver biopsies, which have become part of the routine follow-up of HCV-infected liver transplant recipients. Early histological damage after transplantation correlates with long-term outcome and identifies patients at high risk of graft loss **(Yosri et al., 2008)**.

One of the limitations of liver biopsy is sampling variability which might become a relevant issue in individuals with rapid disease progression, liver biopsy also is expensive and invasive which is a concern if it is mandatory to be done frequently during the follow up **(Bedossa et al., 2015 and Rousselet et al., 2013).**

## Non-invasive serum markers of liver fibrosis

There is a compelling need for non-invasive methods of liver fibrosis given the limitations of currently available methods of fibrosis assessment. 'Serum markers' broadly refers to the measurement of one or more molecules within a blood or serum sample as a surrogate marker of fibrosis in the liver **(Scott et al., 2014).** No single marker fulfills all of the criteria sufficiently to merit routine clinical use yet. However, recent efforts to assay several markers from the same serum sample promise a greater likelihood of success in discriminating minimal from severe fibrosis. Current assays are directed at measuring breakdown products of extracellular matrix (ECM) constituents and the enzymes that regulate their production or modification, including:

(a) Glycoproteins including antibodies to hyaluronic acid, laminin or undulin (type IV collagen);

(b) Propeptides from ECM molecules that are generated by cleavage from ECM molecules as they are incorporated into scar, for example the propeptides of types I, III and IV collagens;

(c) Enzymes involved in ECM synthesis including lysyl oxidase, prolylhydroxylase and lysyl hydroxylase **(Rosenberg et al., 2014).**

**Transient Elastography (TE), Fibroscan**

A recent noninvasive and reproducible method based on the measurement of liver stiffness has recently been developed. This method, named transient elastography, has been shown to correlate with the liver fibrosis stage and is able to identify accurately the presence of histological cirrhosis. The results obtained by this noninvasive method have been compared with those obtained by liver biopsy, the current gold standard **(Foucher et al., 2015).**

Combining TE with serum markers increases diagnostic accuracy and as a result, liver biopsy could be avoided for initial assessment in most patients with chronic hepatitis C. Evaluation of this strategy post LT warrants further evaluation and it is of great concern if repeated evaluation for the development and progression of fibrosis is needed during follow up of HCV infected liver transplant recipients **(Carrion et al., 2015).**

We hypothesized that we could be able to avoid using liver biopsy in the initial assessment and follow up of HCV infected liver transplant and replacing it with non-invasive serum biomarkers and/or Transient Elstography (TE).

# AIM OF THE WORK

1- This study aims to predict recurrence of fibrosis in HCV infected liver transplant recipients with serum markers and TE or fibroscan.

2- To validate the diagnostic accuracy of serum biomarkers and TE or fibroscan compared with liver biopsy, which is the current gold standard for diagnosis of hepatic fibrosis.

# LIVER TRANSPLANTATION

## Introduction:

Liver transplantation is widely accepted as an effective therapeutic modality for a variety of irreversible acute and chronic liver diseases for which no satisfactory therapy is available **(Rogiers et al.,2013).**

**Types of liver transplantation:**

**(1) Auxiliary liver transplantation: (ALT)**

Healthy liver tissue is introduced leaving the native liver in situ. It may be indicated in acute liver failure where there is a chance that the patients own liver will regenerate.It may be also be used in the treatment of some metabolic defects. **(Rogiers et al.,2013).**

**(2)Split liver transplantation:**

Split liver transplantation (SLT) was developed as an alternative to meet the great demand for grafts from the scarce supply of donors. It consists of dividing the donated liver into 2 grafts typically transplanted to an adult and a child. **(Rogiers et al.,2013)**

**(3) Hepatocyte Transplantation:**

Advances in the understanding of hepatocyte engraftment and the remarkable proliferative potential of hepatocytes have brought liver cell transplantation to the doorstep of application in the treatment of inherited and acquired human diseases. Hepatocyte transplantation is metabolically less stressful than transplantation of the whole organ and the consequences of graft loss are much less severe**.**