# Application of Newer Diagnostic Modalities for Childhood Autoimmune Hepatitis

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BY

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# ABSTRACT

**Background**: AIH and cryptogenic chronic hepatitis are important causes of liver failure in children. No single clinical or biochemical test proves the presence of AIH.

**Aim:** The aim of this study was both to apply the IAIHG scoring system and testing for SLA and pANCA in children with AIH and cryptogenic CLD.

**Materials and methods**: The study included 28 children with AIH, 15 with cryptogenic CLD and 40 healthy age and sex matched children as controls**.** The patients' clinical, laboratory, and histological data have been analyzed. The IAIHG scoring system was used to score patients both before and after treatment.

**Results:** SLA antibody was positive in 17.8% and pANCA in 32% of AIH cases. The IAIHG score was applied before treatment to 24 AIH cases as liver biopsy was not available for 4 cases; 14 (58.4%) scored as definite AIH and 10 (41.6%) scored as probable AIH. When score was reapplied after therapy; one out of the 10 cases with probable AIH was shifted to the definite group and vice versa one of the definite AIH cases was shifted to the probable group. Nine (60%) of cryptogenic CLD patients was scored as probable AIH.

**Conclusion:** No factor by itself can contribute to the diagnosis of AIH in children. SLA is an additional diagnostic marker for type 1 AIH. pANCA is useful for diagnosis of AIH especially in patients seronegative to conventional autoantibodies. The IAIHG score can be used in diagnosis of AIH in children with a need for more simplified scoring system for every day use.



**Key words:** Autoimmune Hepatitis - AIH Scoring System – Soluble Liver Antigen - Cryptogenic Chronic Liver Disease – Children.

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| AIC | Autoimmune Cholangitis |
| AIH | Autoimmune Hepatitis |
| AILD | Autoimmune liver disease |
| AIRE | Autoimmune Regulator |
| ALP | Alkaline phosphatase |
| ALT | Alanine Aminotransferase |
| AMA | Antimitochondrial Antibodies |
| ANA | Antinuclear Antibodies |
| ANCA | Antineutrophil Cytoplasmic Antibodies |
| APC | Antigen-presenting cells |
| APS-1 | Autoimmune Polyendocrine Syndrome type 1 |
| ASC | Autoimmune Sclerosing Cholangitis |
| ASGPR | Asialoglycoprotein Receptor |
| AST | Aspartate Aminotranferase |
| CAH | Chronic Active Hepatitis |
| CCH | Cryptogenic chronic hepatitis |
| CD | Celiac disease |
| CLD | Chronic Liver Disease |
| CMV | Cytomegalovirus |
| DILI | Drug-induced liver injury |
| EBV | Epstein Barr Virus |
| ELISA | Enzyme-Linked Immunosorbent Assay |
| GGT | Gamma Glutamyl Transpeptidase |
| HAV | Hepatitis A virus |
| HBcAb | Hepatitis B core Antibody |
| HBsAg | Hepatitis B surface Antigen |
| HBV | Hepatitis B virus |
| HCV | Hepatitis C virus |
| HDV | Hepatitis D virus |
| HEV | Hepatitis E virus |
| HLA | Human Leukocyte Antigen |

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|---|---|
| HSV | Herpes Simplex virus |
| IAIHG | International Autoimmune Hepatitis Group |
| IBD | Inflammatory Bowel Disease |
| IDDM | Insulin Dependant Diabetes Mellitus |
| IFN- γ | Interferon-gamma |
| IgA | Immunoglobulin A |
| IgG | Immunoglobulin G |
| IgM | Immunoglobulin M |
| IIF | Indirect Immunofluorescence |
| IL | Interleukin |
| LE | Lupus Erythematosus |
| LC-1 | Liver Cytosolic Antigen 1 |
| LKM | Liver-Kidney Microsomal |
| LP | Liver-pancreas Antigen |
| LSP | Liver specific protein |
| MHC | Major Histocompatibility Complex |
| NK | Natural Killer |
| pANCA | perinuclear Antineutrophil Cytoplasmic Antibodies |
| pANNA | perinuclear Antineutrophil nuclear antibodies |
| PBC | Primary Biliary Cirrhosis |
| PBS | Phosphate buffered saline |
| PCR | Polymerase Chain Reaction |
| PSC | Primary Sclerosing Cholangitis |
| SAIH | Seronegative autoimmune hepatitis |
| SD | Standard Deviation |
| SLA | Soluble Liver Antigen |
| SLE | Systemic Lupus Erythematosus |
| SMA | Smooth Muscle Antibodies |
| SPSS | Statistical Package for Social Sciences |
| Tc | T cytotoxic |
| TGF-β | Transforming Growth Factor β |
| TNF- α | Tumour Necrosis Factor Alpha |
| ULN | Upper limit of normal value |

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|---|---|
| UNL | Upper Normal Limits |
| UDCA | Ursodeoxycholic acid |
| VZV | Varizella zoster virus |

# CONTENTS

# List of Figures

# List of Tables

# تطبيق وسائل جديدة لتشخيص الالتهاب الكبدي المناعي في الأطفال

**خطة بحث لرسالة**

**مقدمة توطئة للحصول على درجة الدكتوراه في طب الأطفال**

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**كلية الطب- جامعة القاهرة**

الأستاذة الدكتورة/ منى عزيز

**أستاذ الباثولوجيا الإكلينيكية**

**كلية الطب- جامعة القاهرة**

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# INTRODUCTION AND AIM OF THE WORK

Autoimmune hepatitis (AIH) is a chronic progressive inflammatory liver disease characterized by an inflammatory liver histology, circulating non-organ specific autoantibodies and increased levels of immunoglobulin G (IgG) in the absence of a known etiology **(Mieli-Vergani and Vergani, 2003).**

Autoimmune liver disease (AILD) in children progresses to cirrhosis and liver failure if not diagnosed and managed in time. Early diagnosis and immunosuppressive treatment are essential in preventing severe liver damage. Unfortunately, lack of diagnostic certainty in establishing a diagnosis can lead to delay in treatment and the continued progression of the disease **(Yachha et al., 2001).**

AIH is classified into three serological subgroups: antinuclear (ANA) and smooth muscle antibody (SMA)- positive in type 1, liver-kidney microsomal antibody (LKM) -positive in type 2 and soluble liver antigen (SLA) antibody - positive in type 3 AIH **(Strassburg and Manns, 2002).**

Autoantibodies against SLA show a high specificity for AIH (**Luxon, 2003).** Several reports have shown that many patients with AIH negative for ANA and SMA show positive SLA reactivity, making these antibodies an important diagnostic marker **(Ballot et al., 2000).**

SLA autoantibodies are the only immunologic marker found in 15–20% of hepatitis cases previously considered cryptogenic. In about 13% of cryptogenic hepatitis patients, initially seronegative, detection of SLA autoantibodies contributed to their diagnostic clarification **(Manns and Strassburg, 2001; Ballot et al., 2003).**