Prevalence of HCV Infection in Children with Arthritis

Thesis

for fulfillment of master degree in pediatrics

Presented by

Shaimaa Emad Abass

M.B.B.Ch

Supervised by

Prof. Dr. Samia Salah El-Dien Mahmoud

Professor of Pediatrics Faculty of Medicine

Cairo University

Prof. Dr. Mona El-Said El-Raziky

Professor of Pediatrics Faculty of Medicine

Cairo University

Dr. Marian Yousry Fahmy

Assistant Professor of Pediatrics Faculty of Medicine

Cairo University

Cairo University

2012

Acknowledgement

I would like to thank **ALLAH** *a lot for his kindness, patience and strength he gave me to achieve this work and made me able to finish it.*

I would like to thank **Professor Dr/ Samia Salah El-Dien Mahmoud,** *Professor of Pediatrics, Faculty of Medicine, Cairo University for her meticulous supervision and her kind support. I greatly appreciate her efforts to guide me to accomplish this work.*

I'm extremely grateful to **Professor Dr / Mona El-Said El-Raziky,** *Professor of Pediatrics, Faculty of Medicine, Cairo University for her continuous strict supervision, and revision of this work, she gave me much of her time, experience and support, her valuable comments, efforts and collaboration were the causes to complete this work properly.*

My special thanks to **Dr / Marian Yousry Fahmy**, *Assistant Professor of Pediatrics, Faculty of medicine, Cairo University, for her sincere guidance and encouragement so to her I express my deepest gratitude.*

I would also like to thank my dearest **Dr/ Hanan Mina Fouad**, *fellow of Pediatrics, National Hepatology and Tropical Medicine Research Institute who helped me a lot in finishing this work and was always beside me.*

Very special thanks to **Professor Dr/ Magda Abd-Elfatah,** *who gave me an example to follow and taught me about the gift of being a doctor and the gift of being a human being and added a meaning for all that.*

A special dedication to **my family** *for their never ending care. They were always supporting me and encouraging me to continue and to be successful especially my mother* **Fatma Osman Abd-Elsalam** *the best gift that God gave me.*

Abstract:

Background/Aim: Hepatitis C virus (HCV) infection can induce immunological extrahepatic manifestations including arthralgia and arthritis mimicing rheumatoid arthritis. Our aim is to report the prevalence of HCV infection in children presenting with arthritis or arthralgia.

Methods: The study included 40 children presenting with arthritis or arthralgia as a cases and another 40 age and sex matched children, not complaining of liver disease or arthritis as a control group. All cases and controls were subjected to full history taking, clinical examination and HCVab detection by rapid test. To all positive cases with rapid test a confirmatory HCVab ELISA test was done and HCV PCR as well.

Results: Cases were 45% males and 55% females, with a mean age of 10.5 ± 3.7 years. Among cases, prevalence of HCVab as detected by rapid test and confirmed by ELISA was 5%. HCV RNA was positive in 2.5%. In the control group HCVab was 2.5% by rapid test and confirmed by ELISA and HCV RNA. Both arthritis and lower limb oedema were more prevalent in HCVab positive cases than negative but with no statistical significance difference. By examination; HCVab positive cases had a higher prevalence of presence of scratch marks and they also have a significantly higher AST and ALT levels than HCVab negative cases.

Conclusion: HCV infection is prevalent in children with arthritis or arthralgia.

Key words: HCV, arthritis, arthralgia, HCVab, HCV RNA, rapid test, children.

List of Contents

List of Tables

List of Figures

List of Abbreviations

AA	Amyloid A
ALT	Alanine transaminase
AKA	Anti Keratin Antibody
AST	Aspartae transaminase
ANA	Anti Nuclear Antibody
APF	Anti Perinuclear Factor
APR	Acute Phase Reactant
BMC	Bone Mineral Content
BILAG	British Isles Lupus Assessment Group
CRP	C Reactive Protein
COMP	Cartilage Oligometric Matrix Protein
CTLs	Cytotoxic T Lymphocytes
CRF	Chronic Renal Failure
CLA	chemilminescence immunoassay
CNS	Central Nervous System
CVD	Coronary Vascular Disease
CD2BP1	CD-2 binding protein-1
CYC	Cyclophosphamide
DEXA	Dual Energy X-ray Absorptiometry

ESR	Erythrocyte Sedimentation Rate
EDHS	Egyptian Demographic Health Survey
ELISA	Enzyme Linked Immunosorbont Assay
EVR	End Viral Response
FMF	Familial Mediterranean Fever
GN	Glomureolo Nephritis
Hp	Haptoglobin
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HCVab	Hepatitis C Virus antibody
HIV	Human Immunodeficiency Virus
IDDM	Insulin Dependent Diabetes Mellitus
IASL	International Association for the Study of The Liver
IFN-α	Interferon-α
IGg	Immunoglobulin g
IGM	Immunoglobulin M
ILD	Interstitial Lung Disease
ITP	Idiopathic Thrombocytopenia
JRA	Juvenile Rheumatoid Arthritis
JIA	Juvenile Idiopathic Arthritis
LEF	leflunomide

LLN	Lower Limit of Normal
MEFV	Mediterranean Fever
MHC	Major Histocompatibilty
MMF	Mycophenolate mofetil
MRI	Magnetic Resonance Image
MTX	Methotrexate
NAFLD	Non alcoholic Fatty Liver Disease
NHANES III	national health and nutrition examination survey
NP	Neuropsychiatric
NSAIDs	Non Steroidal Anti Inflammatory Drugs
Oligo JIA	Oligoarticular juvenile idiopathic arthritis
PAPA	pyogenic arthritis, pyoderma gangrenosum, and acne
PCR	Polymerase Chain Reaction
PEG	Polyethylene glycol
pSLE	Pediatric Systemic Lupus Erythematosus
PSTPIP1	proline serine threonine phospatase-interacting protein 1
Poly JIA	Polyarticular juvenile idiopathic arthritis
RA	Rheumatoid Arthritis
RFs	Rheumatoid Factors
RIBA	Recombinant Immunoblot Assay
RVR	Rapid Viral Response

SAARDs	slow-acting antirheumatic drugs
S-JIA	Systemic juvenile idiopathic arthritis
SLE	Systemic Lupus Erythematosus
SVR	Sustained Viral Responce
TMA	Transcription mediated amplification
TNF	Tumor Necrosis Factor

Introduction:

Hepatitis C virus (HCV) is an RNA flavivirus with six major genotypes and several subtypes, HCV is an important causative agent of liver diseases. However, HCV infection is more than just a liver disease and has been associated with numerous hematologic, renal, dermatologic, rheumatic and autoimmune disorders **(Cacoub et al., 2000, Ramos-Casals and Font, 2005)**.

Recent studies have reported that more than half (54%) of the HCV infected Egyptian children had persistently elevated ALT levels **(El-Raziky et al., 2004)**. The worldwide seroprevalence of HCV ranges between 0.2-2% **(Wilber, 1995)**. In 2007, an HCV seroprevalence of 2% was reported in healthy Egyptian children **(El-Raziky et al., 2007)**.

HCV infection is usually asymptomatic and may be detected incidentally; it also induces immunological extrahepatic manifestations including arthralgia and arthritis which can mimic rheumatoid arthritis (RA). HCV is associated with a variety of rheumatic disorders and autoimmune phenomena. This includes arthralgia, arthritis, vasculitis, sicca syndrome, myalgia and fibromyalgia **(Palazzi et al., 2008)**. Arthralgia is the most common rheumatic manifestation. Arthritis is less common and may present as a rheumatoid arthritis-like, non deforming arthritis mainly involving small joints with RF and absence of rheumatoid nodules and less commonly a mono-oligoarthritis usually of large joints **(Sterling and Bralow, 2006).**

Associations have been reported between HCV infection and other autoimmune diseases including systemic lupus erythematosus, Sjogren's syndrome and antiphospholipid antibody syndrome (APS) **(Lormeau et al., 2006; Ramos-Casals and Font, 2005).**

Rosner and colleagues in 2004 summarized the clinical characteristics of HCV associated arthritis. Arthritis, not otherwise explained, has been noted in 2% to 20% of HCV patients, that arthritis was rheumatoid- like in two thirds of the cases and a waxing waning oligoarthritis in the rest. It was concluded that HCV arthropathy should be considered in the differential diagnosis of new onset arthritis

The pathogenesis of HCV-related arthritis is not entirely clear, but three possible mechanisms have been suggested, namely: synovial tissue damage by direct viral invasion, synovial autoimmune response induced by the virus and immune complexes or cryoglobulins deposition **(Zuckerman et al., 2001).**

Aim of work:

The aim of this study is to report the prevalence of hepatitis C virus infection in children and adolescence with arthritis or arthralgia.