

שם: רשא דניאל

שם העבודה:

Epidemiology of Hepatitis E Virus Infection in Israel and Potential Risk Factors, a Multicenter, Comparative, Cross-sectional Study

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Abstract

Background:

Hepatitis E virus (HEV) has emerged as an important cause of epidemic and sporadic autochthonous acute viral hepatitis worldwide. Four different HEV genotypes were reported (1-4). HEV genotype 1 and 2 are mainly transmitted by the feco-oral route in endemic areas (Asia, Africa and Central America). Hepatitis E was considered to be a travel-associated disease in Western countries, since only individuals returning from HEV endemic areas were affected. However, sporadic indigenous hepatitis E cases with genotypes 3 and 4 were observed in later periods, suggesting autochthonous infections. A zoonotic transmission from animal reservoirs to human has been reported (mainly genotype 3), while additional routes of transmission such as blood borne, human to human and vertical transmission have also been proposed. In most cases HEV infection is usually a self-limiting disease, in the past years multiple reports have emerged on immune compromised patients, developing chronic HEV infection caused by genotype 3.

Recent data shows that the prevalence of HEV seropositivity had been underestimated worldwide including Western countries, but it is still not clear whether HEV prevalence rates in non-endemic areas are actually changing or if more cases are detected through increased surveillance. The main risk factors associated with the increased sero-prevalence include age, consuming uncooked meat, preexisting disease and traveling to endemic regions.

In Israel, there is no HEV prevalence data based on neither general population study nor high risk groups, and there is no sufficient data regarding risk factors associated with high HEV sero-prevalence.

Aim:

The aim of this study is to investigate the epidemiology of hepatitis E virus infection among general and high risk populations in Israel and to explore potential risk factors.

Methods:

A multicenter, comparative, cross-sectional study will be conducted. The study will include sera from individuals with acute/chronic hepatitis of unknown etiology, individuals with hepatitis C chronic infection, immune-compromised individuals, and subjects who are in close daily contact with swine

who represent a high risk population as well as sera of healthy periodic check-up attendees and career soldieries representing the general population. A probability systematic sampling will be used for collecting sera from health examination attendees whereas, convince sampling for the rest groups. Recruited subjects will undergo blood sampling, and sera will be aliquoted and stored until analysis. Outcome variables including HEV serological status and HEV RNA- status will be measured using commercial enzyme-linked assays that detect immunoglobulin G (IgG) and IgM against HEV and PCR technology for detecting HEV RNA respectively. Structured questionnaire will be used in order to evaluate the exposure variables including demographic and socioeconomic status, habitual factors, health and sanitation evaluation and traveling. Univariate analysis will be performed including Chi-square test, Fisher's exact test for analyzing categorical variables whereas, student's t-test, Mann-Whitney test will be used for continuous variables. Multivariate logistic regression analysis will be carried out to identify which variables are significantly associated with anti-HEV seropositivity. The magnitude of the association between variables and seropositivity will be expressed as odds ratio with 95% confidence interval.

Significance:

The results will contribute to the understanding of the health burden of HEV infection in different groups of the Israeli population and to define the high-risk population. High prevalence of the virus may indicate that the infection is no longer a traveler's disease as previously assumed, and actually, there is an autochthonous HEV infection. This may be an indication to consider the addition of routine HEV test in the high-risk Israeli population. In particular, since a mortality of up to 75% in patients with pre-existing chronic liver disease or immunocompromised patients was described, and since there are HEV effective treatments, it is important to better understand the epidemiology of this pathogen and to develop public health strategies that target the most vulnerable and high-risk groups.