



صندوق العلوم والتنمية التكنولوجية  
Science and Technology for Development Fund



**Project ID:** 1784

**Project Type:** TC/2/Health/2009/hep-1.3\*: modes of transmission of HCV infection.

**Project Title:** Multicenteric study of epidemiological aspect in intrafamilial spread of HCV infection and genetic susceptibility in Egyptian population

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**Duration:** 3 years

**Total budget:** 2412400

## background

Egypt has the highest prevalence of hepatitis C Virus (HCV) worldwide. Prevalence of HCV was 13.9% among healthy populations and 78.5% among hepatocellular carcinoma (HCC) cases. Over 50% of those infected with HCV will suffer from chronic hepatitis, cirrhosis or even develop HCC. HCV is most efficiently transmitted primarily by parenteral routes. In recent studies, strong correlations reported in Egyptian populations with HCV seroprevalence between first degree relatives. These correlations could be accounted for by a combination of specific modes of intrafamilial viral transmission and genetic predisposition to HCV infection. **Objectives:** To identify the possible risk factors of transmission of HCV among Egyptian families, investigate the transmission of HCV by genotyping and sub-genotyping of HCV RNA sequences and finally to investigate the role of genetic factors in HCV susceptibility. **Methods:** A multicenter study involving 3 research centers (Upper & Lower Egypt) where one Thousand HCV index cases and their families will be recruited from multicentric areas & will be subjected to HCV RNA quantification, genotyping, sequencing, and phylogenetic analysis. HLA genotyping for host DNA to ascertain genetic susceptibility. **Outcome:** understanding the risk factors that lead to intrafamilial transmissions and to improve our knowledge of the mechanisms leading to infection, and will pave the way for the development of new strategies of control for this major public health problem. **Consequences:** This research program represents an integrative approach towards the control of HCV infection in Egypt with high scientific value as well as potential economic revenues.

## **Aim of the project**

Aim of this project is to:

- 1- Highlight on intrafamilial spread of HCV in Egyptian families to estimate the magnitude of the problem.
- 2- Identify the mode(s) of transmission of HCV among Egyptian families.
- 3- Investigate the transmission of HCV from one family member to other member by genotyping and sub-genotyping of HCV RNA sequences
- 4- Compare the transmission of HCV from Upper and Lower Egypt
- 5- Investigate the role of genetic factors in the susceptibility of HCV in Egyptians by:-
  - Investigate the role of the protective alleles of MHC class I and class II in the susceptibility of HCV.
  - Investigate the role of other candidate genes including Interferon gamma and interferon gamma receptor genes, CCL3L1 genes.

**Statement of the proposed research:**

- 1- Establish a local network between the different Egyptian contributing centers(Cairo, Mansoura, Assiut))to facilitate communication between them and to standardize the protocols ( 2 months).
- 2- Training of the team and personnel sharing in the proposal on questionnaire conducting, patient evaluation blood sampling and data collection and assessment (3 m)
- 3-Multicentric pilot study will be conducted for validation &testing reliability of the questionnaire, as well as measuring the time needed to conduct the single interview in order to organize the manpower needed to conduct the work properly (3 months).
- 4-Identify the index case of our study and recruit the other family member according to inclusion and exclusion criteria.
- 5- Evaluate the risk factors responsible for HCV transmission among Egyptian families (6 months).
- 6-Collection of blood samples from different centers. Blood samples of patients diagnosed at Cairo, Ain Shams and Assiut Universities, will be batched and sent to Mansoura laboratory in Mansoura University for testing (18 months).
- 7-Molecular quantitation of HCV RNA and laboratory assessment of our subjects (12 months)
- 8-Molecular testing of HCV genotypes and sub-genotypes by direct sequencing of HCV RNA (six months).
- 9-Verify the interfamilial transmission using Phylogenetic analysis of the sequences obtained from HCV sequences of index case and of other family member(s) for each family (6 months).
- 10- Testing the genetic susceptibility (host factor) for HCV infection by molecular testing of alleles of MHC class I and class II in affected individuals compared with non affected persons (three months).
- 11-Molecular testing of other candidate genes for genetic susceptibility of HCV infection (Three months).
- 12-Statistical analysis for genetic susceptibility using family based study software.
- 13-Testing the possibility of heterogeneity between Upper and Lower Egypt.

### **Subjects:**

1,000 index HCV cases and their families (household contacts and family members) will be recruited from the three research centers representing Dakahlia, Assuit and Cairo governorate. All patients from different centers will be selected under exactly the same criteria in terms of ethnicity and diagnosis.(Cross sectional study). The average size of Egyptian families around  $4.5 \pm 0.5$ . Positive cases of HCV antibodies and or HCV RNA will be served as cases group. All household member who are negative for either HCV antibodies and RNA by PCR will be served as –ve control for comparative analysis.

#### **Inclusion criteria for index case:**

- 1- HCV positive by PCR
- 2- Adults (above 18 years) of both sexes.
- 3- Any stage of HCV related liver diseases

#### **Exclusion criteria for index case:**

1. Patients co-infected with HIV or HBV (HBV core antibodies).
2. Patient with anti-HCV antibodies positive and no detectable PCR-HCV in the serum.

#### **Inclusion criteria for household members:**

- 1- Age > 3 years of both sex
- 2-first and second degree consanguinity to the index case living and Sharing usual life activity with index case.

#### **Exclusion criteria for household members-:**

- 1-Age < 3 years for exclusion of the vertical transmission.

**NB:** Household members with history of hepatitis, auto-immune and metabolic liver disease or household members with history of repeated blood transfusion, occupational exposure (nurses, doctors, lab. technicians, health workers)& Intravenous drug users Will be included in the assessment of the familial risk but only will be excluded during statistical analysis to avoid any cofounders for genetic susceptibility of HCV & any bias for intrafamilial transmission,

**Questionnaire:**

The questionnaire will include questions regarding individual-level and household-level variables. Individual level variables recorded on participating contacts included:

- 1- Demographic variables as (age, sex, occupation education level and relationship to the index patient),
- 2- Behaviors of family contacts of the index cases as regards: (sharing towels, gum/ sweets, partially eaten, toothbrush with carrier)
- 3- Bitten by the index case, scratched the back of carrier, handling blood-tinged clothes of carrier, kissing of carrier).
- 4- Extra-familial factors (including various potential parenteral exposures to blood or blood products, e.g., past hospital admissions, operations, injuries needing hospital interventions, blood, or blood product transfusions, and history of parenteral injections, intravenous drips received, and dental treatments) known to be associated with HCV transmission and were compiled from literature.
- 5- Household- level variables included mother tongue ,total monthly income, family size, age of index patient, sex of index patient, and RNA status (positive or negative) of the index patient.

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