Prevalence of IL28B genotypes among Saudi population In Jeddah city

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1. Title of Proposal:

2. Type of Project: (Please check all applicable options)

Chart Review ☐ Diagnostic ☐ PhD Project ☐ Qualitative Research ☐

Human Research ☐ Laboratory ☐ Msc Project ☐ Quantitative

Therapeutic ☐ Basic Science ☐ Other ☐ _____

3. Starting Date:	4. Duration:	5. Total Fund Requested (SR):
05-08-2015	one month	_____

6. Principal Investigator (PI):

Name: Dr.Rayan Azeb Alharthi
Affiliation & Address:
_____
Title/Position: clinical scientist E-mail: abunaif.com@gmail.com

8. Principal Investigator's Assurance:

The undersigned agrees to accept responsibility for the scientific and technical conduct of the proposed research and submission of progress reports if this application is approved.

_____ _____ _____

Name of Principal Investigator Signature Date

DEPARTMENT APPROVAL:

_____ _____ _____

Name of Chairman Signature Date

9. Background:

Hepatitis C (HC) is one of the infectious diseases that has major impact on public health [1]. Approximately, 180 million people (3%) are infected with HC virus worldwide[2, 3] where the HC oscillation about three to four million new infected cases per year [4]. Although 30% of patients with acute HC infection get spontaneous clearance, there are 54,000 deaths annually in acutely infected patient worldwide. The remaining patients have high tendency to develp into chronic progressive liver disease, cirrhosis or hepatocellular carcinoma [5] where 350,000 deaths are reported annually due to chronic HC-related causes [4]. In the United States, it is currently considered as the primary indication for liver transplantation [6]. The seroprevalence of HC among Saudi nationals reflected that, the overall anti-HC antibodies were found in 7.3% (1124/15323) of the examined individuals[7].

Consequently, the mainstay for treatment of HC is pegylated interferon-α (PEG-IFN) plus ribavirin involved a 24/48-week coursewith 50% response over 12 month. Viral genotype has been considered as important predictor of response with only 40% of patients with genotype 1 responding to PEG-IFN/ribavirin treatment, compared to 90%, 80%, and 60% of patients with genotype 2, 3, and 4, respectively. Therapy with PEG-IFN/ribavirin is has some burden on certain patients because of the duration of treatment and extensive side effects as well as the high cost [3, 8]. In addition to the viral genotypes the host's genetic factors (IL28B) have played an important role in response to treatment [9]. The most important baseline factor for treatment response is variation of the IL28B genotype, so that patients with the IL28B-CC genotype (SNP rs12979860) achieved SVR significantly more frequently than those bearing the unfavorable genotypes (CT or TT)[9]. Single nucleotide polymorphism (SNP) plays an important role in the management of HC virus infection, but distribution of the IL28B SNP is widely varied among populations and ethnicities [10].

Recently, A large number of new therapies are in development for chronic HC including direct-acting antiviral (DAA) drugs [11]. DAAs have been FDA-approved in manegment of HC infection even in patients with cirrhosis, interferon-based triple therapy including telaprevir or boceprevir had been more effective than peginterferon and ribavirin, although some safety concerns may exist [12].

Thus, the aim of this study is to identify the percentge of IL28B genotype among HCV patient in Saudi Arabia which help to plan effective HC treatment .

Objectives of the Study:

10.1 Aim of the Study:

To identify the rate of IL28B genotype among HCV patient compared to healthy individuals in Jeddah, Saudi Arabia which help to calculate the cost effectiveness of HC treatment .

10.2 Specific Objectives:

1. Identify common IL28B genotypes in in Jeddah.
2. Assess disease outcome in association with HCV genotypes and IL28B genotypes.

10.3 Secondary Objectives:

1. To calculate the cost effectiveness of hepatitis C treatment based on the prevalent genotype.

Materials and Methods:

11.1 Study Area/Setting:

Medical records in many Hospitals in Jeddah .

11.2 Study Subjects:

Case definition :
Hepatitis C patients diagnosed.

Inclusion criteria:
Hepatitis C patients who had been tested for IL28B genotype test
Exclusion criteria:
Patients with HBV infection

Control definition :
Healthy individual who attend to the Blood Banks .

Inclusion criteria:
Healthy blood donors.
Exclusion criteria:
Positive for any exclusion criteria of blood donors.

Study Design:

Case control study.

11.4 Sample Size: (Instructions: mention the input criteria for sample size estimation.)

35 infected patients and 35 healthy individuals.

11.5 Sampling Technique:

Convenience sample .

Data Collection methods, instruments used, measurements

Data Collection methods:

Retrospective Chart review : medical records of Hepatitis C patients who meet inclusion criteria
Prospective analysis of IL28B genotype of healthy individuals attending Blood Banks .

Instruments :

- Data Collection form based on Medical Records .
- Il28B SNP test will be performed as per manufacturer recommendation (Tib-MolBiol) on Roche LC-II system following genomic DNA extraction on MagNAPure compact system.

11.7 Data Management and Analysis Plan: (Instruction**:** Describe the analysis plan, tests used for data analysis and statistical package(s) used)

All data will be entered in SPSS program for statistical analysis.

The apropriate T-test will be used.

12. Bibliographic References:

1. Andrade, L., et al., *Association between hepatitis C and hepatocellular carcinoma.* Journal of global infectious diseases, 2009. **1**(1): p. 33.
2. Al-Qahtani, A.A., et al., *The association of Toll-like receptor 4 polymorphism with hepatitis C virus infection in Saudi Arabian patients.* BioMed research international, 2014. **2014**.
3. Al-Qahtani, A., et al., *Correlation between Genetic Variations and Serum Level of Interleukin 28B with Virus Genotypes and Disease Progression in Chronic Hepatitis C Virus Infection.* Journal of immunology research, 2015. **2015**.
4. Mohd Hanafiah, K., et al., *Global epidemiology of hepatitis C virus infection: New estimates of age-specific antibody to HCV seroprevalence.* Hepatology, 2013. **57**(4): p. 1333-1342.
5. Balagopal, A., D.L. Thomas, and C.L. Thio, *IL28B and the control of hepatitis C virus infection.* Gastroenterology, 2010. **139**(6): p. 1865-1876.
6. Khullar, V. and R.J. Firpi, *Hepatitis C cirrhosis: New perspectives for diagnosis and treatment.* World Journal of Hepatology, 2015. **7**(14): p. 1843.
7. Abdel-Moneim, A.S., et al., *HCV infection among Saudi population: high prevalence of genotype 4 and increased viral clearance rate.* PloS one, 2012. **7**(1): p. e29781.
8. Moghaddam, A., et al., *IL28B genetic variation and treatment response in patients with hepatitis C virus genotype 3 infection.* Hepatology, 2011. **53**(3): p. 746-754.
9. Rivero-Juarez, A., et al., *The IL28B effect on hepatitis C virus kinetics among HIV patients after the first weeks of pegylated-interferon/ribavirin treatment varies according to hepatitis C virus-1 subtype.* AIDS, 2013. **27**(12): p. 1941-1947.
10. Sixtos, A., et al., *A Genetic Variant in the Interleukin 28B Gene Is a Major Predictor for Sustained Virologic Response in Mexican Patients with Chronic Hepatitis C Virus Infection.* Archives of medical research, 2015.
11. Pockros, P.J., *Review: New direct-acting antivirals in the development for hepatitis C virus infection.* Therapeutic advances in gastroenterology, 2010. **3**(3): p. 191-202.
12. Nakamoto, S., et al., *Antiviral therapies for chronic hepatitis C virus infection with cirrhosis.* World J Hepatol, 2015. **7**(8): p. 1133-1141.

13. Ethical Considerations:

Consent form will be signed by the healthy individuals attending blood banks.
Confidentality of patients and cotrol individuals will be respectd.

14. Workplan: (Instructions: Please use this form as a template for the timeline of your project)

Task	MONTH											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Progress report												

15. Other Funding Agency

Does this study need fund? Yes [ ] No [ ]

Is your study funded by another funding agency? Yes [ ] No [ ]

(If yes, specify the agency and available funds)

16. Budget (Please use the attached documents for the price list of equipments used in the project if applicable)

Budget Breakdown	Unit Cost (SR)	Total (SR)	Remarks
Personnel *			
Total			
Supplies and Equipment			
Total			
Patients Cost			
Total			
Others (please, specify and justify briefly)			
Total			
GRAND TOTAL			

17. Appendices: (Instructions: Data collection instruments, elaboration on methods and procedures to be used, etc.) (Please attach the related documents)