

HOW TO ERADICATE HEPATITIS C FROM PAKISTAN?

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Date Received: February 06, 2017

Date Revised: February 10, 2017

Date Accepted: February 12, 2017

This editorial may be cited as: Farooqi JI. How to eradicate hepatitis C from Pakistan? J Postgrad Med Inst 2017; 31(1): 1-3.

Hepatitis C virus (HCV) was identified as a cause of Non-A, Non-B (NANB) hepatitis in 1989^{1,2}. Hepatitis C virus belongs to the hepacivirus genus within the Flaviviridae family. It is an enveloped single stranded positive sense, 9.6 kb and about 50 nm in diameter RNA virus. It is a bloodborn virus and the most common sources include unsafe injection practices, blood transfusion, unsterilized or inadequately sterilized medical equipment and vertical transmission from mother to child and the sexual contact. Hepatitis C virus has 6 major genotypes with variable global distribution: genotype 1 is mostly found in USA and Europe, genotype 3 mostly in South-east Asia, genotype 4 mostly in Middle East, Egypt and Central Africa and genotype 5 almost exclusively in South Africa. The incubation period for HCV is 2 weeks to 6 months.

By and large, hepatitis C infection exhibits 80:20 rule: 80% acute hepatitis C patients are asymptomatic and 20% symptomatic. Out of symptomatic patients, 80% patients have mild symptoms with mildly raised liver enzymes and 80% significant symptoms with significantly raised liver enzymes. Out of these acute hepatitis C patients, 80% progress into chronic hepatitis and 20% recover spontaneously within 6 months of acquiring infection. Out of chronic hepatitis C patients, 80% remain stable and 20% develop cirrhosis with its sequelae including hepatocellular carcinoma.

Approximately 130-150 million people have chronic hepatitis C infection worldwide³. An estimated 4.8% of the general population is infected with HCV in Pakistan which roughly equals to 10 million people today. Ninety percent cases are genotype 3. True prevalence is elusive due to the asymptomatic nature of the HCV infection and lack of surveillance infrastructure in our country. Pakistan has the highest number of people with active HCV infection of all countries except China in the world,

but unlike China the total number of infections in Pakistan is not declining⁴.

HCV can lead to liver cirrhosis with life threatening complications like hepatic encephalopathy, variceal bleeding, ascites and hepatorenal syndrome and certainly fatal hepatocellular carcinoma until identified and treated early in its course. Because of lack of dedicated liver care centers and services in our country, most of these cirrhotic patients are treated by general physicians and even non-doctors like quacks, hakims and so-called peers. As a result they are either treated sub-standardsly or even totally wrongly. Majority of these patients reach a stage where they need liver transplant to live a healthy life. Liver transplant has been started in our country and is quite successful program as per results, but it's a very expensive therapeutic option and practically out of reach of pocket of a common man. As a result, these advanced cirrhotic patients are very frequently brought to doctors for consultation and admitted in hospitals, thus resulting in huge economic burden on family resources as well as community resources. Therefore the only way to overcome this enormous challenge is to successfully eradicate HCV from our country.

By and large viral eradication has remained a persistent public health challenge across the world except smallpox and polio. Smallpox was successfully eradicated from the world by 1979 and now polio is almost eradicated except 3 countries^{5,6}; and unfortunately Pakistan is among these 3 countries where polio still exists. Eradication of these two viral infections became possible mostly because of vaccine that reduced transmission and curtailed new infections. Unfortunately we don't have any vaccine available against HCV till date, and even if it had been available to us, it would have been very difficult to solely depend upon this, as we haven't been able to eradicate polio from our country

despite the free availability of its effective vaccine, because of our local factors.

Whether we can eradicate HCV from our country or not, depends upon the proper understanding of the dynamics of the problem: Identified number of patients with active HCV infection is the tip of iceberg; accounting for less than 20% of the total patients pool existing at any given time; which in turn is determined by entry of newly HCV acquired cases and exit of treated and cured HCV cases from this pool. Eradication of HCV is only possible if we block entry of new cases and ideally increase exit of treated and cured cases. Before 2015, only interferon and ribavirin were the available therapeutic options for patients with chronic hepatitis C with an average success rate of 60%-70%; but for the last 2 years oral antiviral drug (sofosbuvir) is now available in Pakistan and soon we shall be having daclatasvir and velpatasvir available in our Pakistan. All these oral drugs have therapeutic efficacy of more than 90% and 96%-99% in easy to treat cases. Another good news is that the price of sofosbuvir is very low as compared to the original price of these drugs. Excellent efficacy and low pricing brings hope to extinct greater number of HCV cases from the existing pool of active infection.

Therefore we need to adopt a multifaceted national policy to become able to successfully eradicate HCV from our country. Our intervention strategies should include:

1. Prevention of spread of HCV to others
2. Successful treatment of known cases of active HCV
3. Screening for unidentified cases of HCV

Prevention: In 2015, on Center for Disease Assessment (CDA) platform with Homie Razavi, local expert panel including myself reviewed local and international publications as well as analyzed local data. We found that 230,000 new cases occur and 85,000 patients are treated each year; resulting in constant expansion of the HCV pool. Injections have been found to be the greatest risk factor for spread of HCV in our country, followed by surgical instruments and unscreened blood transfusions. Other known risk factors play a minor role⁴. Therefore we need to limit the number of unnecessary injections use and advocate the use of new disposable syringes every time injection is needed to be given. We need to address this issue at different levels starting from government level to healthcare institutions to healthcare workers to general public. Government needs to make legislation about mandatory disposable syringes, safe blood transfusions and safe surgical procedures. Healthcare institutions need to implement policy of hepatitis free surgical and instrumental interventions and safe hospital waste disposal. Healthcare

workers need to adopt safe procedures and advocate hepatitis C prevention strategies in the public. There is a great responsibility on public as well especially barbers, beauticians, professional personnel involved in ear piercing etc. to adopt hepatitis free strategies. We need to create public awareness in rural as well as urban areas particularly with high prevalence of HCV. We may use electronic and social media as well as lectures and videos in schools, colleges and universities. We may use platform of madrassas, religious speeches in mosque, public messages by public celebrities, public leaders and scholars.

Treatment: In our country, HCV treatment is mostly via "out of pocket" approach by patients. Most of our patients belong to low socio-economic group and find difficult to afford anti-HCV treatment and related investigations. Since 2005, we have patients support program run by government but till date it has not achieved its targets. We need to ensure treatment to each and every diagnosed case of hepatitis C in our country; if unable to afford treatment by himself/herself; then via patients support program. We need to motivate philanthropists, social organizations and NGOs to come forward and help in providing free treatment to poor patients with HCV. We need to negotiate with pharmaceutical companies to provide subsidized anti-HCV drugs to these poor patients. We need to ensure proper and complete anti-HCV treatment to patients with proper follow-up and in time treatment of those who fail to respond to initial antiviral treatment. We need to ensure quality of anti-HCV drugs and proper prescription of these drugs. Not only the drugs, we need to train healthcare personnel at all levels to educate and train on protocols of these new drugs in form of refresher courses and CME activities. We need national guidelines on hepatitis C by our liver societies, which must be freely available to all concerned.

Screening: Because of the asymptomatic nature of HCV infection, almost 80% of HCV-positive people are unaware of their infection and therefore remain unidentified reservoirs for further transmission in the family and community. Therefore it is important to plan national hepatitis screening program, which should be properly funded, well coordinated and multi-phased as explained below:

- **Mass Screening:**
 - In first phase, high-risk people need to be screened. These include family members of HCV patients, those who need regular blood transfusions or hemodialysis, those who have underwent surgery and dental extraction, IV drug abusers and sex-workers, etc.
 - In second phase, people residing in areas with high prevalence of HCV.

- In third phase, rest of the general population need to be screened.
- **Mandatory Screening:**
 - At the time of blood donation
 - At the time of surgery or other interventional procedure
 - At the time of admission to school
 - At the time of employment
 - At the time of making NIC and passport

During devising screening strategy, we need to ensure proper budgeting of the project, quality screening methods, proper counseling and awareness, and then adopting "go to person and screen" rather than "come and get screened" policy. It must be realized that screening must be followed by effective treatment and it brings responsibility to the screening authority and body to ensure effective treatment of HCV accordingly.

Fortunately we have national hepatitis control and treatment program in our country since 2005; it was run by Federal government as 'Prime-Minister' program from 2005 to 2010 and since 2010 it is run as "Chief-Minister" program by all provinces. It is important to understand that we need to work on all the above mentioned three aspects to ensure eradication of hepatitis C from Pakistan, which is otherwise going to engulf all our resources in years to come.

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