

## Hepatitis B Virus: An Overshadowed, Misunderstood and Under Diagnosed Epidemic in Pakistan

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### Abstract

Hepatitis B Virus (HBV) is the most prevalent cause of chronic liver disease in the developing world. It is often an overlooked entity as it does not garner as much attention as other diseases in this day and age. Flawed perceptions, myths and non pragmatic vaccination programs have led to a dire situation. Things have pretty much remained stagnant with respect to HBV in the last few decades. With no new drugs or interventions in sight for HBV, it is time to rethink strategy and come up with novel ideas and solutions to tackle this epidemic once in for all.

**Keywords:** Hepatitis B Virus; Epidemic; Vaccination; Anti-vaccination

### Introduction

As a medical student, one tends to over simplify real life problems and challenges that shape our world. Participating in screening camps throughout college years it became apparent that Hepatitis B virus (HBV) was the most prevalent active infectious disease in our society. As a gastroenterology trainee I expected HBV to be the talk of the town. One can only imagine my surprise once I saw how little lime light it was given even by the experts. Attending multiple internal medicine, hepatology and gastrointestinal meetings or conferences as a resident I could not initially explain the disproportionate time and resources given to topics such as Hepatitis C virus (HCV), fatty liver disease and liver transplantation all the while ignoring HBV. This was off putting, after all HBV is still the most common cause of liver disease in the developing world [1]. Furthermore new research endeavors into the evolving nature of HBV were all but absent. Were the experts downplaying the significance and impact of HBV? Was it a foregone conclusion? Why were there no new data on HBV coming out frequently? Why did HBV infect so many young individuals and yet so few knew about it? Why are the vaccination programs for HBV not as stringent as that for Polio? Was all that could be done already done? There were no easy answers to all these questions, but it did get the ball rolling for us and led to some surprising results.

### Review Literature

#### All eyes on HCV

HCV to date is the most common cause of chronic liver disease and cirrhosis in the westernized world [2]. For a long time HCV was associated with great morbidity and mortality [3]. Treatment options were limited to Interferon based regimen. Even with high dose therapy with or without cirrhosis outcomes were miserable [4]. All of this changed drastically with the introduction of directly acting antivirals (DAAs). Sofosbuvir (SOF) a NS5B inhibitor, the first of DAAs was approved by the Food and Drug Administration of the US in 2013 [5].

SOF was a revolutionary drug. It redefined what “cure” meant with respect to HCV. Viral eradication rates nearing 100% rates were seen even with advanced liver disease. Furthermore relapse rates were much lower compared to any Interferon based regimen irrespective of duration of treatment or stage of liver disease [6]. Within a year of its approval SOF was one of most financially successful drugs in the world. Several DAAs followed soon, all demonstrating excellent viral eradication rates. Shortly thereafter real life studies eventually validating the results of previous trials were initiated by almost all concerned institutes. It simply made more economic sense to direct more academic and industrial resources towards this novel cure. Unlike HBV, HCV could now be eradicated. Goals were already set to eliminate HCV from the developed world [7]. While this goal was unrealistic for most non developed nations, it none the less provided an excellent option to halt progression of liver disease in a large proportion of population. There is a certain sense of achievement associated with treating HCV, one that was previously not felt with any of other viral hepatitis; eliminating a known carcinogen has that affect. For all the reasons mentioned above HCV has been garnering more and more attention. Outcomes have only gotten better over time. HBV has been pulled back into the background. It's an old problem with the same old solutions. There are no new attractive medications that can be marketed to the masses. HBV remains more of a preventable disease than a treatable one. There are no new interventions for HBV in the foreseeable future. But, for millions of people already infected with HBV, it is imperative that it be brought back to the fray.

#### Under diagnosed and misunderstood

Pakistan is an intermediate endemicity region for HBV, with an estimated 2-4% of the population harboring the infection [8]. This amounts to a disease burden of 4-8 million patients, this might be actually be an under estimation of the actual number as we discuss below. Further confounding matters is the fact that most of these estimated cases have not been diagnosed neither are there any mechanisms in place at time of writing to screen such a large population. There have been appreciable attempts by the local and federal government to improve screening. One such effort is the ‘Hepatitis Free Sindh Program’ [9]. A great initiative, it provides free

vaccination to adults and infants. Some of the sentinel sites from this program have posted vaccination numbers in excess of a hundred thousand over the last three years, all free of cost [9]. Yet, this is comparable to a bucket in the sea (of HBV). Some areas of Sindh have recorded incidence rates of nearly 25%, this would put the disease burden at 8-12 million patients in Sindh alone [10]. Similar rates have also been seen for other cities in other provinces as well [11]. The real number of patients infected with HBV might never be known! HBV is quiescent in large number of its carriers. Therefore, a strategy to screen people based on signs or symptoms is out of the question. The best course of action is to screen relatives of known HBV carriers. This game plan may sound reasonable, but it has rarely delivered the desired results. The routes of transmission of HBV are several and varied, In fact, the most consistent route of transmission according to previous data has been via barber shops [12] as such infection cannot be limited the family per se, it is much more likely to be a community problem. Of course, the perfect scenario would have us screening everyone. The recent novel corona virus pandemic has made it painfully clear that healthcare systems (around the globe) just don't have the capacity for this; at the moment there is no clear answer. I have heard myths such as HBV is untreatable, you can get it by sitting in the same chair (furniture) as a patient, it's a hoax, it's supernatural, mixed in local water supply, associated with hilly areas (or its people), can be treated with herbal medications and is treatable with sunlight or heat. Honestly a lot of this mirrors current state of confusion that surrounds the current COVID-19 pandemic. People choose to believe such inaccuracies all the while disregarding proper precautions including getting tested and vaccinated, sanitizing surgical tools, sanitizing shaving tools and kits, screening blood products and using protection. These issues have to be addressed if we are to tackle HBV efficiently. Myths need to be busted, but the message must be conveyed in a kind and empathetic manner to the public. Negative views are a result of lack of education and a sense of disenfranchisement; lack of delivery from the health care system has led to many a false notion. Human behavior must be understood affectionately before people are expected to understand the truth of HBV itself.

### **To vaccinate or not to vaccinate?**

Anti-vaccination movements have propped up in the last few decades especially in North America. Fueled by distrust and resentment towards the government and "big pharma", these misguided campaigns use misinformation and debunked scientific data to propagate their claims. Supporters of the anti-vaccination campaigns cite personal experiences, religious beliefs and one of occurrences as definitive proof of damage that vaccines cause. Basically, it is a thought process that does not confer to modern scientific data and processes, be it in an individual, a group or a community as a whole. Developed health care systems that have the infrastructure to deal with such situations tend to do better at controlling infectious outbreaks or epidemics. However, it would appear that these movements are actually gaining momentum, but for the time being their impact is easily negated. This is easier said than done in developing nations. Anti-vaccination movements are much less organized in the third world and are far few in between, but because of the lack of effective counter measures their effects are much more disastrous. One catastrophic example of such line of thinking is Polio. It is endemic in Nigeria, Pakistan and Afghanistan only as of 2020 [13]. This can be attributed to anti vaccination attitudes wholly. HBV vaccination programs face similar problems in Pakistan, but perhaps not as severely. For one HBV vaccination programs are not as

well advertised nor do they receive international funding. As previously discussed HBV is an old problem and probably not news worthy ergo has markedly reduced coverage. This has led to two distinct obstacles. One, there are unfounded concerns among some that HBV vaccination may cause impotence, loss of virility, skin abnormalities, chronic diarrhea, exacerbate HBV infection, actually cause infection or sepsis and cancer to name just a few. Secondly and far more prevalent is the lack of knowledge that a vaccine for HBV exists at all. This plays in with the under diagnosed nature of HBV. When the majority of the population is unaware of a threat, how can they be expected to know about one of its precautions? In general, public attitudes towards HBV vaccination are comparatively positive. Once a family member or a friend is diagnosed as a case of HBV, people are usually up for testing via antibody kits or real time assays. Financial shortcomings play a major part in deciding if or when and how many other members of the family will get tested. The attitudes of 'Market World' are crucial here. Their negative approach has led to reduced screening rates. There is reasonable concern on behalf of their employees of being laid off should they test positive in any capacity or at any stage of liver disease. HBV vaccination is not a part of the national 'Expanded Programme on Immunisation' [14]. The HBV vaccine is about 6-15 USD per dose (depending on the brand and exchange rate). This is an inordinately high amount for a developing nation. Unquestionably this is the single most important factor determining the choice to vaccinate or not. In light of all the evidence it stands to reason that while the masses need to be educated on the importance of vaccination for HBV, this will be to no avail if despite availability and knowledge of it they cannot access the vaccine(s). Perhaps integrating HBV vaccine into national programs is the only logical next step.

### **The more things change, the more they stay the same**

Butt et al. [15] shed light on the current situation of HBV at the tertiary care level, this study was held in Karachi also known as 'Little Pakistan' and is practically representative of the entire nation. According to this study HBV predominantly affects young adolescents, the most common route of transmission is either vertical or via barber shops and it affects all ethnicities and occupations throughout the society. Majority of the patients were diagnosed incidentally. It is as if nothing has changed in the last few decades. All data presented by Butt et al. is consistent with previous reports [12,16]. This has to be considered a great failure for the health care system. With all new technology available and all the advances in communications and travel, why does the situation still resemble that of the 1990's? Clearly the old policies aren't working. Whatever little progress that has been made will become insignificant in coming years, as more and more cases of HBV are diagnosed. Eventually the system will be overwhelmed by this massive influx of patients; this was a major concern years ago and sadly is still a looming threat.

### **What's next?**

Hard hitting introspection is required. There are no new interventions for HBV on the horizon to the best of our knowledge. This epidemic has to be contained with the tools available now. Future endeavors need to take into account and make adjustments for the economic, social, religious, therapeutic and diagnostic aspects of HBV. It's time to earnestly focus on the fight against HBV, lest it be too late. For the moment HBV remains a ubiquitous pathogen.

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