Strategies for the Prevention of Hepatitis B, Hepatitis C and Human Immunodeficiency Virus infection in the Paediatric Population of Developing Countries

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Abstract

After a brief background about the epidemiology of Hepatitis B, C and HIV, strategies for their prevention are discussed in the paediatric population of developing countries. These strategies are focused on mother to child transmission, misuse of injections, use of infected needles, myths and use of material infected with the hepatitis positive patient such as a comb, tooth brush etc. Malnutrition and its relationship with Tuberculosis and HIV infection are discussed. World Health Organization (WHO) guidelines on the management of malnutrition, Tuberculosis and HIV are discussed briefly. A real scenario highlighting the existence of HBV, HCV and HIV is described. Finally role of policy makers, NGO, WHO and local governments in the prevention of HBV, HCV and HIV in the paediatric population is discussed.

Key words: Hepatitis B; Hepatitis C; Human Immunodeficiency Virus infection; Paediatric population

Background

At global level, HBV, HCV and HIV infected population stands at 370, 130 and 40 million respectively. HIV and HBV co-infection are 2-4 million, while HIV and HCV co-infection are 4-5 million(1). Transmission of these infections varies and is dependent upon the geographic region and local practices e.g. in some areas of the world where men who have sex with men, these infections are more common. Hepatitis infections HBV and HCV are endemic in some of the developing countries(1).

Among persons with HBV, HCV and HIV co infections, the presenting features are different. They are dependent upon the epidemiology of the infection in a particular geographical region. As the epidemiology of an infection changes over time, surveys are needed which will detect these epidemiological changes over time and hence can help in developing strategies to prevent these infections in a particular region or communities(2).

HBV is caused by a DNA virus, while HCV by a RNA virus. These viruses cause acute and chronic liver disease worldwide, leading to cirrhosis and hepatocellular carcinoma (HCC). There is difference in the clinical presentation, pathology and outcome in patients with HCC depending upon whether the cause is HBV or HCV. This difference affects the cure rate and the prognosis(3). HBV and HCV are blood borne viruses; however, HBV can be transmitted by both percutaneous and mucosal exposures and HCV by percutaneous exposure(4). Transmission of these viruses most commonly occurs in developing countries by misuse of infected syringes and rarely by vertical transmission(5, 6) child abuse and possible risk of co-existence of HBV, HCV and HIV infection in garbage scavengers from poor communities(7) (Figure 1) tattooing in older children, drug abuse, and needle piercing(8, 9).

HBV prevention is achieved by immunization for all children according to the Expanded Program for Immunization (EPI) (10, 11). Some centers are giving a booster dose of hepatitis B vaccine, 11-15 years after the primary vaccination. A study done in China indicates that in those children with a low level (0.1-0.9 and <0.1mIU/mL) of the anti-HBs titer, prior to the booster vaccine may need more than one booster dose vaccination. While in those children with a higher level of pre-booster anti-HBs titer of 1-9.9mIU/mL, additional booster vaccination dose is not required. Hence, the protective levels of the HBs antibody decrease more rapidly in those with low titers(11, 12).
The vaccine for HCV is not available, even though trials on the vaccine development are being conducted(12). Lack of availability of the vaccine against HCV is a serious concern as there will be an upsurge of HCV infections compared to HBV infection, leading to more cases of HCC. Adolescent children are more prone to infections related to drug abuse and sexual intercourse(13).

HIV infection numbers in Southeast Asia was 320,000 in the year 2001, but has now declined to 210,000 in the year 2010. The countries of the WHO Southeast Asia Region (SEAR) (14) include Bangladesh, Bhutan, South Korea, India, Indonesia, the Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor-Leste. The largest numbers of cases are from Indonesia, where the number of HIV infections is increasing. In the remaining countries of SEAR region, the number of HIV positive cases is decreasing. The maximum number of cases reported from SEARS after Indonesia is from India, which has the second highest number of cases in the region due to heterosexual intercourse(14).

Some older children practice anal intercourse that may also result in HIV infections(15). HIV positive men are more likely to have sexual abuse with children than HIV negative men(16). Knowledge of the children is inadequate regarding HIV infection transmission and they represent the vulnerable group(17).

Prevention strategies for HIV infection in children are the same as for hepatitis viruses and focus on mother-to-child transmission of HIV from an HIV-infected woman to her child during pregnancy, childbirth (also called labor and delivery), or breastfeeding. Mother-to-child transmission is the most common way that children become infected with HIV(18).

Pregnant women infected with HIV are given medications for the HIV infection during pregnancy and at childbirth. Elective Cesarean section may be done to prevent HIV infection from mother to child. A baby born to a mother with HIV infection will receive HIV medication for 6 weeks after birth. The medications will reduce the risk of HIV infection transmitted from the mother to the newborn baby(18).

HIV can be transmitted via breast milk. Hence women in the USA are advised not to breast feed their babies if they are suffering from HIV infection. In such cases formula milk is a safe and healthy alternative to breast milk(19).

However, breast-feeding is promoted in developing countries regardless of HBV, HCV or HIV infection in mother. In developing countries, due to risk of malnutrition in children, the morbidity and mortality is high. Approximately half of the deaths, which occur in children under five years of age, are due to malnutrition. This results in loss of 3 million deaths every year, which could have been prevented. Recurrent infections in children with malnutrition leads to a vicious cycle with delayed recovery and makes the child more prone to susceptible infections leading to death(20). In babies, who are not breast fed, milk is given to them in contaminated bottles and water used is not consumable for health, hence it is advised to continue breast-feeding in these areas. Thus in countries with poor socio-economic backgrounds, with mothers infected with HBV or HCV or HIV, exclusive breastfeeding is recommended. Breast feeding in HIV-infected mothers is continued for the first six months of life, unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for their infants(19, 20).

In areas with poor social and health sector development, incidence of HCV and HIV is high. Drug addicts have to

cope not only with their addiction but also with the process of social exclusion. To the greatest extent possible, any course of action for such a group should be built into integrated, coordinated plans that take a broad approach to the main issues involved(21).

Co-infection of tuberculosis (TB) and HIV

Both children and adults may be co-infected with HIV and tuberculosis. In children, data available on TB and HIV co-infection is rare. However, a strong suspicion of HIV must be kept in mind for HIV when TB is diagnosed in any child, especially if HIV is endemic in that particular region or the child is immunocompromised. Hence the awareness among paediatricians when managing children with severe malnutrition and in case of history of contact with a TB patient, the child must be investigated for HIV also after appropriate counseling of the parents. This may occur in Multi drug resistant cases of tuberculosis (MDR TB) and co-existing HIV infections. WHO has suggested a special team, which can manage these patients (22). Since HIV infection can occur in immuno-compromised children, with tuberculosis, prevention of tuberculosis in developing countries should focus on curtailing the epidemic of TB and HIV especially in endemic areas. Strict control of the vaccination program, protection of children from exposure to infected individuals with TB and prevention of patient transfer with active transfer from one country to another should be monitored(23).

Diagnosis of HIV/TB co-infection in children is challenging. Paediatric TB and HIV(22,23) have overlapping clinical manifestations, which could lead to missed or late diagnosis.

HBC, HCV and Hepatitis D (HDV) Co-infection

HBV and HDV co-infection or HBV and HCV co-infection have a worse prognosis than these infections alone. HDV infection will only occur in the presence of HBV infection and eradication of HDV infection is difficult(24). These co-infections are related to misuse of infected needles and lack of immunization for HBV, a preventable infection, hence, parents should be counseled and law should be passed that every child follows the immunization program of the respective country especially in areas where HBV and HCV is endemic.

Strategies to prevent hepatitis and HIV infections

The strategies depend upon the countries in which the infection is present and related to the epidemiology of the infection. The treatment program in the developing countries will be successful, only after recognition of the country specific epidemiology; this varies and is mostly dependent upon the economic development, which the respective country has achieved.

Immunization

HBV Immunization is mandatory for the prevention of HBV infection in children and adults(25). Despite counseling and advice to parents more than 50 % of the children may not be immunized for HBV in various communities especially in those areas which are economically not well off(26). Hepatitis B virus infects many infants and children - more than 2 billion people have been infected with the virus at some point, and an estimated 350 million are lifelong carriers. However, most don't develop the clinical disease until several decades later when the virus can cause inflammation of the liver and lead to cirrhosis or liver cancer.

More than 30 million children are unimmunized either because vaccines are unavailable, because health services are poorly provided or inaccessible, or because families are uninformed or misinformed about when and why to bring their children for immunization. In such communities HBV and HCV infections continue to increase(26).
HCV is more difficult in terms of prevention of the disease as vaccine is not available, however treatment response in both adults and paediatric patients especially has shown a good response with genotype 2 and 3(27).

It is advisable that all family members are screened for HBV and HCV if a case of HBV or HCV is detected in the family(28). In some hospitals prior to surgery, regular screening of HBV and HCV is done to prevent the infection in the surgeons, in case of a prick with infected blood of patient.

The relative importance of various modes of transmission of HBV, HCV and HIV viruses differs in each country; hence, the choice of specific prevention and control strategies depends primarily on the epidemiology of infection in a particular country. Comprehensive hepatitis B prevention strategies should include (1) prevention of perinatal HBV transmission, (2) hepatitis B vaccination at critical ages to interrupt transmission and (3) prevention of nosocomial HBV transmission and (4) counseling of the parents.

The prevention of hepatitis C is problematic because a vaccine to prevent HCV infection is yet to be developed in the foreseeable future. From a global perspective, the greatest impact on the disease burden associated with HCV infection will be achieved by focusing efforts on primary prevention strategies to reduce or eliminate the risk for transmission from nosocomial exposures (e.g. blood transfusion, unsafe injection practices) and high-risk practices (e.g. injecting drug use). Studies have shown that the risk of infected blood causing hepatitis and HIV is still possible in countries where appropriately screened blood is not available. This is even more apparent in thalassemic children requiring repeated blood transfusion. The infected blood causes increased morbidity and mortality in the children due to thalassemia itself and as there is a high risk of the children being co-infected with HBV, HCV, HDV or HIV (29). A study of thalassemic children from Karachi, Pakistan has shown that 43% of the patients were positive for HCV, 5 % for HBV and none for HIV. This indicates that

the hepatitis B vaccine is protecting the children against HBV and hence HDV. However, due to the absence of vaccine against HCV, there is a higher frequency of HCV in the general population and in thalassemics compared to HBV infection. Also, it is worthwhile to note that none of the patients in this study were positive for HIV. Hence, we have to be extremely vigilant in the prevention of these infections by creating awareness, education and counseling of the parents, children, health workers and policy makers. HIV has not reached the high proportions seen in other countries such as India and Indonesia(14,29) and we have to adopt all preventive strategies to contain HIV.

Lack of international and local organizations interaction and role of NGOs

NGO can play a great role in the prevention and treatment of hepatitis and HIV in the developing world and other parts of the world(30).

The role of organizations such as WHO, UNICEF and local organizations in various countries is important to prevent HBV, HCV and HIV in the paediatric population, due to the wide geographical area of coverage of these organizations, political will and available resources. It has also been observed in some of the developing countries that a decrease in HBV has occurred when compared to HCV, which has continued to rise due to non-availability of the vaccine against HCV. International forums provide treatment of HIV medications at a very low cost(10,11,23, 25).

Role of local paediatricians

Pediatricians taking care of a child should screen all children for HBV and HCV regardless of the status of the parents, especially when working in an endemic area. The child should be referred to a paediatric hepatologist for further investigation and treatment if found to be positive for HBV, HCV alone or co-infected. A Paediatric Infectious disease expert may be consulted in the management of co-infection with HIV. Local paediatricians should repeatedly counsel parents regarding child abuse especially sexual abuse and its relation with HIV or hepatitis to protect the vulnerable child. The local infectious disease experts, should include topics of HBV, HCV and HIV infection in children and their prevention in international conferences in developing countries so to create awareness among the Pediatricians.

Research

There is a need to collect data on the existing infected paediatric cases of HBV, HCV and HIV in the developing countries to determine the prevalence and incidence of these infectious diseases. By doing so strategies can be developed, which would then focus on the treatment of the existing population of children and in the prevention of the remaining paediatric population existing in the country. In a study conducted in Istanbul, Turkey,(31) very early onset of substance and polysubstance use indicated easy accessibility of legal and illicit substances by children and youth. These findings on Turkish children and youth who seek substances at an early age can be corrected by means of early interventions at a stage when the child has just started substance abuse. The diseases such as HBV, HCV and HIV can be prevented in the child at early stage by appropriate early intervention and treatment facility(31).

Challenges in the developing countries

The main challenges that need to be met in developing countries include lack of qualitative ongoing training for health professionals. In some areas of the developing countries, training programs are non-existent, so that some health professionals though aware of the diseases, do not have sufficient knowledge for prevention, treatment or referral to tertiary care hospitals. Inter professional education (IPE)(32), involves close collaboration between health care professionals and can improve patient care. Training and educational programs including, continuing medical education (CME), can be done so that the health professional may work together to reach the objectives, which is primarily patient care. In these countries it is essential that regular seminars for health workers in a systematic fashion are held with ethical coverage by the newsmedia and appropriate discussions with the public and health workers and policy makers is done, so that prevention of HBV, HCV and HIV can be implemented. Children should be highlighted at all levels of the discussion, including that of an expecting mother (unborn baby), her delivery, role of the father and family, so that control of the prevention of HBV and HCV and HIV can be done by immunization and counseling.

Policy makers

The role of policy makers is crucial for the prevention of these infections. Unless the governments are serious about the prevention of these infections, the disease will spread and reach epidemic proportions. Hence, even if few cases are detected in any area, prompt action should be taken in terms of prevention of these infections.

A pertinent example is China where there is a high prevalence of these infections. HBV and HCV co-infection in HIV-infected children in China receiving ART has prompted policy makers to routinely screen for viral hepatitis co-infection, organize an intensive prevention strategy of childhood HBV and HCV transmission, and develop programs for the modification of the management of pediatric HIV infection(33).

Cost effective analysis

Analysts are required to make cost effective analysis of the resources(34) available to decision makers for the implementation of the strategies for the prevention of hepatitis and HIV especially in the poor countries. Existing interventions should be evaluated both in terms of outcome as well as resources, before a new intervention is introduced or approved. Research done in any one country or region or area should be such that it can be applied in another region with minimum cost. Also long-term effects need to be considered; as an example lack of immunization against hepatitis B can eventually lead to

HCC especially if the patient is exposed to the risk factors leading to HBV infection. In such a case the cost effective analysis of the intervention i.e. the immunization for HBV is definitely a good preventive strategy as HCC can be prevented. In the long run cost of immunization is negligible compared to the treatment for HCC and let alone the morbidity associated with HCC.

Hence, an economic analysis should always be done keeping in mind the objectives of the strategies, which will be used to prevent infective diseases such as HBV, HCV and HIV in the very vulnerable human population, our children in regions of the world, which are impoverished(34). In this regard it is essential to develop vaccines for HCV(35) and HIV, which can prevent these infections and will be cost effective in the long run.

Scenario

A young 19 year old woman of Afghani origin is married to a Pakistani man, as her family is very poor and need the money, which will be obtained from this marriage and as is the custom that money is given to the father of the bride.

This is the Pakistani man's second marriage. They are living in an area which is a slum area/camp, where there are migrating individuals from various parts of country Pakistan and people who have fled from Afghanistan due to the war.

Within a year a beautiful healthy baby boy, green eyes and golden hair, resembling his parents and grandparents is born. Living in an area of suburb of a major city of Pakistan, delivery takes place at home. Parents due to lack of awareness do not immunize the baby. Mother breastfeeds for 9 months exclusively. Weaning is inappropriate and the child gradually becomes malnourished and plots on the 3rd centile for both height and weight. Gradually he becomes stunted by the age of 5 years. Mother is unable to give him attention and food due to poverty, lack of awareness and education and little economic support from the husband or the family. The mother herself has lost weight and now looks like a middle-aged woman, even though she is only 26 years of age. She now has 2 more children ages 4 and 2, with the same nutrition history.

These children play in rubbish, (Figure 1) as their only means of recreation in the area. A nearby man has developed tuberculosis and is seen coughing out blood, by some of the neighbors. Another individual aged 23 years; living nearby due to severe depression has started taking drugs of all sorts. Later he is diagnosed to have HIV. Infected needles are thrown by this man and his community in the same rubbish where young children play(36).

Figure 1: Child playing in garbage with infected needles, in a poor community area, with no supervision, lack of awareness and lack of education

Despite the local government emphasizing immunization, very few children in the community are vaccinated, due to their own myths. This community is close knit and do not always welcome NGOs or local doctors. They do not allow their children to go to regular schools and the boys as soon as possible go out to work, which can be anywhere between 8 and 12 years of age.

The young boy aged 5 years now goes on a donkey cart all over the city with his older cousin, picking up old used stuff including used needles and supplying them to a local factory where they are recycled and used again in all major hospitals. He has by now become infected with HBV and HCV. He is also immune-compromised. Due to frequent visits to a distant relative with Tuberculosis; the child is now also exposed to TB.

The child is now 6 years of age, and looks like a wizened old person with no concept of childhood play and is brought to clinic finally as he is listless, severely malnourished with low grade fever every night. On further investigation he is found to be HBV, HCV and HIV positive. There is sharing of toothbrush, comb etc. by all the children due to non-affordability and lack of knowledge and awareness in the family. His sister who also develops HCV is given treatment by the NGO and in part by government funds from a local hospital. The girl becomes HCV negative, but the boy despite available treatment dies.

This scenario exists in many parts of both these neighboring countries and is increasing in frequency. This family like many others will be prone to the following causes of hepatitis and HIV co-infection. The prevention strategies for such children are described in the table on the following page.

Table 1: Strategies for the Prevention of HBV (hepatitis B), HCV (hepatitis C) and HIV in the Paediatric Population of Developing Countries

Causes of Hepatitis and HIV co-infection in children	Prevention strategies (all have to be available free of cost or minimal cost to the population)
Vertical transmission	Screening and immunization of all women of child bearing age, with available vaccines
Lack of immunization	Immunization is available free of cost at all government hospitals. Encourage parents by local media, family physicians, and religious leaders and family elders.
Unsafe injections (contaminated needles and syringes)	Proper disposal by the government, local area in charge. Incinerators in all hospitals. A law has to be passed and implemented for appropriate disposal of all material from the hospitals, dispensaries and local clinics. Early screening of infected individuals.
Unsafe sex	Education of the parents, community and teenage children
Child abuse	Education of the parents and community to be vigilant and keep their children safe
Lack of awareness	Education and social programs in print and electronic media and community level one to one.
Susceptible group	Parents, community and government need to pass laws with strict implementation to protect children. Individuals with problems should be provided psychosocial help.
Economic situation of the country (poverty)	Can be only done if all countries together are sincere and humane to one another and NOT to themselves and their nations alone
Lack of Education	Basic education conducive to the environment the people are living in.
Myths	Education and awareness by family members and religious leaders
Risk factors	Awareness and education
Behavior	Awareness and education
Inappropriate care and treatment of infected persons	Improve government resources, remove corruption, so common man gets the required treatment with ease
Vaccines for hepatitis B, C and HIV	HBV is available at all government hospitals free of cost, HCV and HIV more research is needed

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