Over 15% of all cancers worldwide can be attributed to viral or bacterial infections. Cancers of the uterine cervix, liver, nasopharynx, stomach, some sarcomas and lymphomas are caused by infections.

Since the causal association is well established in these cancers, prevention or appropriate treatment of the infections would be effective strategies for the control of these cancers.

Control of cervical cancer by regular cytological screening has been amply demonstrated. Further, procedures like visual inspection with acetic acid (VIA), or with Lugol’s iodine (VILI) have been tested and shown to be feasible alternatives for South Asia. Primary liver cancer, caused by hepatitis B and C virus infections, is also preventable by observing universal safety precautions, blood safety measures, good sanitation, safe sexual practices and immunization. Food hygiene can prevent Helicobacter pylori infections that cause stomach cancer. HIV associated cancers can be prevented by adopting HIV prevention measures and appropriate treatment of the cases.
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Introduction

People in South Asia are at a greater risk of developing infectious diseases and subsequent mortality which is attributed to associated problems of unhygienic living conditions, malnutrition, illiteracy, and poor access to clean food and water, poor sanitation, warm tropical climate and lack of quality health care. Many of these infections persist for a long time ultimately lead to development of cancer. At least 15% of all cancers worldwide can be attributed to infections with viruses, or bacteria. The largest infection-related cancer burden in the region is primarily of cervical cancer, liver cancer, nasopharyngeal cancer, sarcomas, lymphomas and stomach cancer. These cancers are best controlled by preventive strategies as their causative agents are known.

Control of morbidity and mortality from cervical cancer can be achieved by regular cytological screening of Pap smear. However, this practice is not feasible due to lack of sufficient trained manpower, awareness and resources along with the disadvantage of having large population in the region. The procedures like visual inspection with acetic acid (VIA), or with Lugol’s iodine (VILI) or VIA with magnification (VIAM) are being promoted as cheaper and more practical alternatives. The recognition that cervical cancer is caused by certain specific types of high risk human papillomaviruses (HR-HPVs) has led to the possibilities of employing HPV DNA testing as an adjunct, if not alternative, to cytological Pap test for effective screening and management of cervical cancer or precancer lesions particularly those with negative Pap smear or ASC-US (atypical squamous cells of undetermined significance). There are at least two vaccines against most prevalent oncogenic HPV type 16 and 18 have successfully undergone the Phase III clinical evaluation and are ready to be introduced in the South Asia. This will have a great impact on prevention of cervical cancer, the most prevalent cancer of the region.

Like cervical cancer, the primary cancer of the liver is also quite prevalent in the region and is a preventable cancer which is caused by infection of hepatitis B and C viruses (HBV & HCV). The incidence of liver cancer has been radically reduced by immunization of children against hepatitis B virus which is now a part of national vaccination program of most of countries of the region, and by prevention of hepatitis C virus through improved awareness and sanitation.

AIDS –associated cancers/sarcomas can be avoided by preventing and treating infection with human immunodeficiency virus (HIV). Appropriate awareness programmes
over a century it was believed that cervical cancer is associated with 'sexual behaviour' indicating involvement of a sexually transmissible infectious agent. In the early 1980s, the involvement of HPV was demonstrated by cloning of several HPV genomes, including the most prevalent oncogenic HPV16 from cervical carcinomas. However, it took more than a decade before the causal role of specific types of HPVs in the development of cancer of the cervix and their precursor lesions was accepted. Of more than 100 HPV types described so far, more than 20 types are associated with anogenital cancers. These are broadly classified into High Risk (HR) and Low Risk (LR) groups. Large scale clinico-epidemiological, molecular biological and experimental studies have provided convincing evidence that high-risk HPV are the main risk factors for development of cervical cancer. HPV is also found to be associated with other human cancers such as oral, oesophageal, lungs, laryngeal and skin cancer. Mainly, the most prevalent high risk HPV types 16 and 18 and another less frequent twelve HPV types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, and 73) were defined as the causative agents for cervical cancer. Apart from HPV infection, various epidemiological risk factors such as, sexual promiscuity, exposure to sexual intercourse at an early age, number of pregnancies, long term use of oral contraceptives and smoking have been shown to contribute to the development of cervical cancer. Studies on biological behavior and natural history of HPV infection and cervical cancer indicate a long interval between infection and development of cancer. Persistence of HPV infection in terms of years is essential for manifestation of its carcinogenic activity. This makes primary prevention of cervical cancer feasible. HPV infection is common in South Asia and is primarily symptom-less, transient and thus it is most suitable to use prophylactic approach for its intervention.

**Methods and characteristics of effective intervention**

1. Cytological screening has made little impact on incidence and mortality from cervical cancer in South Asia due to lack of trained manpower and financial and technical constraints. Once in a life-time or selective cytology screening of high risk patients has been proposed but these are also not feasible in resource-poor, rural set-up with lack of awareness in target population. Increasing the awareness among clinicians and primary health care providers can play a major role in successful intervention.

2. Regular cervical cancer screening should be done in different regions within the countries and between the countries through organized cancer awareness and early detection camps and development of cancer control programmes at national and regional levels.

3. Before embarking on organized screening programmes there for hygienic and sexual activities and blood transfusions are actively being pursued in absence of effective therapeutic modalities/vaccines to cure or prevent HIV infection.

Nasopharyngeal carcinoma, Burkitt's and non-Hodgkin's lymphomas have been related with Epstein-Barr virus (EBV) infection which is primarily asymptomatic. EBV induced-cancer development is associated with immunosuppressed state of host. EBV also acts as a co-factor in HIV-induced opportunistic malignancies.

Prevention of stomach cancers caused by Helicobacter pylori is different from that of the other cancers, as the incidence can be controlled effectively by improving hygiene and dietary habits of the individual.

The evidence for association of these infectious agents as human carcinogens have been evaluated by international experts and published as monographs series by International Agency for Research on Cancer (IARC), Lyon. In this chapter, we focus mainly on the extent of the disease and various strategies that can be employed for awareness, prevention and control of infection-associated cancers in the region.

**Human papillomavirus and cancer**

Invasive cancer of the uterine cervix is the most common cancer in the women in South Asia, especially India which harbours more than one fifth of the global burden of the disease. In contrast, Pakistan and Maldives show low cervical cancer incidence. For
Infections should be training and development of cyto-screeners and cyto-pathologists. There is an urgent need for quality control of the diagnostic laboratories both for cytology and for HPV testing, to enforce early detection effectively.

4. Instead of mass cytology, visual screening such as VIA, VILI and VIAM should be introduced for detection of precancerous and cancerous lesions. Also, use of hand-held, battery-operated magnavisionizers could be promoted. VIA-based screening programmes are feasible, safe and easily acceptable to population in rural settings.

5. There has been substantial improvement in the methods used for reliable detection of HPV DNA. Different assays such as hybrid capture 2 (HC2), consensus and type-specific PCRs and several other assays are available that can offer detection of HPV DNA, quantification of viral DNA in clinical samples, identification of high risk genital HPV types, localization of the viral DNA and analysis of viral transcripts. These tests can be optimally utilized for screening of at least high-risk population, if not for all.

6. Based on resources, region can be subdivided into three categories, the most resource poor region should enforce the visual screening, and cytology screening can be utilized by the developing parts and both cytology and HPV-DNA typing by the middle and high income countries.

7. Intervention protocols should target early age of marriage or sexual exposure, sexual promiscuity, number of pregnancies, genital hygiene, use of oral contraceptives and smoking to prevent the persistence of HPV infection and cervical cancer.

8. HPV vaccines, which should be economically viable and attempts to develop indigenous vaccine should be encouraged. For identification of the target population for the vaccine programme, mass scale molecular epidemiological screening program should be taken up to create baseline data for HPV infection in the region.

9. Till date no therapeutic is available for treatment of HPV infection therefore, efforts may be made to develop anticancer microbicides such as curcumin and others that are safe to administer and economically viable for developing countries.

**Advances in HPV research and vaccine program**

There are at least two successful HPV VLP vaccines have been developed and are in Phase III clinical trials. The vaccine developed by Merck, called ‘Gardasil’ is a recombinant quadrivalent L1 VLP vaccine which contains HPV 6, 11, 16 & 18 and is made in yeast, and the other one is called ‘Cervarix’ developed by GlaxoSmithKline, is a recombinant bivalent L1 VLP vaccine made in baculovirus against HPV 16 & 18 20,21. Both the vaccines have showed 100% efficacy in variety of short term (up to 4.5 years follow up) clinical trials in 13-25 year age group women. But nobody knows how long they will provide protection. Since Indian initiatives to develop HPV vaccines are in infancy, India is going to initiate clinical trial of these vaccines shortly. A memorandum of understanding (MOU) has been signed between Merck and Indian Council of Medical Research (ICMR), New Delhi for clinical trial of Gardasil in India for which a protocol is being developed. But before the trial is initiated in the region several issues need to be resolved for effective implementation of HPV program.

- Creating baseline epidemiology data – To identify most prevalent HPV types, use of cost effective tools such as Paper Smear Method should be introduced in resource poor countries.22 This is easy to administer, store and transport samples from the field to the laboratories.

- Target Population - What is the age group of females to be vaccinated, whether males also to be vaccinated?

- Will HPV vaccine prevent the development of cervical cancer? It needs long-term monitoring of vaccinated women till they reach 35-45 years when rate of HPV
infection and cervical cancer is higher.

- Would the vaccine provide lifelong immunity or how long antibody will persist to protect against infection or boosters will be required, if so, then at what interval?

- Will the HPV16 and 18 prototype vaccine have any protection against the cancers caused by other high-risk HPV infections?

- Do the geographical HPV variants affect efficacy of the prototype vaccine? There are geographical variations in the sequence of HPV types which leads to proteins with altered biological functions resulting in different clinical outcome of the disease. Therefore, it may be required to develop region-related-variant-specific HPV vaccine for effective anti-HPV immunity.

- Consideration of ethical and social issues for administration and monitoring of vaccines is most essential. Because of ethical and social stigma associated with unmarried girls in Asian region, non-invasive methods such as self sampling of urine for HPV DNA testing can be employed effectively for vaccine monitoring.

- Both for screening and monitoring of HPV vaccine program there is a need for development of regional reference laboratory with Region-specific HPV diagnostics at par with international standards. In this regard, WHO is making efforts to establish a Regional HPV Laboratory for southeast Asian region. The laboratory will be involved in development of International standards of HPV DNA reagents for reliable HPV diagnosis and vaccine monitoring.

- Is HPV serology reliable as antibody titre following spontaneous HPV infection is very low or undetectable? Good antibody responses occur if vaccine is given in young adolescents (9-10 years olds) but it remains to be seen whether they get protected when they reach sexual maturity and activity. It is also not known if adults can have high antibody titre following vaccination?

- Will the vaccines produced by Merck and GSK be affordable to resource poor countries? Furthermore, these protein-based VLP vaccines are heat-labile, need cold chain for storage and distribution and are not effective in already infected women. To address these issues, there is a need for developing a second generation vaccine which should be easy to produce, cost-effective and can also take care of already HPV infected women. Major efforts, therefore, be directed towards developing HPV DNA-based vaccine which will be highly immunogenic, cost-effective and both prophylactic and therapeutic in nature.

Cancer Awareness, Prevention and Control: Strategies for South Asia — A UICC Handbook

The hepatitis viruses and cancer

Hepatocellular carcinoma (HCC), the major type of primary liver cancer, is one of the commonest cancers contributing nearly 4% of all the malignancies and a leading cause of death in many countries, mainly in Asia and Africa. The heterogeneous geographical distribution of HCC has been instrumental in identification of major risk factors, including chronic infections with hepatitis B virus (HBV), hepatitis C virus (HCV). Although, exposure to hepatocarcinogen aflatoxin B1, alcohol, hemochromatosis, alpha 1-antitrypsin deficiency, tyrosenimia, glycogen storage disease also contribute to the development of HCC, in 70-85% of HCC cases, there is an underlying HBV or HCV infection. HBV infection causes mainly chronic liver disease and as high as 400 million people are chronically infected with HBV and 70 to 80% of these cases occur in Africa and Asia. In several cohort studies, the relative risk of developing HCC increases from 5.3 to 148 fold in chronic HBV surface antigen (HBsAg) positive subjects. The clinical course of acute HCV infection is mostly asymptomatic, but acute infection leads to chronic liver disease. Advanced liver disease and its complications may be the first clinical evidence of chronic HCV infection. It is estimated that about 170 million people are chronically infected with HCV worldwide. The rate is around 1% in North America and Western Europe, while it is up to 10-20% in some African and Asian countries. The number of HCV
Infections

infected people is lower than in case of HBV infection, the chronicity, however, is much higher in every age group, reaching up to 85%. In a study from India, 74 consecutive cases of HCC were studied and evidence of HBV infection was recorded in 71% patients. Infection of HCV alone was detected in 4% and dual HBV and HCV infection in 8% patients. Thus, HBV infection is the predominant factor for the development of HCC which is generally related to mutant forms of the virus. In majority of HCC in India, overt cirrhosis of the liver has been shown.

It is reported that the incidence of HCC is increasing in many countries in parallel to an increase in chronic HCV infection. The death rate due to HCC has been increasing over the last two decades. Recent studies have shown that one of the main causes of this increase is associated with increased infection with HCV.

Methods and Characteristics of effective intervention

Transmission of infection in areas of high prevalence is predominantly occurs in children. However, the modes of transmission in children are unclear. Mother-to-child (perinatal) transmission plays a particularly important role in South Asia. In adults, sexual transmission is a major mode, although intravenous use of drugs and lack of stringent quality control measures during blood transfusion play an important role in some regions.

Vaccination against HBV is the most effective means for preventing transmission of HBV. Recombinant vaccines are highly immunogenic and confer long-lasting protection against acute hepatitis and chronic infection. When administered properly, the vaccine induces protection in 95% of recipients where child and adult infection predominates and greater than 70% in regions where perinatal infection is higher. Evidence that mass immunization is followed by decrease in the incidence of liver cancer has been reported in Taiwan and the Republic of Korea. The efficacy of vaccination in preventing perinatal infection is improved by the addition of hepatitis B immunoglobulin administration soon after birth. Efforts made by the Global Alliance for Vaccines and Immunisation (GAVI) has resulted in inclusion of hepatitis B vaccination in national immunization programme of India and most of South Asia. Due to expiry of intellectual property rights on HBV vaccine and development of its own manufacturing units, the economics of implementing nationwide immunization against hepatitis B has become affordable for the region.

An effective vaccine has been available for prevention of new infection with HBV. However, vaccine against HCV infection is not available as yet. Interferon (IFN) has potent antiviral activity against hepatitis C virus. Previous studies have shown that IFN can reduce the incidence of hepatocellular carcinoma in patients with HCV infection. After complete eradication of HCV by IFN therapy, HCC rarely occurs. The risk of HCC might increase in patients with chronic hepatitis who have complete responses to IFN therapy. New regimens combining IFN with antiviral drugs can improve the rate of HCV clearance.

Interferon is effective in patients with HBV-related chronic hepatitis and is known to reduce serum HBV DNA concentration, improve biochemical data, and consequently suppress disease progression to cirrhosis. Previous studies reported that IFN therapy successfully reduced hepatocellular carcinogenesis in patients with HBV-related cirrhosis and induced tumor regression with inoperable HCC. On the other hand, in terms of HCV-related HCC, it is reported that long-term IFN therapy suppresses tumor recurrence after radical operation for HCC.

How to prevent HBV and HCV infection

Apart from vaccination, various other prophylactic approaches such as avoiding transmission of the infection by blood contacts such as during medical and dental interventions, blood products, tissue/organ transplants, disposable syringes and awareness among adolescents and adults of the need for hygienic sexual practices are the effective approaches to control hepatitis virus infections. In addition, community programmes for control of contamination of food and water with aflatoxins and reduction in alcohol consumption could also reduce the risk for development of liver cancer. Provide counseling and educational programmes through audio-visual and print media for avoiding any type of body piercing activities including tattooing which is very common in Asia, occupational...
exposure, cross-contamination during intravenous drug injections, screening all blood and other human products, and screening of pregnant women for HBV/HCV infections.

**Human immunodeficiency viruses, AIDS and cancer**

The human immunodeficiency viruses (HIV-1 and HIV-2), the etiological agents of the acquired immune deficiency syndrome (AIDS) belong to the lentivirus family of the Retroviridae family. South Asia especially India has the second largest population with HIV infection and AIDS following Africa.5,38 Prevalence rates are lower in other parts of South Asia but rising slowly, particularly in Pakistan and Nepal. The prevalence of HIV in India is heterogeneous; it is concentrated in some southern and western states while most of India has low prevalence. Diagnosis of infection with HIV relies on the identification of specific antibodies to viral proteins, or direct detection of viruses or viral proteins. HIV infection is marked by the decrease in CD4+ lymphocytes and CD4+:CD8+ cell ratio.39 The development of AIDS is defined by the occurrence of one or more specific opportunistic infections especially tuberculosis, malignancies such as non-Hodgkin’s lymphoma, Kaposi’s sarcoma and related diseases occurring in patients with HIV infection. In South Asia, the prevalence of kaposi’s sarcoma is quite low as compared with reports from Africa, USA and United Kingdom.40,41 However, the data from India and Pakistan indicate that patients with AIDS have an increased risk of developing non-Hodgkin lymphoma.42,43

**Scientific evidence for disease etiology**

Epidemiological evidence indicates that the incidence of Kaposi’s sarcoma is greatly increased in persons infected with HIV-1 with a relative risk of 1000 fold with progression of immunosuppression.5 Human herpesvirus type 8 (HHV-8) is the leading candidate as a cofactor for the development of this cancer. HHV-8 seroprevalence was found to be low in South Asia in both the healthy and the HIV-infected populations.48 This correlates with the fact that hardly any AIDS-related Kaposi’s sarcoma has been reported in these countries. Non-Hodgkin’s lymphoma incidence is greatly increased in persons with HIV-1 infection. Co-infection with specific viruses like Epstein-Barr virus (EBV) is associated with primary lymphoma of the brain and body-cavity lymphomas and multicentric Castleman’s disease are associated with HHV-8. Studies of women infected with HIV show increase in development of cervical carcinoma and HPV infection.49 Since HIV-1 tat protein may also enhance the development of HPV-related precancerous and anogenital lesions, it is considered that the immunosuppressive effect of HIV-1 infection is the main cause of development of malignancies in AIDS.

**Methods and characteristics of effective intervention**

More than 40 preventive vaccines for HIV/AIDS are being tested around the world. Aventis, Merck, Chiron and GlaxoSmithKline (GSK) are some of the companies in the forefront of research. But two phase – III trials carried out in Thailand and the USA have not demonstrated any significant level of efficacy. Efforts have also been made to combine two different type of vaccines i.e. VaxGen’s AIDSVAX with Aventis Pasteur’s ALVAC-HIV but it also did not work.46

In the absence of an effective treatment or vaccine, control and prevention of HIV infection continues to rely on behavioral interventions. The main routes of HIV-1 transmission are sexual intercourse, blood-blood contact and from mother to infant, including breast-feeding.5 The risk of transmission through all routes is associated with viral load in the infected person. Other factors like presence of other sexually transmitted diseases, especially genital ulcerative disease also increase the sexual transmission.47 Use of appropriate physical barriers such as condoms during intercourse is the most recommended. However, in some African countries abstinence has been promoted though it is less acceptable. In preventing sexual transmission, reducing the number and modifying the types of sexual contacts and consistent and correct use of condoms are essential. In addition, strong genital hygiene is to be promoted. Transmission from mother to child is associated with vaginal delivery and with breast feeding. Appropriate counseling of HIV positive mothers should be promoted to avoid vaginal delivery and breast feeding of their infants. Drug-dependence treatment programmes and improving the availability of sterile needles are possible effective measures to control
the HIV epidemics among intravenous drug users. Apart from these, stringent screening of blood from donors should be performed to prevent passive infection entry.

New approaches to the treatment of HIV infected people include combination therapy and use of anti-retroviral drugs and protease inhibitors and are the only alternative in the absence of effective and economical preventive vaccine for HIV which still faces many obstacles.

**Human T cell lymphotropic virus and cancer**

Human T cell lymphotropic virus (HTLV-I and HTLV-II) are complex retroviruses and play an important role in the pathogenesis of HTLV associated adult T cell leukemia/lymphoma (ATLL). Evidence of HTLV-I infection was originally found in at least 90% of patients with ATLL in endemic regions. In ATLL, the virus is clonally integrated into the tumor cells. ATLL develops in 2-5% of HTLV-I infected individuals. Infection early in life appears to be important for the development of ATLL. No environmental co-factors promoting the progression to ATLL have so far been identified. A recent study revealed a strong disease association of HTLV-I with haematological malignancies and provided evidence for both horizontal and vertical transmission of the infection in the Indian population.46 HTLV-I infection appears to be common among family members of individuals with HTLV-I associated haematological malignancies.

**Methods and characteristics of effective intervention**

There is no preventive vaccine available for HTLV infection in humans. Therefore, control and prevention of HTLV infection primarily depends on reduced transmission. HTLV-I infection is caused by transmission of live lymphocytes via three routes: perinatal, sexual and parenteral (from mother to child, from males to females, and by transfusion). Familial occurrence of ATL is frequently seen.49 Perinatal transmission can be greatly reduced by avoidance of prolonged breast-feeding. A number of countries have introduced universal screening of blood donors to prevent transmission of HTLV.

**Helicobacter pylori and cancer**

H. pylori, a spiral, flagellated gram-negative bacterium that colonizes the human gastric mucosa was first isolated in 1982. The infection is ubiquitous but the strains are genetically heterogeneous, and this attribute is useful to study its transmission.3, 40 In most cases, it is acquired early in life through oral contamination and persists with no or mild symptoms. H. pylori causes a chronic infection which rarely resolves spontaneously. Its transmission is favoured by overcrowding and low economic status and is most prevalent in developing countries.51 H. pylori can be detected in gastric biopsy specimen and indirectly by serology and analysis of breath after ingestion of labeled urea (as it possesses a strong urease activity). Standard histological and bacteriological techniques and PCR are highly sensitive diagnostic tests. Epidemiological studies currently involve use of serological tests and mainly commercially available ELISA kits. The actual distribution of Helicobacter pylori infection and its related diseases in South Asia is controversial. There is a large inter-country variation in incidence of gastric cancer and H. pylori seroprevalence in South Asia. There is a strong link between H. pylori infection and gastric cancer in many countries, such as Japan. By contrast, the prevalence of H. pylori infection is high in some countries, including India and Bangladesh, but low gastric cancer rates have been reported from these regions.52

**Scientific evidence for disease etiology**

The common gastric disorders that develop in infected persons include chronic gastritis, duodenal ulcer and, in a small number of individuals, gastric cancer or B cell mucosa-associated lymphoid tissue lymphoma. Marshall and co-workers provided the first evidence that H. pylori causes gastric inflammation for this discovery he was awarded the Nobel prize in Physiology or Medicine in 2005. The bacterium has been shown to increase cell replication in the gastric mucosa and induce inflammation through expression of IL-83,54 which results in increased cell replication in the gastric mucosa. The association between prior seropositivity for H. pylori and subsequent gastric cancer has been
evaluated by IACR experts. Significant positive associations were observed with cumulative relative risk of 3.8. The relative risk increased with the increase in the length of follow-up.

Methods and characteristics of effective intervention

The transmission of H. pylori occurs from one person to another; both oral-to-oral and oral-to-faecal routes. Epidemiologic studies of atrophic gastritis which is essential to the development of gastric cancer have also shown an association with dietary factors, especially excessive salt and nitrate intake and inadequate consumption of fresh fruits and vegetables. H. pylori can be cultured and is sensitive to most antibiotics. Therefore, an early detection can lead to bacterial eradication by antibiotic treatment. In two studies of treatment, 75 to 85% gastric cancer patients showed tumor regression after therapy to eradicate H. pylori. However, the option appears to be less feasible in view of prophylactic treatment of a large population at all ages.

Epstein-Barr virus and Cancer

Epstein-Barr virus (EBV) is a gamma-1 herpesvirus found throughout all human populations, with a prevalence of over 90% in adults. Primary infection usually occurs in the early childhood and is asymptomatic, whereas delayed primary infection may cause a self-limiting lymphoproliferative disease, infectious mononucleosis. B lymphocytes are a normal reservoir for latent infection. Only a small fraction of latently infected B lymphocytes spontaneously enters the productive cycle. EBV infection has been primarily related with development of nasopharyngeal carcinomas, Burkitt’s lymphoma, non-Hodgkin’s lymphomas, Hodgkin’s disease and related weakly with lymphoepithelial and adenocarcinomas. Nasopharyngeal carcinoma is a rare malignancy in most populations, although very high rates are seen in populations from southern China and more moderate rates in other parts of South East Asia. Nasopharyngeal carcinoma show higher prevalence rates in some southern states and northeast frontiers of India. However, this carcinoma is quite infrequent tumor in Pakistan and only a small portion of them show presence of EBV.

Scientific evidence for disease etiology

Monoclonal EBV DNA and viral products are consistently detected in malignant nasopharyngeal carcinoma cells but not in normal nasopharyngeal epithelium which strongly implicate EBV as a causative factor in the etiology of the disease. The viral DNA present in Burkitt’s lymphoma cells is also in monoclonal form. However the frequency of this association varies geographically. The importance of EBV in the causation of Burkitt’s lymphoma appears to be greatest when infection occurs in the early years of life. As seen in African populations, malaria acts as an important cofactor in the development of Burkitt’s lymphoma. EBV has particular importance in non-Hodgkin’s lymphomas occurring in immunosuppressed individuals, who are at increased risk. Non-Hodgkin’s lymphomas in transplant recipients and in patients with congenital immunodeficiencies are nearly always EBV-positive.

The consistency of the finding of clonal EBV and the expression of LMP-1 in about half of Hodgkin’s disease cases in many patient populations throughout the world argues strongly against a passenger role for the virus in these cases.

Methods and characteristics of effective intervention

One cause of nasopharyngeal carcinoma in high risk populations is Chinese-style salted fish, a known carcinogen. Other preserved foods and cigarette smoking have also been implicated in its carcinogenesis. Saliva is the usual vehicle of transmission of EBV.

Few drugs are available that prevent viral replication without significant toxicity. Acyclovir and a number of related compounds have been used successfully to reduce viral replication but with no significant effect on persistent infection. Prophylactic, post-infection and therapeutic EBV vaccination strategies are currently being developed with recombinant subunit viral proteins and live recombinant virus vectors. The success of this endeavour will depend on a better understanding of the EBV life cycle and the immune response generated by natural infection in humans.
Conclusions and Recommendations

Evidence-based decision making in human health and disease requires the availability of sound data, but good quality information on the occurrence of premature mortality and loss of healthy life years due to infection related malignancies is unavailable from most of South Asia. Therefore, there is an urgent need to develop a database in this respect to prioritize and to focus the intervention efforts.

Considering the heterogeneity in the prevalent infections and diverse disease patterns, locally relevant intervention programmes are needed to be formulated than a one specific approach for all. As a first step behavioural surveillance programmes have to be initiated to improve the understanding of transmission patterns.

In resource-poor regions, information about the infectious agents, and their role in development of various cancers should be disseminated through audio-visual and print media, awareness camps and community programmes.

Organization of frequent early cancer detection camps for effective cancer control and improving care-seeking behavior of the patients.

Immunization with vaccines at an early age should be promoted wherever the vaccines are available such as in case of HBV and HPV.

Programs may be undertaken to educate masses about cancer-promoting agents including tobacco, and their occupational or otherwise exposure.

Promote personal and community hygiene in food and drug usage.

Training of primary health-care professional for visual inspection of cervix should be imparted which has been demonstrated to be a very effective strategy for control of cervical cancer in resource-poor set-up.

Surveillance systems for infectious diseases are lacking in most of South Asia, which is essentially required for detecting and monitoring the occurrence of infectious diseases important to public health and for measuring the effectiveness of targeted intervention. There should be involvement of staff in the government and private sector, sentinel laboratory surveillance, simple reporting procedures and regular feedback to the data providers.

Monitory support should be provided for creation of epidemiological baseline data on infection-associated cancer in the region.

Support should also be provided for development of low cost vaccines and already developed vaccines should be made available at affordable cost.
References


