

REVIEW ARTICLE**Viral Diseases of Public Health Importance in India: Current Priorities with Special Emphasis on Prevention**

Mageshbabu Ramamurthy^{1}, Sathish Sankar¹, Balaji Nandagopal¹, Gopalan Sridharan¹, Arun R.Risbud²*

¹*Sri Sakthi Amma Institute of Biomedical Research, Sri Narayani Hospital and Research Centre, Sripuram-632055 (Tamil Nadu) India, ²Directorate of Research, Krishna Institute of Medical Sciences Deemed University, Karad-415110 (Maharashtra) India*

Abstract:

India faces problems with both communicable and non-communicable diseases. The major non-communicable diseases are cancer, cardiovascular disease and diabetes mellitus. This article focuses on communicable diseases (infectious diseases) especially viral infections of public health importance. The infections include bacterial, parasitic and viruses. It could be said that fungal infections by the nature of the spread are not of public health concern. The viral infections are transmitted by the respiratory route, water and food-borne route, vectors and blood and blood products, sexual route and are of major concern. Efforts are aimed at early detection, prevention by use of vaccines and sentinel surveillance. For the success of public health programmes sentinel surveillance of diseases is mandatory. India has got several programme initiatives addressing the problem. The programs include IDSP, VBDCP and NACO. The approximate cumulative annual prevalence of infectious disease in India ranges from 100 to 200 million individuals affected in one year. India should aim to improve case detection by strengthening laboratory services with manpower training and nationwide quality control scheme, sentinel surveillance activity and prevention by improving the efficiency and scope of UIP. Also, creation of a single portal of infectious disease data handling hub to collect information from different sources will help avoid overlap and duplication of reporting.

Keywords: Epidemiology, Emerging, Dengue virus, HIV, Acute Encephalitis Syndrome

Introduction:

India is a vast geographical area with different habitats. We have urban centres, rural areas, tribal areas and vast forested areas, each of them posing different public health challenges. India has problems of public health importance including both communicable (infectious disease) and non-communicable diseases [1]. The present article focuses on communicable diseases, especially, viral infections. Historically, viral infection outbreaks have significantly outnumbered the outbreaks of other etiologies. India has successfully controlled or eradicated several communicable diseases by introducing sentinel surveillance and vaccine intervention as well as public health measures. The term sentinel surveillance refers to establishment of field units capable of accurate clinical diagnosis, laboratory diagnosis and data collection. The surveillance site could be hospital or a community-based field epidemiology unit. A long-term data and the data gathered at regular intervals at such field units are of vital importance not only for investigation of epidemics and outbreaks but also for predicting such outbreaks. Universal Immunization Programme (UIP) under the Ministry of Health and Family Welfare (MoHFW) has been significantly expanded by inclusion of newer vaccines over the last fifty years. Successful

control of several childhood illnesses like diphtheria, whooping cough, poliomyelitis and measles has been achieved through vaccination in infancy and childhood booster doses. Previously, as part of the global programme, small pox was eradicated in India forty years ago [2]. Presently, poliomyelitis caused by wild poliovirus has been eradicated in the country [3]. However, Acute Flaccid Paralysis (AFP) polio-like-illness caused by Non-polio Enteroviruses (NPEV) is active throughout the country and is monitored through the AFP control programme under the auspices of WHO and MoHFW which also ensures that the cases of poliovirus infection and disease are not missed [4].

The communicable diseases of public health importance include those that can occur as small outbreaks in communities, epidemics in communities and pandemics that affect large areas of the country. Several infectious diseases have the potential to cause severe morbidity and unacceptable mortality in the community [5]. Presently, among the agents, including bacterial and parasitic, that are of public health concern, viral infections top the list. The acute viral infections with wide spread prevalence in several parts of the country include dengue fever, chikungunya fever, viral diarrheas and respiratory infections [6-8]. There is a major public health problem with enterically transmitted hepatitis viral agents like Hepatitis A Virus (HAV) and Hepatitis E Virus (HEV) as well [9].

Blood borne viral infections which are chronic in nature are widely prevalent in all parts of India and include Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) [10]. The identification of the communicable agents is achieved in different areas by various state and central government health /

research facilities. The national agencies like Integrated Disease Surveillance Programme (IDSP) use the existing laboratory services in medical colleges and District hospitals to collect information on several diseases. Along with certain other viral infections such as Japanese encephalitis surveillance, Dengue fever surveillance and control is presently under the National Vector Borne Disease Control Programme (NVBDCP) established in 2004. In the face of the global influenza pandemic a network of influenza surveillance laboratories was established in 2006 under IDSP. A Multisite virological Influenza surveillance in India was started by Indian Council of Medical Research in 2004. The National AIDS Control Programme (NACP), launched in 1992 as a part of National Aids Control Organization (NACO) has paid rich dividends.

Epidemiological Aspects of Viral Diseases:

Viral diseases active in a country take three major forms, they include, Epidemic: A typical episode of a viral disease occurrence in a population or region of the country not previously affected at that magnitude. The frequency of viral disease known to occur in a given community is exceeded during an epidemic. The appearance and spread of a new etiological agent of a given infectious syndrome also constitutes an epidemic. The term outbreak may be used if the number of human cases is small and occurs only in a restricted area of a metropolitan city or contiguous rural area (few villages). Endemic: The continuous activity of a viral agent in the community at low levels affecting small number of people usually is the characteristic of an endemic viral infection. Pandemic: When large number of people are affected over a wide geographic area inclusive of parts of the country or the entire country and several continents of the globe by a viral agent [11].

Use of standard case definitions is vital for investigating and describing an outbreak/epidemic.

They may be seen to be seasonally related to climatic conditions or vector density. Such infections include Dengue fever and Japanese encephalitis. Outbreaks of infections if not controlled have the potential to become epidemics. It has been pointed out that small outbreaks may disappear due to lack of critical population size of susceptible individuals. On the contrary, when a threshold of infected individuals is reached among the population of susceptible individuals (critical community size), epidemics are prone to occur [12]. Certain epidemics have persisted over long periods like HIV/AIDS now active in the country over the last thirty years. Some infections have originated in certain geographical areas and spread to different regions and countries. These infections which involve large number of people and spread over vast areas constitute a pandemic also referred to as global pandemic. We have had a major pandemic of influenza A virus infection between 2009 and 2010. In addition, preventable iatrogenic infections have been reported as outbreaks of infections by blood-borne viruses due to procedures carried out by infected medical professionals or poor practices. There are proven cases of HBV and HIV acquired in hospital settings [13].

Emerging and Reemerging Viral Infections

An emerging disease could be defined as an infection with clinical disease that has appeared in a population for the first time. It may also have existed previously as geographically restricted and affecting small numbers of people but has rapidly increased in incidence or geographic range. Re-emerging infectious diseases could be

defined as those that were previously major health problems either in certain countries or worldwide. Pattern of occurrence of these infections/diseases over the previous few years suggested that they would have declined significantly, but again started spreading in human populations [14]. Several features which include changing weather pattern due to global warming contributing to vector boom, poor sanitation and water hygiene due to overcrowding and increased travel resulting in spread through carriers or asymptomatic infected individuals and change in life styles. In this category, Arthropod-borne viruses (arboviruses) have become major public health problems in India, with considerable morbidity and mortality. The South East and South Asian regions are particularly affected because of both climatic and environmental conditions conducive for increase in vector population close to human habitation. Infections such as Dengue (DEN) fever, Japanese Encephalitis (JE), West Nile Virus (WNV), Chikungunya (CHIK) fever, Kyasanur Forest Disease Virus (KFDV), are continuing to increase in the different geographical regions of the country. These infections could be referred to as re-emerging viruses. If Zika virus infection is detectable in multiple points in India, it could be deemed as an emerging infection. Even more alarming is the evidence of yet another hemorrhagic fever such as Crimean-Congo Hemorrhagic Fever (CCHF) [15]. In India, a condition termed Acute Encephalitis Syndrome (AES) may have virus etiology as the principal component, but also being recognized is the role of rickettsial species. The viral etiologies identified in AES seen in India include JEV, non-polio enterovirus species and Chandipura virus. The relative contribution of these agents to mortality is shown in (Fig. 1).

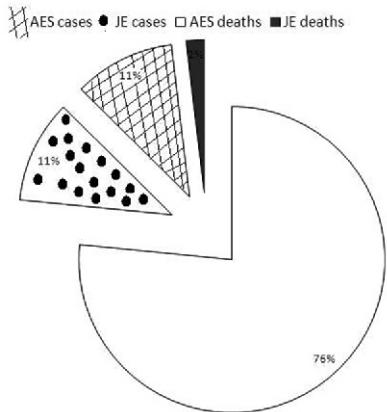


Fig. 1: The Mortality Related to Encephalitic Illness

Dengue fever is active in several parts of the country and the number of laboratory confirmed infections reported to NVBDCP has quadrupled in the reporting period 2010 to 2016. In the year 2016 the number of cases is about 130000 and may be an underestimate, this is shown in (Fig. 2). India has had a major epidemic of Chikungunya for a few years starting in 2005 [16] which was part of a global pandemic affecting several hundred thousand individuals. There were arthropathic complications in thousands of individuals following this epidemic [17]. DEN fever is now active every year in several parts of the country affecting millions of individuals [7].

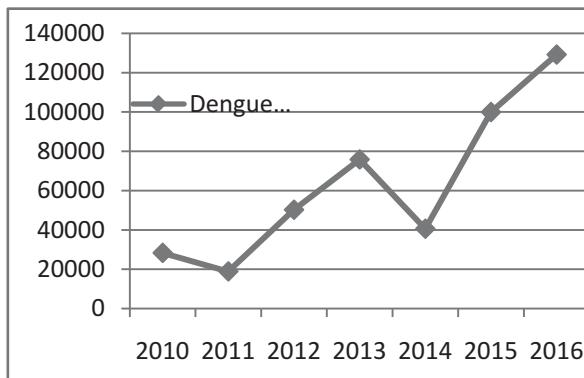


Fig. 2: Dengue Cases from 2010 to 2016 Reported to NVBDCP

In the last two decades, Severe Acute Respiratory Syndrome (SARS) and Ebola epidemics have emerged in South East Asia and Africa respectively causing deadly disease especially with Ebolavirus.

SARS – Coronaviruses (CoV) and Middle East Respiratory Syndrome (MERS)-CoV: Bats have been identified as the natural reservoirs of SARS-CoVs and likely the reservoir of MERS-CoV. However, MERS-CoV affects camels and humans. Infection with SARS-CoV and MERS-CoV infection produce similar clinical symptomatology but infection with MERS –CoV progresses rapidly [18]. These infections have not made a significant appearance in India.

Kyasanur Forest Disease (KFD), a tick borne hemorrhagic fever endemic in India, was first reported in the forested area of Shimoga District of Karnataka. Over the last ten years the virus has moved out of its original geographical boundaries into border areas of Kerala, Tamil Nadu and Maharashtra. Several small outbreaks have been reported in the contiguous four-State forest areas with significant morbidity and mortality [19].

WNV causes fever with or without encephalitis and is transmitted by mosquito (*Culex* spp). The virus is shown to be very active in continental United States. Horses and birds are the natural reservoir. In contrast to date, India has experienced only minimal activity of WND virus [20]. Chikungunya virus was first detected in 1963 in Calcutta. Reports of large scale outbreaks of fever caused by chikungunya virus infection have been recognized in several parts of Southern India starting in late 2005 [16].

Chandipura Virus (CHPV) is a vesiculovirus of Rhabdoviridae is now recognized as a neurotropic pathogen. It causes high mortality in children within a day of start of symptoms. In 2003-2004

there were outbreaks in Central India with high case fatality rates (56-75%). Phlebotomine sandflies are recognized as vectors [21].

NPEV is now gaining attention causing neurological illness like AES and Hand Foot and Mouth Disease (HFMD) in different parts of India. Several serotypes of enteroviruses like Coxsakie virus A16, EV71 are implicated with this illness [22].

CCHF is a tick-borne viral disease causing a fatal hemorrhagic illness in humans but the disease could also be asymptomatic. CCHF was first confirmed in a nosocomial outbreak in 2011 in Gujarat State. Antibodies to CCHF virus (IgG) was detected in domestic animals of the area. The seropositive rate was between 12% and 41% [23]. Zika Virus (ZIKV) is an arbovirus of the Flavivirus genus. The World Health Organization declared ZIKV infection to be an emerging global health threat in 2016. However, considering the subsequent evidence, presently, the alert is downgraded. ZIKV is transmitted by Aedes mosquitoes; also this virus could be spread between humans by transplacental, perinatal, and sexual routes and via blood and body fluids. Neurological manifestations include Guillain-Barré syndrome (GBS), meningoencephalitis, acute disseminated encephalomyelitis, acute myelitis, and transverse myelitis. Infection of mothers during early pregnancy is associated with intrauterine and congenital ZIKV infections which lead to congenital malformations like microcephaly [24]. The MoHFW reported three laboratory-confirmed cases of Zika virus disease in Bapunagar area, Ahmedabad District, Gujarat, State, India

Existing Infrastructure/Programmes in India for Control of Viral Diseases:

Public health delivery is carried out through intervention in the control of outbreaks and epidemics and use of vaccines for vaccine preventable diseases in neonatal to early childhood age groups. The Union Government through the state Government under Universal Immunization Programme (UIP) provides primary vaccination and required boosters in early childhood for a number of vaccine preventable childhood diseases. The viral vaccines used include: trivalent oral polio vaccine (tOPV), now replaced by bivalent-bOPV excluding PV2, Hepatitis B Vaccine and Measles vaccine. Presently, Rubella and killed polio vaccine KPV has been introduced through the Indhradhanush vaccine programme. A major malady is AES which could include cases of Japanese encephalitis. In the face of outbreaks of JE, JE vaccine has also been used in affected geographical areas. In addition, rotavirus vaccine is introduced in several states [25].

IDSP programme is another independent activity under the Ministry of health and family welfare. The objectives are:

1. To carry out surveillance through surveillance units at Centre, State and District level,
2. Training of State Surveillance Officers, District Surveillance Officers, Organize Rapid Response Team and other Medical and Paramedical staff for disease surveillance
3. Application of communication Technology for collection, collation, compilation, analysis and dissemination of data
4. This is vital to strengthening of public health laboratories.

Under the IDSP, India could start a program similar to Epidemic Intelligence Service (EIS) of CDC [26].

Influenza surveillance programme was established under IDSP to strengthening and networking of reference laboratories and re-establishing seasonal influenza surveillance system for India. Initially the network had 12 Regional labs with the Microbiology Division of the National Centre for Disease Control (NCDC), Delhi. In addition, surveillance laboratories were established by Indian Council of Medical Research (ICMR) / Department of Health Research (DHR) with CDC USA funding at several additional centres. Over all, the activities of these centres were strong between 2006 and 2015 and covered the recent influenza pandemic [27].

Data for the year 2015 reported to IDSP on outbreak surveillance is shown in (Fig. 3). The predominant outbreaks reported were diarrheal diseases followed by measles and dengue fever. We have in the country, a NVBDCP under the MoHFW. This programme provides support for outbreak/epidemic investigation and surveillance of vector borne infectious diseases. Under the

scheme, the supply of diagnostic IgM ELISA kits for detection of antibody against Dengue virus, Chikungunya virus and JE virus (<http://idsp.nic.in/index.php>) is undertaken to all participants of IDSP.

One of the priorities to improve the overall efficiency of this system requires strengthening of laboratory services to enable accurate and timely diagnosis of infections especially, those with the potential to spread in the community. From time to time the country has witnessed outbreaks and epidemics of several viral diseases like HAV and HEV infections, dengue fever, chikungunya fever. The diagnosis of these specific infections were achieved or confirmed at district or teaching hospitals. There is a significant participation of institutes under the ICMR which have maintained capacity to diagnose and monitor several viral infections like dengue fever, chickungunya fever and enterically transmitted hepatitis infections. Presently, ICMR under the DHR is working on several objectives as defined are:

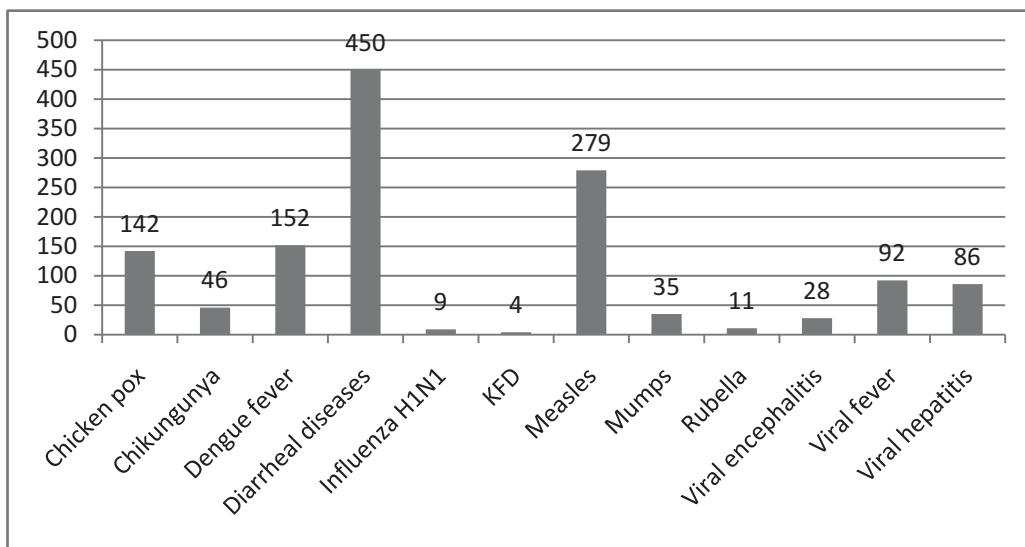


Fig. 3: Outbreaks of Important Infectious Diseases Reported in the Year 2015 (IDSP Data)

1. Create infrastructure for identification of etiological agents (viruses) of outbreaks/ epidemics viruses and other agents for bioterrorism.
2. Development of indigenous diagnostic kits
3. To provide training for health professionals
4. To carry out research on emerging infections.

The programme is enabling a network of laboratories focusing on diagnosis of viral infections under the scheme Virus Research and Diagnostic Laboratories (VRDL) started in 2014.

Currently, ICMR/ DHR is carrying out surveillance for Zika virus in the country using the VRDL network. This scheme has a reporting system to build a national database on sporadic virus infections and outbreaks with National Institute of Epidemiology (NIE), Chennai serving as the principal agency. The National Institute of Virology (NIV), Pune, is presently serving as the apex laboratory for the VRDL network and NIE, Chennai is managing the data generated by the network and performing timely analysis (<http://nie.gov.in/vdln/>). NIE provides the services through REDCap web-based application for building online surveys and databases. It is amenable for direct upload of Microsoft Excel worksheet for common statistical packages (SPSS, SAS, Stata, R) based analysis.

India is successfully controlling the HIV/AIDS global pandemic affecting several continents. The NACP of NACO has played a pivotal role in the control of HIV/AIDS through building up Voluntary Counselling and Testing centres, Antiretroviral Therapy (ART) centres and through supply of testing kits for HIV antibody and CD4 counts and instrumentation as well as drugs for

HIV. NACO has also drawn up and implemented testing and treatment guidelines. The data collected by NACO and given in the annual reports is tabulated in Table 1. It is important to note that both new HIV infection and AIDS related death has shown a steady decline between 2007 and 2015. The number of people living with HIV has remained more or less steady indicating the increased longevity of infected individuals due to access to ART and the widespread awareness among physicians to treat intercurrent opportunistic infections.

India has previously, successfully carried out small pox eradication under the WHO. As of 1979 there have been no cases of small pox in India. The reasons for this success were

- (i) Availability of highly protective vaccine
- (ii) no asymptomatic carriage of the virus with all infected humans being symptomatic
- (iii) The DNA virus was genetically stable and no other natural reservoir of the virus existed [28]. It is important to point out that this remarkable success will be not easily replicated. One has to see how long the control of wild poliovirus will be sustained.

Public Health Priorities in India:

Several communicable diseases are active periodically and some continuously in the country. Some arboviral infections are active in the post monsoon period in several parts of India. The most important infection is DEN fever which has become endemic in the country with hundreds of outbreak per annum in different geographical regions. Chikungunya and JE virus infections are also prevalent in several parts of the country with seasonal outbreaks. More recently KFD has spread in some southern states including the bordering

Table 1: NACO Data Indicating Changes in HIV Related Illness over a 9 Year Period

Year	People Living with HIV	New HIV Infection	AIDS Related Deaths
2007	2225930	15072	148309
2008	2198559	12294	136981
2009	2174594	10613	125522
2010	2156452	9852	115608
2011	2146839	9253	104327
2012	2143446	8776	96189
2013	2127958	8312	87946
2014	2119881	7900	76494
2015	2116581	7524	67612

areas of Maharashtra adjoining Karnataka. The live attenuated tetravalent DEN vaccine though licensed in four countries has not yet been introduced in India. The delay may be related to concerns regarding seroconversion rates and susceptibility to complications of DEN fever. JE and KFD vaccines are used in areas where there is disease activity.

One of the problems posed by communicable diseases like tuberculosis and HIV/AIDS is the disease burden for the community. Disease burden is a measure of the impact of the health problem in terms of financial cost, mortality, morbidity, or other indicators. Quality-adjusted Life Years (QALYs) or Disability-Adjusted Life Years (DALYs), both of which quantify the number of years lost due to disease and give an estimate of the impact of the particular disease [29].

We looked at WHO statistics on tuberculosis in relation to HIV status and mortality due to TB. This data is shown in Table 2. Data from India indicates that the percentage of TB mortality among HIV

negative individuals is 0.037% and in HIV positive individuals it is 0.009% which indicates the lower prevalence of HIV in the general population compared to TB. This is different from Africa where the mortality associated with TB is higher among individuals with HIV. This reflects the higher prevalence of HIV in the general population.

Infections with HIV and development of AIDS have slowed down in India with the multipronged strategy of NACO. The major effort initiated and maintained has been to ensure safety of blood and blood products in the country through appropriate testing of blood borne pathogens like HIV, HBV and HCV in blood banks and product testing by manufacturers [30].

Today, the total number of People Living with HIV (PLHIV) in India is estimated at 20 lakhs. The highest prevalence was recorded in Nagaland (1.29%), followed by Mizoram (0.81%), Manipur (0.60%), Gujarat (0.56%) and Chhattisgarh (0.41%). Telangana (0.39%), Bihar (0.37%),

Table 2: TB Mortality as Related to HIV Infection as per WHO Statistics for the Year 2015

Countries	HIV Negative TB Mortality	HIV Positive TB Mortality	Total TB Incidence	HIV Positive TB Incidence	Population	Percentage of TB Mortality among HIV Negative Individuals	Percentage of Individuals with HIV-TB Coinfections
India	480000	37000	2840000	113000	1310000000	0.037	0.009
Africa	450000	300000	2720000	834000	989000000	0.045	0.084
Americas	19000	5900	268000	32000	991000000	0.002	0.003
Eastern Mediterranean	80000	3000	749000	13000	648000000	0.012	0.002
Europe	32000	4900	323000	27000	910000000	0.003	0.003
Western Pacific	89000	5700	1590000	34000	1860000000	0.005	0.002

Karnataka (0.36%) and Andhra Pradesh (0.35%) were other States which recorded HIV prevalence of more than the national average. PLHIV on ART was over 9 lakhs. It is estimated that the scale-up of free ART since 2004 has saved cumulatively around 4.5 lakhs lives in India until 2014.

Hepatitis infection broadly classified as enterically transmitted and blood borne infections are a major public health problem. The enterically transmitted infections caused by hepatitis A virus and E virus tend to occur as epidemics, especially the latter. A good vaccine is available for HAV. The vaccine is used only in the private sector. The blood borne hepatitis B and C are wide spread in the community and endemic. They affect several million individuals. Liver cirrhosis as a long term complication of such infections is second most common to alcoholic liver disease and a leading cause of liver carcinoma. India is a middle level endemic country in terms of prevalence of

Hepatitis B virus. It is estimated that there are at least 40 million Indians who are chronically infected by HBV as measured by hepatitis B surface antigen and serve as a source for spread of infection. The vaccine against hepatitis B is available to children under the UIP [31, 32].

Suggested Plan of Action for the Future:

India has had an active public health programme with a strong mandate to control infectious diseases over the last sixty years. Many organs of the central government work under the union ministry of health and family welfare in addition to state authorities. The approach has been diagnosis (detection), treatment (where possible) and appropriate vaccination programs. India's vaccination programme is good in many states but needs sustained effort to improve it in a few large states of the union.

A vital activity is to strengthen the laboratories to help detect major problems. There should be an

effort to use state-of-the-art technologies with good quality control measures in place. In this context the National Accreditation Board for Testing & Calibration Laboratories (NABL) is making advances both in private sector and public sector to improve quality of medical diagnosis laboratories [33]. Efficient drug availability for HIV control under the national programme should be strengthened. The UIP may need to include few additional vaccines to their programme like more developed countries. Introduction of countrywide use of Rotavirus vaccine is being considered under UIP. These newer vaccines could be rubella vaccine, Human papilloma virus vaccine for young teenagers.

Establishment of a single portal for Integrated Data Handling for infectious diseases avoiding duplication in annual reports to MoHFW from all agencies including ICMR, IDSP, RNTCP, NVBDCP, NIE-VRDL will allow to develop a comprehensive picture of the massive public health problem that India faces in this area. India has had success in creating several National portals for data handling in other areas like banking and finance, Unique Identification Authority of India (UIDAI) and Income Tax (IT) filing of returns. Only a signal portal on ID issues will help in planning country wide public health measures and vaccine delivery.

Conclusion:

Communicable diseases still pose a major public health problem in India. The estimated annual prevalence of infectious disease in India ranges from 100 to 200 million individuals affected in one year. Some of the infectious diseases periodically cause outbreaks and India has experienced two major pandemics, the HIV pandemic is slowing down, where as the influenza A pandemic has abated since, 2014. We do face the risk of several outbreaks / epidemics of diarrheal diseases and Arboviral infections like Dengue fever, Chikungunya fever. Success is being gained in the control of several childhood infections like diphtheria, pertussis, measles and poliomyelitis. In addition India previously eliminated the small pox virus infection and recently poliovirus disease. Improvement in environmental sanitation, availability of safe drinking water and use of appropriate nation-wide vaccination programme under the UIP will make a significant dent in the problem of infectious diseases. In order to successfully implement disease prevention Public health surveillance is mandatory. It involves a continuous systematic case recognition and appropriate sample collection and analysis. Based on this information the officials could do the interpretation of data, planning, implementation, and evaluation of the programme initiatives.

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***Author for Correspondence:** Dr. Mageshbabu Ramamurthy, Sri Sakthi Amma Institute of Biomedical Research, Sri Narayani Hospital and Research Centre, Sripuram-632055 Tamil Nadu, India
Email: rimageshbabu@rediffmail.com Cell: 09442505480