Plague in India: A Review

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Abstract

Plague, most ancient, dreadful and formidable pestilential rodent borne disease was a major public health problem in India till the mid twentieth century A.D. Plague is one of the three epidemic prone diseases still subject to the International Health Regulations and notifiable to the World Health Organization (WHO). In India mortality due to plague reached zero level during 1967. However, sporadic cases of suspected human plague were reported from Himachal Pradesh during 1966 and 1983-1984 and Karnataka during 1984 and at times localized sylvatic plague incidence encountered in the last decade from the trijunction of Karnataka, Andhra Pradesh and Tamil Nadu in peninsular India. During 1994 a bubonic plague outbreak at Beed district, Maharashtra and pneumonic plague outbreak in Surat, Gujarat were recorded. After 8 long years of quiescence a localized outbreak of pneumonic plague occurred in Himachal Pradesh in 2002. In 2004, a bubonic plague outbreak occurred in Uttarkashi district, Uttarakhand.

Plague continues to exist as a major public health problem in many countries of the world. In several countries plague has remained quiescent for years together before reappearing all of a sudden. The enzootic foci of plague in India is believed to be present in four groups of foci in northern, central, western and southern India. From 1989 to 1994 active zoonotic foci of plague were detected from the trijunction of Tamil Nadu (Krishnagiri district), Andhra Pradesh (Chittoor district) and Karnataka (Kolar and Bangalore rural district). As the sylvatic rodents live in wild and peri-domestic situations and maintain the natural transmission in enzootic foci for centuries together, eradication of the disease is highly impossible. Natural decline in plague incidence would not justify the conclusion that plague has disappeared from the area. Since the beginning of the 1990s, the number of plague cases shows rising trend worldwide, and outbreaks are reappearing in various countries of the world after decades of quiescence.

Under reporting of plague cases may be attributed to lack of diagnostic facilities for the confirmation of the cases and cessation of plague surveillance work by number of erstwhile plague endemic countries, where non-occurrence of cases for long years gave false impression that *Yersinia pestis* are no longer circulating.

A plague outbreak may cause widespread panic, as occurred in India in 1994 when a relatively small outbreak, with 54 deaths, was reported in the city of Surat. Plague should not be relegated to the sidelines. It remains a poorly understood threat that we cannot afford to ignore.

Potential new foci should be confirmed and investigated, with special attention to harbours with international trade. National plague surveillance programmes and regional collaboration are needed to be strengthened.

**Keywords:** Epidemic, Pandemics, *Yersinia pestis*, Biovars, Resurgence, Enzootic, Sylvatic, Insecticide resistant, Bamboo flowering

Introduction

Plague, one of the most ancient, dreadful and formidable pestilential rodent borne zoonotic diseases continues to exist as a major public health problem in many countries of the world. Plague, a disease of antiquity was well known to the mankind as a communicable disease initially started with unusual increase in deaths of rodents termed as rodent...
epizootics or rat fall in domestic or peri-domestic situation. Epidemics of human plague usually followed by rodent epizootics. Plague as a disease was mentioned in Bhagvata Purana (155- 600 BC). An account of pestilence among the Philistines exists in 5th & 6th chapters of the first book of Samuel. Similar description finds places in the first book of Kings (vulgate version). Before the discovery, acceptance of theory of microbial causation (discovery of a bacterium as a causative agent of plague was made by Yersin and Kitasato in 1894 in Hong Kong) and for prevention of the disease people were advised to leave the places where rodents carcasses found in large numbers due to unnatural deaths and occurrence of bubonic case started.3,11

Plague, was a major public health problem throughout India till the mid twentieth century A.D. The authenticated plague epidemic started in the year 1895-1896 and reached its peak in 1907. During the two decades from 1898-1928 there were over 12 million deaths in undivided India. The decennial death rate due to plague in India per 1,00,000 population during these decades were 183.3,133.8 and 51.9 respectively. During 1949-1958 mortality rate due to plague was calculated to be 1.8 per 1,00,000 population. Since then mortality had declined and reached zero level during 1967 (Table 1).11

Table 1. Decennial Mortality trend from Plague in India during 1898-1968*

| Period     | Total Deaths from Plague | Specific mortality rate/100,000 | Plague as percent of total deaths 1898-1968 |
|-----------|--------------------------|-------------------------------|---------------------------------------------|
| 1898-1908 | 6,032,693                | 183.3                         | 47.47                                       |
| 1909-1918 | 4,221,529                | 133.8                         | 33.32                                       |
| 1919-1928 | 1,762,718                | 51.9                          | 13.4                                        |
| 1929-1938 | 422,880                  | 11.7                          | 3.33                                        |
| 1939-1948 | 268,596                  | 6.8                           | 2.11                                        |
| 1949-1958 | 90,059                   | 1.8                           | 0.46                                        |
| 1959-1968 | 942                      | 0.2                           | 0.001                                       |
| After 1968-1993* |                      |                               |                                             |

* Source: NICD/WHO Publication on Plague

**Dramatic Reduction of Plague cases in India**

The reasons for dramatic reduction in plague incidence in India since 1948 and a sudden recrudescence in certain areas can only remain in speculation. However, two important anti-plague measures to combat the disease were made available immediately after the second world war. Streptomycin and Sulphonamide were found to be very specific for plague treatment and universal use of DDT in rural areas in India since 1958 under National Malaria Eradication Programme (N.M.E.P) intercepted plague transmission among the commensal rodents by reducing the rat flea index below critical level (≥1.0). This led to a marked reduction in human plague incidence in all ecological zones except in peninsular India.

**Resurgence of Plague in Peninsular India**

There was a resurgence of plague in bordering districts of Tamil Nadu, Andhra Pradesh and Karnataka states during 1959 to 1966 (Fig.1,2,3). This may be attributed to discontinuation of DDT spray under National Malaria Eradication Programme in these areas. The last human plague case in India during the period was reported from Mulbagal in Kolar District, Karnataka in 1966.1,2
Though human plague cases were not reported from India since 1967, yet sporadic cases of suspected human plague were reported from Tangnu, Himachal Pradesh during 1966 and 1983 and Attibele, Karnataka during 1984 and at times localized sylvatic plague incidence encountered in the last decade from the trijunction of Karnataka, Andhra Pradesh and Tamil Nadu in peninsular India. During 1994 a bubonic plague outbreak at Mamla village, Beed district, Maharashtra and pneumonic plague outbreak in Surat, Gujarat were recorded.

After 8 long years of quiescence a localized outbreak of pneumonic plague occurred in Hatkoti, Shimla district, Himachal Pradesh in 2002. In 2004, a bubonic plague outbreak occurred in Dangud village, Uttarkashi district, Uttarakhand.\textsuperscript{11,21}

Plague continues to exist as a major public health problem in many countries of the world. In several countries plague has remained quiescent for years together before reappearing all of a sudden.
Natural foci of plague exist in the tropical and sub-tropical latitudes, and in the warmer parts of the temperate latitudes around the globe, between the parallels 55° North and 40° South. Endemic foci of the disease are found in all continents except Australia. Since 1989-90 number of human plague cases and outbreaks started reappearing after long years of quiescence in various countries of the world.

Due to the high public health significance and the risk of its re-emergence after long years of quiescence, the present review on plague was carried out with the aim of evaluating the current situation of the disease in India and to make us understand the importance of continuous surveillance for the suitable prevention and control measures.

### Epidemics and Pandemics

Several epidemics were on record before the Christian era. There were records of 109 epidemics and three great pandemics during 541, 1347, and 1894 CE, each time causing devastating mortality of people and susceptible animal population across countries and continents.

#### First Pandemic

First pandemic ("the Justinian plague") was started from Palusium (lower Egypt) during the reign of Emperor Justinian (543 AD) and spread to southern Europe and moved to Asia trespassing north Africa, Syria, Palestine and Constantinople. From Asia it progressed to north Europe and engulfed the world in 50-60 years (543 to 602 AD).100 The disease advanced along the tin and opium routes to British India and reached the provincial capital of K’unming in 1866, from there it spread to Korea, Japan, and China. The first recorded outbreak of plague occurred in China in the 1330s, a time when China was engaged in substantial trade with western Asia and Europe. The plague reached Europe in October 1347. It was thought to have been brought into Europe through the port of Messina, Sicily, by a fleet of Genoese trading ships from Kaffa, a seaport on the Crimean peninsula. When the ship left port in Kaffa and reached Messina, the infected rodents that took passage with the ship slipped through mooring ropes unnoticed to shore and carried the disease with them and their fleas. In 1347 the ‘Black Death’ originated in Asia and spread to the Crimea then Europe and Russia.

#### Second Pandemic

The second pandemic ("the Black Death") originated in 1347 AD from Jaffa in Crimea and continued up to the beginning of 19th century. It started in Europe in the 14th century and recurred intermittently for three centuries as ‘Black death’ and estimated to have caused death of 25 million people. From 17th century onwards second pandemic showed a declining trend and the last case was probably in 1841. This pandemic also spread to China and Indian subcontinent. It was believed that *Yersinia pestis* was the causative agent of the Black Death.3,11,20,26

#### Third Pandemic

Third pandemic started from Yunnan province of China in 1860, spread to Hong Kong in 1894, reached India in 1896 and spread to Japan and part of Europe. It reached Madagascar and Mauritius in 1897, Western Europe, Latin American countries and South Africa in 1898 and U.K., Australia, U.S.A. in 1900.3,11,20,26

### Biovars of *Yersinia pestis* responsible for pandemics

Three biovars of *Yersinia pestis* have been identified which can be differentiated on the basis of reduction of nitrate and fermentation of glycerol and melibiose. These biovars are virulent for humans. Each pandemic was believed to be caused by different biovar of *Yersinia pestis*, respectively, *antiqua* (prevalent in Africa and Central Asia), *medievalis* (currently limited to Central Asian countries), and *orientalis* (almost worldwide in its distribution). Biovar *antiqua* was found to be responsible for first pandemic, *medievalis* for second pandemic and *orientalis* linked to the third pandemic.3,11,20,27,28

### Sea route transmission of Plague by rodents

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Plague re-emerged from its wild rodent reservoir in the remote Chinese province of Yunnan in 1855. From there the disease advanced along the tin and opium routes and reached the provincial capital of K’unming in 1866, the Gulf of Tonkin in 1867, and the Kwangtung province port of Pakhoi (now Pei-hai) in 1882. In 1894 it reached Canton and then spread to Hong Kong. The third pandemic in 1894, originated in Yunnan, China and spread to Hong Kong and India, then to the rest of the world. Scientists were in general opinion about the role of rodents and fleas in transmission of plague, and the main means of dissemination - carried from port to port by merchant ships. It had spread to Mumbai by 1896 and by 1900 had reached ports on every continent, carried by infected rats travelling the international trade routes on the new steamships.

### Table 2. World Notification of Plague 1989 to 2009-after long years of quiescence

| Country   | Year of Reappearance | Duration of Quiescence |
|-----------|----------------------|------------------------|
| Botswana  | 1989                 | 45 years               |
| Kenya     | 1990                 | 10 years               |
| India     | 1994                 | 27 years               |
| Indonesia | 1997                 | 27 years               |
| Zambia    | 1997                 | 33 years               |
| Algeria   | 2003                 | 50 years               |
| Libya     | 2009                 | 25 years               |
In India the plague was initially spread in port cities, beginning with Mumbai, but later emerged in Pune, Kolkata, and Karachi (now in Pakistan). By 1899, the outbreak spread to many regions of India. The impact of plague epidemics during third pandemic were more in the provinces then designated as Bombay, Punjab, and the United Provinces while eastern and southern India were not as badly affected. From 1896–1918 the plague swept through undivided India (India, Pakistan and Bangladesh), taking the lives of over 12.5 million people. According to the World Health Organization, the pandemic was considered active until 1959, when worldwide casualties dropped to 200 per year. The third pandemic waxed and waned throughout the world for the next five decades, in that time plague had caused over 15 million deaths, the majority of which were in India.

### Plague a notifiable disease

Plague was one of the three epidemic prone diseases subject to the International Health Regulations and notifiable to the World Health Organization (WHO). An assessment of the effectiveness of the International Health Regulations in control of cholera, plague, and yellow fever reveals that WHO member states have not observed the regulations strictly. One reason could be the lack of surveillance capacity in many WHO member states. To help monitor and control of four serious communicable diseases that had significant potential to spread between countries International Health Regulations (IHR) was adopted by the Health Assembly in 1969, having been preceded by the International Sanitary Regulations adopted by the Fourth World Health Assembly in 1951. The 1969 Regulations, which initially covered six “Quarantinable diseases” were amended in 1973 and 1981, primarily to reduce the number of covered diseases from 6 to 3 (Yellow fever, Plague and cholera) after the global eradication of small pox. In consideration of the growth in international travel and trade, and the emergence or re-emergence of international diseases threats and other public health risks, the International Health Regulations (2005) were adopted by the fifty eighth World Health Assembly on 23 May 2005. It came into force on 15th June 2007. The purpose and scope of these Regulations are to prevent, protect against, control and provide a public health response to the international spread of the disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade.

### IHR in reference to Plague

- Surveillance and response
- Notification in 24 hrs to WHO and countries
- Report newly discovered or reactivated foci of plague
- Apply measures to: ships, aircrafts, land transport
- All ships should be free of rodents
- Rat proof buildings at seaports/airports
- International travelers prior to departure from an area (epidemic of pulmonary plague) having significant exposure should be isolated for 6 days after last exposure
- On arrival of an infested ship/aircraft, travelers be dis-insected and kept under surveillance for 6 days

### Rodents

Rodents are among the most important competitors globally with humans for food and other resources, particularly through the pre-harvest damage they cause to cereals. Rodents destroy more than 42 million tons of food (1/5 th to 1/3 rd of total food production) worldwide, approximately ten times more through urination and defecation than they actually eat. In past century alone more than ten million people died due to rodent borne diseases. Rodents are the most successful animals on earth, 2000 valid forms in world,1/4th of families and 36 percent of genera in class Mammalia. Rodent species are distributed in India from snowy heights of about 5700m to extremes of deserts. It has vast breeding potential and different modes of life: arboreal to subterranean. Rodents are characterized by the presence of one pair of chisels shaped ever growing (0.4mm/day) incisor teeth. Of the 128 species of rodents belonging to 46 genera in India 8 are considered to be the zoonotic reservoirs of different diseases. They are *Rattus rattus, Rattus norvegicus, Mus musculus, Tatera indica, Bandicota bengalensis, Meriones hurrianae*, the Southern palm squirrel- *Fanumbulus palmarum* and Marmots- *Marmota himalayana*.

Rodents are the carriers of viral, rickettsial, nematode and bacterial diseases. They are responsible for the transmission of more than 35 communicable diseases including Hunta viruses. In indirect transmission of diseases, rodents may serve as intermediate hosts for parasites that ultimately infect man and may serve as reservoirs of disease agents which may be picked up by arthropod vectors like fleas, ticks or mites and transmitted to humans through bites. In direct transmission, rodents may transmit the viruses by inhalation of aerosolized excreta, ingestion of excreta or by direct contact with the rodent itself and may directly transmit a pathogen to man through bite.

### Fleas

#### Vector Efficiency

- Survival rate (depends on frequency of feeding and micro-climatic conditions prevailing in the area) should allow the pathogen to multiply in its body
- Capable of passing the pathogen
- Feeding habits must be related to the foraging habit of the host
Seasonal Prevalence

The seasonal prevalence of rodent fleas are markedly influenced by temperature and humidity. In Penninsular India *Xenopsylla cheopis* show the peak density from August to October in domestic situations. Warm season with mean temperature of 23.2/22.9°C with occasional rainfall (mean total rainfall 182.2/221.4 mm) with relative humidity about 78 percent are the main factors responsible for the high flea indices during the period. The period of greatest prevalence of the rodent fleas is also the season of the maximum intensity of the disease. Studies undertaken by Brooks et.al., (1977)12 in Myanmar showed that seasonal distribution of plague positive rodents as characterized by antibody to *Y. pestis* followed closely to high indices of *Xenopsylla* species which occurred in April and May23.

Distribution of Vector Fleas

The ancestral home of *X.cheopis* is believed to be the valley of Nile. *X.cheopis* is distributed throughout the world. *X.astia* is restricted in its distribution to the oriental region and in India it is widely distributed in peri-domestic and wild situations. *X.brasiliensis*, originally distributed from Africa was very common species on rodents in domestic and peri-domestic situations in Penninsular India. However, the species is not abundant now-a-days in India. Rats especially *Rattus rattus* (domestic) and *Rattus norvegicus* (peri-domestic) are the most common hosts of these vector fleas though these species are occasionally found on other rodents and domesticated animals.

Host Association

High flea indices cannot be co-related with rodent density in a given biotope. Fleas do not uniformly infest all rodents of a locality but show unequal distribution due to interference of certain natural ecological variation in the host-parasite relationship. Fleas usually spend part of their life as ecto-parasite on rodent or other animals for feeding only. Adult fleas in large numbers are often found in loose soil in indoor situations and rodent burrows in peri-domestic and wild situations. Thus rat fleas retrieved only from the animal or rodent bodies may not give the actual flea index in a given area.

| Common Name       | Flea species                 | Distribution               |
|-------------------|------------------------------|----------------------------|
| Oriental Rat flea | *Xenopsylla cheopis*         | Widely distributed         |
| Rat flea          | *Xenopsylla astia*           | East Africa, Oriental origin|
| Rat Flea          | *Xenopsylla brasiliensis*    | Africa, Brazil, India.     |
| Mouse Flea        | *Leptopsylla segnis*         | world wide                 |
| Northern Rat Flea | *Nosopsyllus fasciatus*      | world wide                 |
| Human Flea        | *Pulex irritans*             | world wide                 |
| Cat flea          | *Ctenocephalides felis*      | world wide                 |
| Dog flea          | *Ctenocephalides canis*      | world wide                 |
| Chigoe flea       | *Tunga penetrans*            | America, Africa, India     |
| Rat flea          | *Stivalius ahale*            | South India & Sri Lanka    |

Table 3. Flea species attacking man

Global plague situation

According to notification received by WHO during the period 1987 to 2015, plague affected 28 countries with 56,744 cases and 4650 (8.19 percent) deaths. During the period the maximum number of plague cases (5419) occurred in 1997 and the minimum (320) occurred in 2015. Between 2004 to 2009, a total of 12,548 cases of human plague, including 845 (6.7 percent) deaths, were reported by 13 countries in Africa, Asia and Americas. During 2010 to 2015, a total of 3248 cases and 584 (17.98 percent) deaths were recorded from 11 countries in the world.

In Africa previous epidemics were reported from Angola, Botswana, Burkina Faso, Egypt, Equatorial Guinea, Ghana, Kenya, Lesotho, Malawi, Mauritania, Morocco, Namibia, Nigeria, Republic of Guinea, Senegal, Somalia, South Africa, South Sudan (in Juba), Tunisia, and Zimbabwe. Natural foci of plague are known to exist in the Democratic Republic of the Congo, Kenya, Lesotho, Libya, Madagascar, Mauritania, Mozambique, Namibia, Senegal, South Africa, Tanzania, Zambia, Uganda, and Egypt.

In USA human plague is recorded with an average of 11 cases per year. In North America, natural foci of plague occur in 15 western states of the United States, in southwestern Canada on the border with the United States, and in northern Mexico. Endemic foci in South America exist in Argentina, Bolivia, Brazil, Ecuador, Peru and Venezuela, two of which have no report of current cases. Plague was
found to be present for one or more years in 14 out of 25 countries in Latin America (1899–2012). Active enzootic plague foci exist in the Americas among wild rodent and flea populations in Bolivia, Brazil, Ecuador, Peru and the United States of America.

There has been a major shift in human plague incidence from Asia to Africa. 96.2 percent of all cases and 88.9 percent of deaths in the last five years (2010–2015) were reported from African countries—Madagascar, Tanzania (URT), Uganda, and the Democratic Republic of the Congo (DRC). Most of the cases were bubonic. However, pneumonic plague outbreaks also occur in these countries. In Asia, China, Cambodia, India, Indonesia, Iran, Kazakhstan, Mongolia, Myanmar, Nepal, Philippines, Lao People’s Democratic Republic, Russian Federation, Kyrgyzstan and Vietnam reported the cases and deaths from 1954 to 2015. Endemic foci are found in Cambodia, China, India, Indonesia, Iran, Mongolia, Myanmar, Nepal, Vietnam. The Central Asian region has active enzootic plague foci in deserts, mountains and steppes. China reported human plague cases almost all the years to WHO. Nearly 30 percent of the vast Mongolian territory consists of endemic plague foci.23,31,32,33

Table 4. Global distribution of human plague cases and deaths from 1987-2015

| Continent       | Country                                      | Number of cases | Number of deaths |
|-----------------|----------------------------------------------|-----------------|------------------|
| Africa          | Algeria                                      | 15              | 5                |
|                 | Botswana                                     | 173             | 12               |
|                 | Democratic Republic of Congo                 | 14,175          | 1331             |
|                 | Kenya                                        | 44              | 8                |
|                 | Madagascar                                   | 19122           | 1995             |
|                 | Mozambique                                   | 2387            | 28               |
|                 | United Republic of Tanzania                  | 6448            | 414              |
|                 | Uganda                                       | 1260            | 182              |
|                 | Zambia                                       | 1629            | 32               |
|                 | Zimbabwe                                     | 417             | 34               |
|                 | Libya                                        | 5               | 1                |
|                 | Malawi                                       | 835             | 16               |
|                 | Namibia                                       | 2189            | 81               |
|                  | **Total**                                    | **48699**       | **4139**         |
| Americas        | Bolivia                                      | 44              | 9                |
|                 | Brazil                                       | 173             | 0                |
|                 | Ecuador                                      | 14              | 14               |
|                 | Peru                                         | 1643            | 81               |
|                 | USA                                          | 213             | 24               |
|                  | **Total**                                    | **2087**        | **128**          |
| Asia            | China                                        | 584             | 80               |
|                 | India                                        | 900             | 61               |
|                 | Indonesia                                    | 106             | 1                |
|                 | Mongolia                                     | 123             | 40               |
|                 | Myanmar                                      | 784             | 6                |
|                 | Vietnam                                      | 3425            | 187              |
|                 | Kazakhstan                                   | 24              | 7                |
|                 | Lao People’s Democratic Republic              | 10              | 0                |
|                 | Russian Federation (2010-2015)               | 1               | 0                |
|                 | Kyrgyzstan                                   | 1               | 1                |
|                  | **Total**                                    | **5958**        | **383**          |
|                  | **Worldwide Total**                          | **56744**       | **4650**         |
Epidemiological cycle of Plague in India

From 1989 to 1994 serological evidence of plague was detected in wild and peri-domestic rodents in peninsular India. All the rodent species were shown to be the hosts for three important flea vectors i.e. Xenopsylla cheopis, Xenopsylla astia and Xenopsylla brasiliensis (now rarely found in India) in the area. Plague is transmitted between mammals via fleas, cannibalism or contaminated soil. Human plague most commonly occurs when an infected flea bites a man. Before human epidemics, rats frequently died in large numbers, precipitating the movement of the flea population from its natural rodent reservoir to humans. In rare occasions, rodents can transmit the infection to humans through direct contact.

*Tatera indica* and *Bandicota bengalensis*, reservoirs of plague in India were found to be the most favourable hosts of Xenopsylla astia.

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**Figure 4.** Global distribution of natural plague foci as of March 2016 (number of cases reported)

Sylvatic plague in wild, peri-domestic rodent population occurred throughout the year but with a peak incidence in September-October. This may be attributed to the breeding activity of the rodents, which is at a peak during post monsoon season when the availability of nutritive food is more. Availability of green and nutritive diet also increase the survival rate of the fresh recruitees in the population. Another factor, which is responsible for the peak incidence is the high flea indices during the period is the warm season with mean temperature of 23.2/22.9°C with occasional rainfall (mean total rainfall 182.2/221.4 mm) with relative humidity about 78 percent.\(^{23}\)
Figure 6. Areas with potential plague natural foci based on historical data and current information

It was established from the study that *Y. pestis* infection is maintained amongst wild rodent population in enzootic foci by *Tatera indica / Bandicota bengalensis > X. astia > Tatera indica / Bandicota bengalensis* chain from season to season over the number of years.23,34,35,36,37

Main Epidemiological Types of Plague

- **Epizootic Plague**: Widespread infection in rodents in domestic and peri-domestic situations
- **Enzootic Plague**: Live plague foci in wild situation with rodents/animals
- **Sylvatic Plague**: Asymptomatic plague among wild rodents
- **Demic Plague**: Pneumonic plague

Epidemiology of plague depends upon the existence of optimum relationship of the causative organisms (*Yersinia pestis*), reservoirs (Rodents), the vector fleas and human host, resulting in a complex phenomenon. Plague is primarily a disease of rodents, which inhabit the natural foci where ecological conditions ensure the persistence of the plague organisms for a considerable period. The natural focus is responsible for sylvatic plague and entirely independent of human population.

Plague transmission occurs due to ecological imbalance when rodents migrate from their natural habitats and intermingle with tolerant or susceptible rodent population in peri-domestic or domestic situations and transfer the infection through fleas causing 100 percent mortality in susceptible rodent population in domestic situations (Rodent Epizootic or Rat fall). In absence of live rodents during rodent epizootics the infected fleas attack/bite the human population causing bubonic plague.

Epidemiological cycle of Human Plague

- Wild rodents > Rodent flea > Man (in feral situations)
- Wild rodents > Rodent flea > Commensal rodents (Rodent epizootic) > Flea > man (Bubonic plague)
- Man > Human flea (*Pulex irritans*) > Man (Interhuman transmission-rarely occurs)
- Man > Man (Pneumonic plague by droplet infection)
- Wild animals/ rodents > Man (Due to handling of infected animals/rodents)
Enzootic Foci of Plague

Detection of plague foci was made in the erstwhile plague endemic areas mainly to unravel the existence of sylvatic rodents in the maintenance of the reservoir of the infection and to study the population stress under which migration takes place from sylvatic to peripheral and commensal habitats.

An active enzootic plague foci is a permanent nidus in a delimited biotope, where ecological condition ensures the persistence of the disease for long periods. The enzootic foci of plague in India is believed to be present in four groups of foci in northern, central, western and southern India. The northern focus is composed of three endemic centres in the Himalayan region covering Himachal Pradesh, Uttarakhand, Uttar Pradesh and Bihar. The central focus is confined to Madhya Pradesh covering Vindhya Bhanrer, Maikal ranges and Mahadeo hills. The western focus is confined to Beed and Latur areas in Maharashtra and Surat areas in South Gujarat. The southern foci are localized in the watersheds of Western ghat of Tamil Nadu (Salem, Cumbam Valley, Theni district, Dharmapuri, Krishnagiri, Coimbatore, the Nilgiris and Madurai districts), Karnataka (Kolar and Bangalore rural districts) and Andhra Pradesh (Chittoor district). Investigations on reservoirs of plague were commenced early in 1964 in peninsular India plague foci. Evidence of the presence of plague infection amongst small mammals of different species i.e. Rattus rattus (0.54%), Tatera indica (4.76%), Bandicota bengalensis (0.6%), M.m.maltada (1.2%) and Funumbulus palmarum (8.0%) was detected by National Institute of Communicable Diseases (Now NCDC) in the course of their intensive studies during 1970.

Detection of plague antibodies was made again in peninsular India amongst wild and peri-domestic rodents. From 1989 to 1994 active zoonotic foci of plague were detected from the trijunction of Tamil Nadu (Krishnagiri district), Andhra Pradesh (Chittoor district) and Karnataka (Kolar and Bangalore rural district). A total of 4,73,736 rodent sera samples were individually tested serologically to detect the evidence of plague antibodies. Of the total rodents collected, Tatera indica cuvieri (Hardwicke), the Indian gerbil was by far the most numerous (41.9 per cent) followed by Rattus rattus rufescens Gray and Rattus rattus wroughtoni Hinton (Rattus rattus group) and Bandicota bengalensis (Gray). Haemagglutinating antibodies were detected in 243 sera samples from three different rodent species i.e. Tatera indica, Bandicota bengalensis and Rattus rattus at a titre of 1:16 and above. High sero-positivity rate with Tatera indica cuvieri (0.04 percent amongst total rodents tested) in wild habitats indicates that the species has high degree of resistance to Y.pestis infection and are also involved in maintaining enzootic foci in nature. High sero-positivity rate found in Rattus rattus which was considered to be the most susceptible rodent population in plague transmission suggested that this species acquired high tolerance to Y.pestis infection particularly from the peri-domestic habitats.

Figure 8. Enzootic Foci of Plague, India
Plague in India

The principal plague affected states in India since 1939 were Bihar, Maharashtra, Andhra Pradesh, Madhya Pradesh, Karnataka, Tamil Nadu, Uttar Pradesh and Punjab. Within this period, West Bengal and Assam were newly affected. No plague death was recorded in Punjab since 1951; in Bihar since 1952; in West Bengal and Maharashtra since 1953; in Madhya Pradesh since 1954; Andhra Pradesh and Assam since 1957. The last three states in which human plague deaths were recorded up to 1966 were Uttar Pradesh, Karnataka and Tamil Nadu. Kerala state were not affected much with human plague cases like other states in peninsular India.24

Table 5. Feral and Peri-domestic rodents with natural infection of Yersinia pestis in India

| Rodent species       | Area reported                                                                 | Reported by                  |
|----------------------|-------------------------------------------------------------------------------|------------------------------|
| Tatera indica        | Northern UP                                                                    | Baltazar, 1952               |
| Tatera indica        | Kolar, Karnataka                                                               | NICD, 1970                   |
| Tatera indica        | Bombay                                                                         | NICD, 1963-72                |
| Tatera Indica        | Hyderabad                                                                      | NICD, 1963-72                |
| Tatera Indica        | Kolar, Attibele, Bangalore Rural (Karnataka) Chittoor district (Andhra Pradesh) Krishnagiri and Dharmapuri districts (Tamil Nadu) | Biswas, NICD, 1989-1994      |
| Bandicota bengalensis| Kolar (Karnataka)                                                             | George & Webster, 1934       |
| Bandicota bengalensis| Calcutta (West Bengal)                                                        | Sharif & Harasimkar, 1934    |
| Bandicota bengalensis| Kolar, Attibele, Bangalore Rural (Karnataka) Chittoor district (Andhra Pradesh) | Biswas, NICD, 1989-1994      |
| Mus platythrix       | Kolar (Karnataka)                                                             | Rao, 1947                    |
| Mus booduga          | Madras (Tamil Nadu)                                                           | Lal & Seal, 1949             |
| Rattus rattus        | From peri-domestic areas Kolar, Attibele, Bangalore Rural (Karnataka) Chittoor district (Andhra Pradesh) Krishnagiri and Dharmapuri districts (Tamil Nadu) | Biswas, NICD, 1989-1994      |
| Mus m. maltada       | Kolar (Karnataka)                                                             | NICD, 1970                   |
| Funambulus palmarum  | Kolar (Karnataka)                                                             | NICD, 1970                   |

Table 6. Human cases and deaths due to Plague in India*

| Year         | Number of cases | Number of deaths |
|--------------|-----------------|------------------|
| 1963         | 197             | 22               |
| 1964         | 106             | 13               |
| 1965         | 1               | 0                |
| 1966         | 46              | 2                |
| 1967 to 1993 | Nil             | Nil              |
| 1994         | 876             | 54               |
| 1995 to 2001 | Nil             | Nil              |
| 2002         | 16              | 4                |
| 2003         | Nil             | Nil              |
| 2004         | 8               | 3                |
| 2005-2017    | Nil             | Nil              |

*Source: NICD/WHO Publication on Plague

In August–October 1994 human plague was reported in India for the first time in 28 years. Although the exact circumstances are unknown, factors contributing to the re-emergence of plague in India have been identified by the National Technical Advisory Committee on Plague constituted by the Government of India.23,24
Bubonic Plague outbreak in Beed district

Bubonic plague outbreak occurred during August, 1994 at Mamla and its surrounding villages under Beed district after long years of quiescence. Ecological changes created by the devastating earthquake in September 1993 in adjoining districts of Latur and Osmanabad disturbed the equilibrium density of domestic rodents (Rattus rattus) and their fleas (Xenopsylla cheopis). It was believed that the impact of devastating earthquake in September, 1993 forced the villagers of Mamla to vacate their old houses and shift to new temporary shelters erected by the state authorities. Old houses were then used for the storing of harvested groundnuts and other food grains. At the same time due to ecological imbalance the wild and peri-domestic rodents mostly Tatera indica from the adjoining areas migrated towards periphery in groundnut fields of Mamla and surrounding villages and mingled with local commensal rodents i.e. Rattus rattus and Mus musculus, susceptible population for plague. Simultaneously, due to abundance of stored food grains there was a gradual but persistent growth of susceptible rodent population. The density of Xenopsylla cheopis was also increased due to favourable ecological conditions prevailing in the abundant structures.

During the first week of August, 1994 the inhabitants of Mamla village experienced heavy flea nuisance and flea bites. Several rodent epizootics (Rat falls) were reported from the area. Subsequently, a number of human cases clinically resembling bubonic plague were reported from Mamla and other surrounding villages too. These were all confirmed by the Central Plague laboratory, NICD, Delhi (now NCDC).

Pneumonic plague outbreak in Surat

The resurgence of plague in Surat, Gujarat State, was related to a record high rainfall during the September monsoon. Tapi river flood waters inundated localities in the north, south–west, central and eastern zones of Surat City. Many rodents and other animals were found dead when the water floods receded 5 days later. While cleaning up local residents have become infected after contact with dead animals. Shortly after the flood the Ganapati festival brought huge crowds of people together in the city which would facilitate the spread of acute respiratory illness. Based on the clinical picture and the plague outbreak in neighbouring Maharashtra State, the outbreak in Surat was declared as pneumonic plague on 21 September 1994. The epicenter of the plague was Surat, Gujarat. 54 people lost their lives and close to a quarter of the city’s citizens fled the area for fear of being quarantined. Although the plague only lasted a little over two weeks, it caused widespread panic. Tourism was negatively affected, flights to India were cancelled.

There were several lines of evidence strongly suggesting that it was a plague epidemic: blood tests for Yersinia were positive, a number of individuals showed antibodies against Yersinia and the clinical symptoms- suspected fever, blood stained sputum, breathlessness, chest pain, sore throat and persistent cough displayed by the affected were all consistent with the disease being plague.

Plague outbreaks in Himachal Pradesh

Himachal Pradesh had reported human plague cases during the year 1959. Sporadic cases of suspected human plague had been reported from Himachal Pradesh during 1966, 1969, 1971 (Mahasu), 1983 (Tangnu) and 1984 (Jubbal area). A localized outbreak of pneumonic plague occurred in Hatkoti, Shimla district, Himachal Pradesh in February 2002. A total of 16 cases and four deaths were reported. All the patients were adults (7 males and 9 females) and epidemiologically linked with each other. The diagnosis of plague was confirmed by the laboratory in 10(63%) cases.

To determine the presence of enzootic plague foci in Himachal Pradesh a study was undertaken by the National Institute of Communicable Diseases during 1971 in Mahasu, Kotkhai and Rohru. During the investigations, reports of rat fall with two human deaths associated with fever and glandular enlargement in Duedi village were also investigated. The isolation of Y.pestis from the rat carcasses collected at Duidi village and the occurrence of sero-positive rodents in the area provide positive evidence of continued underground transmission and persistence of plague infection in the area.

The results of human sera examined by N.I.C.D. (Now NCDC) suggests the retrospective diagnosis that the outbreaks in 1966, 1969, 1971, 1983 in Tangnu and 1984 in Jubbal area were of plague. Rohru tehsil and the other adjacent areas in Himachal Pradesh has the active enzootic plague foci. The area is maintaining the typical cyclic pattern of plague transmission.

Bubonic plague outbreak in Uttarakhand

An outbreak of bubonic plague was reported from Dangud village (Population-332), Barkhot tehsil, Uttarkashi district in the second week of October, 2004. During the episode a total of eleven human cases and three deaths were recorded. All the 3 fatal cases and five surviving cases had enlargement of inguinal lymph nodes. None of them had pneumonia. There was no clear history of rat fall in the village. No flea was found on rodents or animals. 16 animal serum samples were found to be negative for antibodies against F-1 antigen of Y. pestis. However, Y. pestis was isolated from two rodents (Rattus rattus and Mus musculus) trapped in the village. One human and three animal sera showed borderline sero-positivity against...
rickettsial infection. The diagnosis of plague was confirmed by detection of four fold rise of antibody titre against F-1 antigen of *Yersinia pestis* in paired sera of three cases (one of the WHO approved criteria of diagnosis of confirmed plague).

The village Hatkoti (Gallu) in Rohru tehsil, Himachal Pradesh which reported confirmed cases and deaths due to plague during 2002 is bounded by Arakot areas of Barkhot tehsil, Uttarkashi district, Uttarakhand. Arakot is only 25 kms. away from Rohru town by motorable road. Villages around Arakot areas are directly connected with Hatkoti village by mountainous deep forest route. One of the victims of Hatkoti plague episode in Himachal Pradesh was reported to be the resident of Arakot areas (Banpur) village of Uttarkashi district, Uttarakhand.

**Risk Factors in International Sea Ports**

Ports receive and manage goods and people from all over the world. Therefore, ports are exposed to the risk of introduction of vectors from any other part of their host country or any other port in the world. The activities undertaken at ports, such as handling foodstuffs, attracts many species of vermin. Contaminated ships transport disease across geographical boundaries. Rodents can gain access to ships directly by mooring ropes, hulls and gang ways. Rodents may be concealed in cargo, ship’s stores and other materials taken on to the ship.

**Risk factors during Gregarious bamboo flowering**

Spontaneous increase in rodent population due to high nutritive value of bamboo fruits, reduction in cannibalism due to the availability of plenty of food during bamboo flowering and change in the ecological conditions resulting in ‘r’-pattern of rodent breeding might be the probable reasons for the rodent outbreaks in North Eastern Hilly Region, India.

The rats and mice reproduce in numbers due to sudden and constant supply of bamboo fruits for a period of 5 years. When the source of food is finished, rodents migrate towards crop fields, plantations and human habitations and consume everything and thus spread the rodent borne diseases.

Rodent migration after gregarious bamboo flowering in North Eastern Hill Region of India, Myanmar and Bangladesh can trigger a consequence far more serious than crop destruction and famine - an increase in the frequency of transmission of rodent-borne pathogens to human and animals.

**Discussion**

Plague is primarily a disease of rodents and man gets the infection mainly through the infected flea bites to bubonic form which later turns out as pneumonic form of plague. As the Sylvatic rodents live in wild and peri-domestic situations and maintain the natural transmission in enzootic foci for centuries together, eradication of the disease is highly impossible. Natural decline in plague incidence would not justify the conclusion that plague has disappeared from the area. Plague is not static but shift from place to place through contiguity of colony infection amongst wild rodents which eventually transferred the infection to the commensal rodents on their path. Many biotic and abiotic factors influence the persistence of the disease in wild population and causing epizootic plague. Natural foci of plague are known to be completely independent of man, have a cyclic pattern of activity and can transmit the disease to man.

Plague is a re-emerging zoonotic disease. It is one of the three epidemic prone diseases still subject to the International Health Regulations and notifiable to the World Health Organization (WHO). Plague can re-emerge, vaccination is useless and mass killing of rodents is not the solution for the eradication of the disease. The emergence and spread of multi-resistant strains of *Y. pestis* to antibiotics and vector fleas which have developed resistance to organochlorine, organophosphate and synthetic pyrethroids insecticides in most of the endemic countries may pose a serious threat to global outbreak of the disease.

Since the beginning of the 1990s, the number of plague cases shows rising trend, and outbreaks are reappearing in various countries of the world after decades of quiescence. Presently, plague continues to occur in Africa, the former Soviet Union, the Americas, and Asia (WHO Report). Under reporting of plague cases may be attributed to lack of diagnostic facilities for the confirmation of the cases and cessation of plague surveillance work by number of erstwhile plague endemic countries, where non-occurrence of cases for long years gave false impression that *Yersinia pestis* are no longer circulating.

Although the number of human cases of plague is relatively low, it would be a mistake to overlook its threat to humanity, because of the disease’s inherent communicability, rapid spread, capability of the agent to cause epidemic, rapid clinical course, high mortality if left untreated and international importance and economical impact. *Yersinia pestis* bacterium is widely available in microbiology banks around the world, making a biological attack a potential problem. A plague outbreak may also cause widespread panic, as occurred in India in 1994 when a relatively small outbreak, with 54 deaths, was reported in the city of Surat. This led to a nationwide collapse in tourism and trade, with an estimated cost of US$600 million.

Surveillance of plague includes the collection and estimation of rodent density in a given biotope, detection of plague antibodies among rodents by PHA /HI test using Fraction 1 antigens of *Yersinia pestis*. Under reporting of plague cases may be attributed to lack of diagnostic facilities for the confirmation of the cases and cessation of plague surveillance work by number of erstwhile plague endemic countries, where non-occurrence of cases for long years gave false impression that *Yersinia pestis* are no longer circulating.

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(F1) antigen, the recovery, identification and calculation of absolute and specific flea indices, pathological examination of certain rodent organs and detection of Y. pestis in vector fleas by animal inoculation. The inadequate management of the outbreaks in Beed and Surat (1994) triggered improvements in the surveillance, prevention and control of plague in India. As a result, the outbreak of pneumonic plague in Shimla (Himachal Pradesh) in 2002 and bubonic plague outbreak in Uttarkashi district, Uttarakhand in 2004 were contained in the shortest possible time, with early diagnosis, antibiotic treatment, mass chemoprophylaxis, quarantine and vector control measures performed in a timely manner 48,49. Now, regular surveillance of plague is not being carried out in India due to non-availability of indigenous serological test kits (being manufactured by Haffkine Institute, Mumbai, India) and closing of all state plague surveillance units in the endemic states.

Rodent and vector surveillance is useful for detecting plague circulation in reservoir populations, assessing epidemic risk factors and surveying the susceptibility of fleas to insecticides. In addition to routine surveillance activities, new strategies based on use of geographical information systems, climatic and ecological data and mathematical models are improving the prediction of outbreaks. The resistance of fleas to various insecticides gave us warnings for appropriate use of residual insecticides and insecticide dust powders (insufflations) for efficient anti flea measures. Since newer pesticide molecules are being flooded into the market and the availability of recommended old pesticides becoming scarce, farmers unknowingly purchase and spray some non-recommended pesticides to solve the pest problem. The indiscriminate use of insecticides in agricultural sector has direct impact on resistance problem in flea population breeding outdoors. Effective flea resistance management depends on early detection of the problem and rapid assimilation of information on the resistant insect population so that rational pesticide choices can be made66. Many insecticides are also massively used to control domestic pests, and therefore, impact will be more on the vector species which are breeding and resting indoors like fleas. Furthermore, in some circumstances, resistance can persist in populations for very long periods after regular use of an insecticide has ceased. In these cases, resistance to new insecticides is inherited from the past as a result of the previous use of other insecticides66. Plague should not be relegated to the sidelines. It remains a poorly understood threat that we cannot afford to ignore.

International sea ports were the entry point for plague. Ships arrived from plague-endemic countries brought the infected rodents and fleas with Y. pestis infection. Potential new foci should be confirmed and investigated, with special attention to harbours with international trade. National plague surveillance programmes and regional collaboration are needed to be strengthened.

Conflict of Interest: None

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