



Plague: Symptoms, Transmission, Diagnosis, Prevention and Treatment

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Plague is a contagious disease caused by the zoonotic bacteria, (*Yersinia pestis*) but transmitted by fleas. It is found on rodents and their fleas. The most common ways for humans to contract plague are through handling a plague-infected animal or by getting bitten by a rodent flea that is carrying the pathogen. Septicemic, pneumonic, and bubonic plague are the three most prevalent types. The bubonic plague typically takes 2 to 8 days to incubate. Patients experience weakness, one or more enlarged, painful lymph nodes, headache, chills, and fever (called buboes). The bite of an infected flea results in plague, which is the most widespread type of plague. Pneumonic plague, a more severe form of bubonic plague, can progress and disseminate to the lungs. Septicemic plague incubation period isn't exactly known but, it most likely happens within days of exposure and is

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accompanied by high temperature, chills, intense exhaustion, stomach discomfort, shock, and maybe, bleeding into the skin and other organs. Pneumonic plague often only takes 1 to 3 days to incubate and is accompanied by a fever, headache, weakness, rapidly progressing pneumonia, shortness of breath, chest pain, coughing up occasionally bloody or watery mucus, and other symptoms. Generally, fever, chills, headaches, and nausea are some of the general plague symptoms. There is also the case of lymph nodes enlargement, coughing, chest pain, and hemoptysis. Plague can be transmitted through; bites by fleas, contact with contaminated fluid or tissue, and infectious droplets. The symptoms of plague are typically non-specific; hence laboratory investigation is necessary for a certain diagnosis. *Y. pestis* infection can be detected using a microscope and by bacteria culture. The sample (buboes) can be gotten from blood, mucus (sputum), or an aspirate taken from swollen lymph nodes. Polymerase chain reaction (PCR), can also be employed to diagnose plague (F1 capsule antigen). It is also possible to identify plague by using blood tests that look for antibodies to *Y. pestis*. Plague can be prevented by eliminating rodent's habitats around living houses, workplace, and leisure locations, and elimination of bushes, rock piles, garbage, cluttered firewood, and potential rodent food sources such as pet and wild animal food. Plague vaccines are only recommended for high-risk categories such as laboratory professionals who are constantly exposed to the risk of contamination, and health care workers. All forms of plague respond to antibiotic treatment if they are diagnosed early. Those suspected to have made contact with infected patients or animals should be isolated and observed. Plague remains one of the most infectious diseases worldwide. Although as at the time of this review, there is no recent case of plague in Nigeria, or in Africa, effort is still required to create robust awareness among the population on the subject of plague. The focus of this review is to educate and create more awareness among the citizens on plague as a highly infectious disease.

Keywords: Flea; plague; pneumonia; rodent; *Yersinia pestis* fever.

1. INTRODUCTION

From time to time, the public is faced commonly with outbreaks of infection and less commonly with pandemics like COVID-19. [1-3]. Many species of rodents in different countries are dangerous animals in terms of the spread of zoonotic diseases [4-7] According to a report by the World Health Organization (WHO) [8], plague is a contagious disease caused by the zoonotic bacteria, *Yersinia pestis*, but transmitted by fleas. It is found on rodents and their fleas. The most common ways for humans to contract plague are through handling a plague-infected animal or by getting bitten by a rodent flea that is carrying the pathogen [9]. Septicemic, pneumonic, and bubonic plague are the three most prevalent types [9]. Millions of people were killed by plague in Europe throughout the Middle Ages, which is not of good repute. If left untreated, the case-fatality ratio for the plague ranges from 30% to 100% in humans, especially in its septicemic (a systemic infection caused by circulating bacteria in the bloodstream) and pneumonic forms [8]. Also, if not treated promptly, the pneumonic type is almost always fatal. It is usually contagious and has the potential to spread through airborne droplets, causing major outbreaks [8]. Each year, 600 cases are documented worldwide [8]. The Democratic Republic of the Congo, Madagascar, and Peru had the highest cases worldwide in

2017. Other countries encountered lesser number of outbreaks of plague as compared to Democratic Republic of the Congo, Madagascar and Peru. Large outbreaks of it have historically taken place, with the greatest being the Black Death in the 14th century, which claimed over 50 million lives. In current history, incidences have been split between rare outbreaks or isolated instances in endemic regions and tiny seasonal outbreaks that mostly affect Madagascar [8].

A study conducted by Wilson [10] reported that in 2022, human remains from three cemeteries in Kyrgyzstan that were dated to 1338 and 1339 were discovered to include the potential source of all modern strains of *Yersinia pestis* DNA. According to legend, the first plague outbreak began at the siege of Caffa in the Crimea in 1346, and subsequent strains later swept over Europe. Using DNA sequencing to create a family tree of the bacteria, it is compared to other ancient and contemporary strands. As the strain of bacteria found in the tombs is most similar to the bacteria infecting marmots in Kyrgyzstan today, this suggests that this is also the site where plague spread from animals to humans [10]. Human plague infections still happen occasionally in rural areas of western United States, but Africa and Asia currently have a much higher number of cases [9].

With respect to Africa, the human plague continues to be very important for public health. The prevalence of plague is higher on the continent. Over 90% of all documented human cases worldwide originate in Africa [11-12]. The Democratic Republic of the Congo (formerly Zaire), Madagascar, Mozambique, Uganda, and the United Republic of Tanzania are the countries most severely impacted. The nations with the highest endemicity rates worldwide are Madagascar and the Democratic Republic of the Congo [11]. Algeria [13], DR Congo [14], Madagascar [11], Libya [15], Mozambique, Uganda [16], Zambia [17], and Tanzania [18], are reported to have active foci of the human plague in Africa [9]. Africa also has nations that have experienced human plague in the past and may currently have zoonotic foci. Such zoonotic cases can trigger the resurgence of human illness. The epidemiological state of the disease's most recent outbreaks in these nations is not documented in the literature, however Angola [19-21], Botswana, Egypt, Kenya, Equatorial Guinea, Ghana, Lesotho, Malawi, Mauritania, Morocco, Namibia, Republic of Guinea, Senegal, Somalia, South Africa, South Sudan (in Juba), Tunisia, and Zimbabwe and Nigeria has previously recorded epidemics [16]. In these countries, the number of plague outbreaks has significantly decreased during the past few decades, though the rate of reduction has not been captured in literature as at the time of this review. This does not rule out the possibility that the infection still exists in many places where the human plague has been absent for some time. Previous outbreaks have demonstrated that the plague can return to places that have long been silent, such as Algeria in 2003, after 48 years of stillness [11]. Civil wars, climate change, trade, deforestation, migration, mining, poverty, and urbanization are a few variables that may have contributed to the disease's resurgence [20-21]. In Nigeria, there has been no recent case of plague, however, the aim of this review is to educate and create more awareness among the citizens on the subject.

2. SIGNS AND SYMPTOMS

Nelson *et al.* [22] in his research reported that there are numerous distinct clinical signs and symptoms of plague. Ocular plague, plague meningitis, and plague pharyngitis are further clinical symptoms [22-23]. Fever, chills, headaches, and nausea are some of the general plague symptoms [9]. The CDC [9] also reported cases of lymph nodes enlargement as a common

symptom of bubonic plague in many persons. Coughing, chest pain, and hemoptysis may (or may not) be signs of pneumonic plague in affected individuals.

2.1 Bubonic Plague and Symptoms

The bubonic plague typically takes 2 to 8 days to incubate. Patients experience weakness, one or more enlarged, painful lymph nodes, headache, chills, and fever (called buboes) [9]. The bite of an infected flea results in plague, which is the most widespread type of plague [8,9]. *Y. pestis*, the plague bacillus, enters through the wound and moves through the lymphatic system to the closest lymph node where it multiplies. The lymph node is therefore referred to as a "bubo" and experiences inflammation, tension, and pain. In more severe cases of infection, swollen lymph nodes can develop into pus-filled open sores. Bubonic plague transmission from person to person is uncommon. Pneumonic plague, a more severe form of bubonic plague, can progress and disseminate to the lungs [3,9].

2.2 Septicemic Symptoms

Although the exact timing of septicemic plague incubation is unknown, it most likely happens within days of exposure [9]. Patients have a high temperature, chills, intense exhaustion, stomach discomfort, shock, and perhaps even bleeding into the skin and other organs. Particularly on fingers, toes, and the nose, skin and other tissues have the potential to turn black and perish. Septicemic plague may manifest as the initial sign of the disease or may progress from untreated bubonic plague. This kind is brought on by handling an infected animal or by flea bites [9].

2.3 Pneumonic Symptoms

Pneumonic plague often only takes 1 to 3 days to incubate [9]. Patients experience a fever, headache, weakness, rapidly progressing pneumonia, shortness of breath, chest pain, coughing up occasionally bloody or watery mucus, and other symptoms. Pneumonic plague can emerge from untreated bubonic or septicemic plague after the germs disseminate to the lungs, or it might arise from inhaling infectious droplets [8]. The pneumonia may result in shock and respiratory failure. The only type of plague that can transfer from person to person is pneumonic plague, which is the most dangerous

variation of the illness (by infectious droplets) [8,9].

3. TRANSMISSION

According to the CDC [9], plague can be transmitted through; bites by fleas, contact with contaminated fluid or tissue, and infectious droplets [9].

The bite of a flea carrying the plague germs is the most common method of transmission [9]. Many rodents perish during plague epizootics, which prompts fleas in search of alternate blood supplies. Flea bites can spread plague to people and animals who visit areas where rodents have recently perished from the disease. Infected fleas from dogs and cats may potentially enter houses. Exposure to flea bites can cause primary septicemic or bubonic plague [24].

Upon making contact with the body fluids or tissue of an animal that has the plague, animal-human transmission can occur [9]. For instance, a hunter who doesn't take the necessary procedures when skinning a rabbit or other sick animal risk contracting the plague bacteria [24]. The plagues that are most frequently contracted by this type of exposure are bubonic or septicemic.

Those who have plague pneumonia may cough up airborne droplets of the plague bacterium [24]. These bacteria-filled droplets can spread pneumonic plague if they are inhaled by another individual. This usually necessitates close proximity to the pneumonic plague victim. The only way the epidemic can spread between humans is through the transmission of these droplets. Although this kind of dissemination has not been observed in the United States since 1924, it still happens occasionally in underdeveloped nations [24]. Cats are particularly vulnerable to the plague and can contract it by eating rodents that have the disease. Sick cats run the risk of infecting their owners or veterinarians with infectious plague droplets.

4. DIAGNOSIS

The symptoms of plague are typically non-specific, hence laboratory investigation is necessary for a certain diagnosis [21]. The CDC [24] reported that plague may be suspected as an illness's source if an infected person has previously been bitten by a flea or a bubo is found on them. Jullien and colleagues [25] noted

that in order to determine whether someone has a case of plague, *Y. pestis* can be detected using a microscope and by cultivating a sample. Blood, mucus (sputum), or an aspirate taken from swollen lymph nodes can all be used to get the sample (buboes). False negative results could occur if an individual is given antibiotics prior to having a sample collected, if transportation to the lab is delayed, and/or if the sample was improperly maintained [25].

4.1 Polymerase Chain Reaction (PCR)

Plasmodium activator (pla) and caf1 genes, among others, can be found in bacteria, and their existence can be determined using polymerase chain reaction (PCR), which is also used to diagnose plague (F1 capsule antigen) [25]. Both live and dead bacteria can be successfully tested with PCR, which only needs a very tiny sample. Because of this, if an individual takes antibiotic before a sample is taken for testing in a lab, the results of the culture may be falsely negative while the results of the PCR may be positive.

It is also possible to identify plague using blood tests that look for antibodies to *Y. pestis*, although doing so necessitates collecting blood samples over time to look for variations in the F1 antibody titres during the acute and convalescent phases of illness [25]. A study conducted by Jullien et al. [25] on rapid diagnostic tests to identify the F1 capsule antigen (F1RDT) using sputum or bubo aspirate samples was published in 2020. According to the findings, the quick diagnostic F1RDT test cannot be utilized on asymptomatic individuals but can be applied to those who have a suspicion of pneumonic or bubonic plague. While studies suggest that F1RDT is extremely sensitive for both pneumonic and bubonic plague, it may be valuable in delivering a quick result for timely treatment and a quick public health response. When employing the rapid evaluation however, both positive and negative outcomes must be validated in order to establish or reject the diagnosis of a confirmed case of plague, and the screening outcome must be interpreted within the epidemiological context, as research findings show that while 40 out of 40 people with the plague in a population of 1000 were correctly diagnosed, 317 people were falsely diagnosed as positive [26,27].

5. PREVENTION

Joel and Vikas [9] reported that in 1897, bacteriologist Waldemar Haffkine created the first

plague vaccine. Between 1897 and 1925, he led a huge immunization program in British India, and it is believed that 26 million doses of Haffkine's anti-plague vaccine were distributed from Bombay, lowering plague mortality by 50-85%.

The CDC [28] reported that plague can be prevented by minimizing the habitat for rodents around living houses, workplace, and leisure locations. Eliminate any bush, rock piles, garbage, cluttered firewood, and potential rodent food sources such as pet and wild animal food. Rodent-proof your home and sheds. Gloves can be worn when handling or skinning potentially affected animals to avoid coming into touch with plague bacteria. If there is any question concerning the disposal of dead animals, local health department should be contacted [28]. Additionally, repellants should be used during camping or outdoor meeting if there is suspicion of rodent fleas in that environment. DEET-containing products can be applied to the skin as well as clothing, while permethrin-containing products can be administered to clothing (always follow instructions on the label) [28]. Flea-control products can be applied on pets to keep them flea-free. Free-roaming animals are highly likely to come into contact with plague-infected animals or fleas and bring them into households. If pets become ill, veterinary assistance should be sought as soon as possible. Also, free-roaming dogs or cats in endemic regions should not be allowed to lie on beds [28].

According to Jullien and colleagues [25], early diagnosis of plague reduces the disease's transmission or spread. Preventative strategies can also include notifying individuals when zoonotic plague is prevalent in their community and encouraging them to avoid handling animal carcasses and take precautions against flea bites [8]. People should be cautioned to avoid direct contact with contaminated body fluids and tissues in general. Standard measures such as wearing of appropriate Personal Protective Equipment (PPE) such as gloves, goggles or face shield, gown and respiratory protector, and also perform hand hygiene before and after patient contact by washing with soap and water or use of an alcohol-based hand sanitizer should be taken should be taken when handling possibly contaminated patients and collecting specimens.

With respect to vaccination, apart from high-risk categories such as laboratory professionals

who are constantly exposed to the risk of contamination, and health care workers, the WHO does not recommend immunization [8].

6. TREATMENT

According Nelson *et al.* [22] and Jullien and colleagues [25], all the manifestations of plague respond to antibiotic treatment if they are diagnosed early. The WHO [8] also reported that the inability to diagnose plague in time can reduce the chance of survival and increased complications. Streptomycin, chloramphenicol, and tetracycline are common antibiotics. Gentamicin and doxycycline, two antibiotics from the younger generation, have been shown to be efficacious in the monotherapeutic treatment of plague [22]. If left untreated, pneumonic plague can be lethal within 18 to 24 hours, however simple medicines for enterobacteria (gram negative rods) can effectively cure the sickness if given early [8]. Individuals who come into contact with severely ill pneumonic plague sufferers may be assessed and placed under observation [9].

7. CONCLUSION

This review has highlighted the ongoing threat of plague in Nigeria and Africa, particularly in remote villages. Despite a decrease in overall cases, the presence of infected rodents and fleas in these areas raises concerns about potential outbreaks. To address this, active surveillance is crucial in accurately assessing the true status of the disease. Establishing robust surveillance systems in remote villages is essential to enable early detection and prompt response to outbreaks. This can be achieved through strengthening local healthcare providers, enhancing laboratory infrastructure, and fostering collaborations among stakeholders. By actively monitoring and reporting plague cases, authorities can mobilize necessary resources, implement targeted interventions, and minimize the spread of the disease. Moreover, active surveillance plays a vital role in raising public awareness and understanding of plague, empowering communities to take necessary precautions and actively participate in disease control efforts. By intensifying efforts to establish comprehensive and sustainable surveillance mechanisms, Nigeria and Africa can effectively combat the challenge of plague, protecting the health and well-being of their populations.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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