

Pertussis: Re-emergence or underdiagnosed?

Sir,

Pertussis (whooping cough) is an extremely contagious, vaccine-preventable, respiratory infection caused by *Bordetella pertussis*. Pertussis spreads rapidly from person to person through contact with airborne droplets. Recent years have witnessed a surge in pertussis cases, and it is now the most common vaccine-preventable disease.^[1] In 2016, the World Health Organization reported 139,535 cases of pertussis worldwide, with a mortality rate of 4%.^[2] More recent trends also suggest that cases of pertussis continue to increase globally, with an estimated 151,074 cases reported in 2018.^[3]

Children in whom *B. pertussis* was detected from throat swab and/or nasopharyngeal swab were included in the study. The clinical course, laboratory findings, treatment, and outcome of the patients were recorded.

B. pertussis was detected in four infants out of a total of 76 infants whose nasopharyngeal swabs were tested for upper respiratory tract pathogens by multiplex real-time polymerase chain reaction (PCR) between January and June 2018. The patients in whom *B. pertussis* was detected were aged 28 days (patient 1), 1 month (patient 2), 2 months (patient 3), and 9 months (patient 4). The patients 1, 2, and 4 were not vaccinated against pertussis. At <6 weeks of age, the first two patients were not vaccinated; the third patient had received one dose of the acellular vaccine at 6 weeks of age. The pertussis vaccine was not administered to the 4th patient as the baby suffered intractable convulsions since birth. All patients presented with severe cough and respiratory distress and required admission in the pediatric intensive care unit.

The first patient (28 days old, female baby) had a history of cough and cold for the past 10 days and was being symptomatically treated at home. The mother also suffered from a persistent cough for the past 15 days. The baby was brought to the outpatient department as she had suddenly become drowsy and stopped taking feeds. She was advised for urgent admission. During the time of admission, she suffered an apneic spell and had convulsions. She was immediately ventilated and managed with all supportive care. At the time of admission, the total leukocyte count was 73,800 mm⁻³ with predominant lymphocytosis. The total count further increased to 90,780 mm⁻³ the following day. The initial antibiotics of cefotaxime and amikacin were substituted after the first dose by meropenem and

azithromycin following the detection of *B. pertussis* from nasopharyngeal swab by multiplex PCR. Exchange transfusion was initiated, but the patient succumbed to the infection on day 2 of admission.

The second, third, and fourth babies had a history of cough, cold, and mild fever for 10, 7, and 10 days, respectively. On account of respiratory distress and falling oxygen saturation, the babies were admitted to the intensive care unit. The total count was highly elevated in all the three patients (34,600 mm⁻³, 28,000 mm⁻³, and 716,000 mm⁻³, respectively), and differential count showed predominant lymphocytosis. They were managed in the pediatric intensive care unit with intravenous fluids, antibiotics, nebulization, and oxygen support. All of them received macrolide antibiotics (azithromycin at dose of 10 mg/kg bodyweight/day for 5 days and clarithromycin in two divided doses of 15 mg/kg/day for 7 days) following the establishment of pertussis diagnosis. All the three babies recovered with antibiotics and supportive therapy.

Pertussis in young infants is a severe, afebrile, cough illness that is frequently fatal. Pertussis has re-emerged on a global scale and is an ongoing public health problem, even in countries with high vaccination coverage. Declining vaccine-induced immunity, pathogen adaptation, and enhanced surveillance as well as advancements in molecular diagnostic facilities are some of the reasons thought to be responsible for the increased incidence of pertussis.^[4]

Reports of pertussis resurgence and outbreaks are mostly available from the developed world with sophisticated diagnostic facilities and improved surveillance systems of infectious diseases. It is possible that pertussis is being underreported from developing countries with large populations. Recently published data from a multinational serosurveillance study of *B. pertussis* infection among 10–18-year-old Asian children and adolescents which included patients from South Korea, Taiwan, China, Sri Lanka, Thailand, Japan, and India showed that there is a significant circulation of *B. pertussis* among Asian children and adolescents, with one in twenty having serologic evidence of recent infection regardless of vaccination background.^[5]

Microbiological diagnosis of pertussis is challenging. Culture, the traditional reference standard for diagnosis,

is only 20%–80% sensitive and requires special media and extended incubation. The recovery of *B. pertussis* from nasopharyngeal swabs in culture is an arduous procedure and is not a timely option for confirming the diagnosis as opposed to molecular tests that provide a higher sensitivity and swiftness than culture techniques. The availability of the Food and Drug Administration-cleared real-time multiplex PCR from nasopharyngeal swabs in a fully automated platform with a rapid turnaround time has greatly helped in the laboratory confirmation of pertussis. If pertussis is diagnosed in a timely manner, antibiotic treatment of the patient can mitigate the symptoms and prevent further transmission.

An increased white blood cell (WBC) count observed in almost all cases of pertussis is thought to be caused by the pertussis toxin. The fact that pertussis is associated with very high leukocyte count is evident from the above-described cases. All the patients had very high leukocyte count at presentation, and in the fatal case, leukocyte count increased to $90,780 \text{ mm}^{-3}$ despite optimum clinical management. The possibility of pertussis should be kept in mind in evaluation of young children with paroxysmal cough and respiratory distress with greatly elevated WBC counts. In the absence of reliable diagnostic facilities to detect *B. pertussis* infection, these indirect evidences along with a high degree of suspicion will help in the detection of clinical cases. Several studies have also shown that hyperleukocytosis is predictive of death among pertussis infected infants.^[6,7]

Macrolide antibiotics, erythromycin, azithromycin, and clarithromycin are the preferred drugs for the treatment of pertussis, provided they are initiated sufficiently early in the course of the disease. The diagnosis of pertussis is often not considered until the paroxysmal phase, which occurs 1–2 weeks after the onset of infection, and the administration of antibiotics at this stage may not yield desired results. Macrolide resistance is still rare and had been sporadically reported from China and Iran.^[8]

The availability of an effective vaccine against *B. pertussis* since the 1940s led to a substantial reduction in the morbidity and mortality caused by pertussis worldwide. Under the Expanded Programme of Immunisation (EPI) scheme in India, the pertussis vaccine is administered as a conjugate vaccine commencing from 6 weeks of age, initially as three doses 4 weeks apart. In our study, we found that pertussis occurred in infants who were not vaccinated or partially vaccinated. Young infants below the age for pertussis vaccination are highly vulnerable for contracting the infection. It is estimated that in India over 700 million episodes of acute respiratory infections (ARI) and over 52 million episodes of pneumonia occur every year in children under 5 years of age. ARIs result in ~1.9

million childhood deaths per year in developing countries, and 20% of these deaths are in India.^[9] It is possible that pertussis also contributes significantly to the disease burden. In such a scenario, vaccinating pregnant women with one dose of tetanus, diphtheria, and acellular pertussis (Tdap) vaccine in the third trimester of pregnancy would help to protect the very young children at risk for the infection. The Indian Academy of Pediatrics also recommends the use of Tdap during each pregnancy to provide protection to the very young infants.^[10]

Pertussis is making a resurgence worldwide. As is evident from the study, infants who are unvaccinated or partially vaccinated are at the highest risk of contracting the very severe form of the infection. Molecular diagnostic tools are useful for early and rapid diagnosis. A high index of suspicion is required to diagnose cases sufficiently early and improve outcomes.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

Ujjwayini Ray, Soma Dutta

Dr. Ujjwayini Ray, Department of Microbiology, Apollo Gleneagles Hospitals, Kolkata, West Bengal, India.

E-mail: dr_uray@rediffmail.com

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