



Challenges in diagnosis and treatment of pneumonic plague in Tamatave, Madagascar: retrospective cohort study

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Background

- Plague is caused by *Yersinia pestis*, with two main forms, bubonic and pneumonic
- Transmitted by inhalation of aerosol droplets. Highly contagious and usually fatal if treatment is not started within 24 hours of onset of symptoms
- In Madagascar, plague has been recognized as endemic
- A significant problem is the difficulty in reaching an accurate diagnosis for many patients presenting with symptoms
- A total of 2417 cases of plague were reported during this outbreak in Madagascar, including 209 deaths with a case fatality rate (CFR) of 9%.

Objectives

We aimed to describe:

- Epidemiology of patients with pneumonic plague treated at the Tamatave Respiratory Hospital between September and November 2017
- Characteristics, clinical signs and symptoms, and outcomes of treated patients
- Correlation between rapid diagnostic test (RDT) results done in the hospital, and RDTs and PCR tests done at the central laboratory

Methods

Study duration: 1st of August to 26th of November 2017

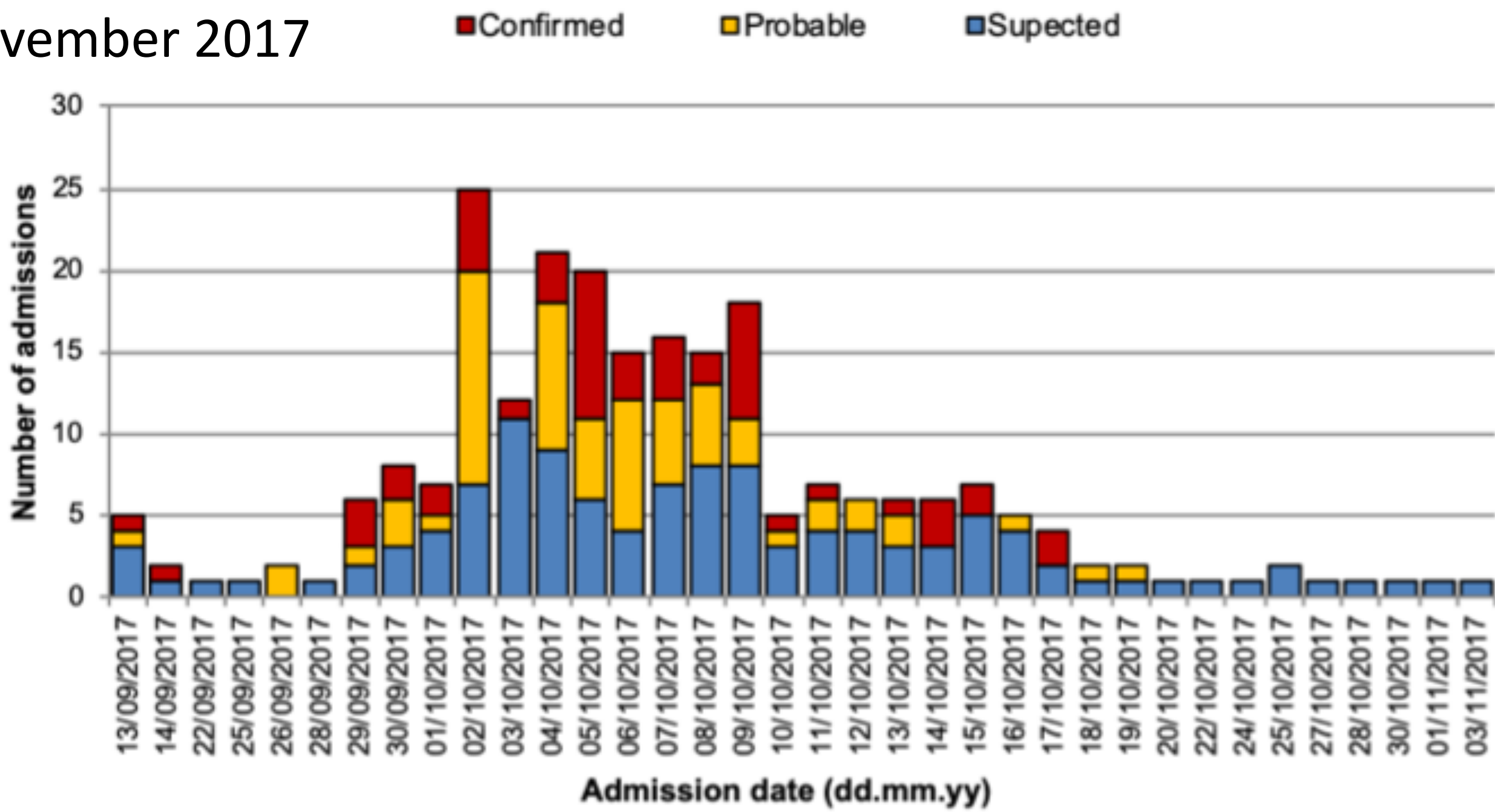
Study site: University Hospital of Tamatave, Madagascar

Study population: All patients admitted to Tamatave Hospital, during the MSF-supported intervention

Organisation of testing: RDTs were performed on most patients admitted to the hospital. Confirmation involved RDTs and PCRs, re-analyzed in the central laboratory in Antananaviro, Madagascar

Results

Number of daily admissions of suspected, probable and confirmed cases during a plague outbreak in the Tamatave Plague Treatment Centre (Madagascar) September to November 2017



This research was conducted through the Structured Operational Research and Training Initiative (SORT IT), a global partnership led by the Special Programme for Research and Training in Tropical Diseases at the World Health Organization (WHO/TDR). The model is based on a course developed jointly by the International Union Against Tuberculosis and Lung Disease (The Union) and Médecins sans Frontières (MSF/Doctors Without Borders).

- 235 pneumonic plague patients were admitted
- 116 (49.4%) were suspected, 66 (28.1%) were probable and 53 (22.6%) were confirmed cases
- Mean age of 28.6 years, 12.8% were minors
- Sex distribution was even
- The largest proportion of patients were students, followed by unskilled workers and healthcare staff
- Cough and chest pain were the most common symptoms
- Mortality rate at discharge was low, with five deaths (CFR of 2.1%).

Box Treatment protocol used during a plague outbreak in the Tamatave Plague Treatment Centre (Madagascar) September to November 2017

Madagascar Pneumonic plague treatment protocol:

Streptomycin (injectable)

- First 4 days: 0,5 g, 8 times a day
- Last 4 days of treatment 1g, 2 times a day

Table Demographics, clinical characteristics and treatment outcomes of patients during a plague outbreak in a treatment centre in Tamatave, Madagascar, Sept 13/17 to Nov 03/17

	N	%
Total number of patients	235	100
Age [years]		
0-4	2	0.9
5-17	28	11.9
18-34	147	62.6
≥35-64	52	22.1
≥65	4	1.7
Missing	2	0.9
Sex		
Male	122	51.9
Female	112	47.7
Missing	1	0.4
Occupation		
Students*	67	28.6
Unskilled workers	67	28.5
Missing	45	19.1
Health staff	32	13.6
Qualified workers	15	6.4
Unemployed	9	3.8
Symptoms		
Major symptoms		
Cough	150	24.8
Fever (≥ 38.5 °C)	57	9.4
Minor symptoms		
Chest pain	133	22.0
Haemoptysis	81	13.4
Headache	55	9.1
Weakness in legs	38	6.3
Asthaenia	35	5.8
Dyspnea	38	6.3
Chills	14	2.3
Others	3	0.5
Patient outcomes		
Cured	219	93.2
Died	5	2.1
Left against medical advice	8	3.4
Missing	3	1.3

- Hospital RDTs had a positive predictive value (PPV) of 60.5% (95% CI: 55.2%-65.6%) when compared to PCR
- Laboratory RDTs had a PPV of 73.5% (95% CI: 59.0%-84.3%)

Table Association between the results of PCR vs RDT tests carried out in the hospital and in the laboratory during a plague outbreak in the Tamatave Plague Treatment Centre, Madagascar, September to November 2017

PCR	Total	RDT Hospital						RDT Laboratory					
		Positive		Negative		Not Tested*		Positive		Negative		Not tested	
		N	%	N	%	N	%	N	%	N	%	N	%
Positive	57	49	86.0	7	12.3	1	1.8	25	43.9	32	56.1	0	0.0
Negative	47	32	68.1	15	31.9	0	0.0	9	19.1	38	80.9	0	0.0
Not tested	131	21	16.0	20	15.3	90	68.7	21	16.0	21	16.0	89	67.9
Total	235	102	43.4	42	17.9	91	38.7	55	23.4	91	38.7	89	37.9

The study was approved by the Ethical Biomedical Research Commission of the Ministry of Health of Madagascar. Nr062 MSANP/SG/-AGMED/CNPV/CERBM. This research fulfilled the exemption criteria set by Médecins Sans Frontières.

Conclusions

- One quarter (22.6%) of patients had a confirmed diagnosis of plague
- A large number of patients were treated with a regimen which has potentially serious side effects, which could not be confirmed as plague cases.
- The CFR was surprisingly low, when compared with those from a previous outbreak in 2015 (Moramanga et al; 71%)
- Results confirm a reasonable sensitivity/specificity and PPV for the RDTs used in hospital
- A more systematic diagnostic tool and treatment protocol could better target true plague cases and avoid overtreatment.