Investigation of a Haemorrhagic Disease with Unknown Origin in Kyrandia, 2005: A Teaching Case-Study

Student's Guide

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Abstract

A number of diseases are classified as hemorrhagic disease and differences between them relate to etiologic factors, being infectious or non-infectious, geographic distribution, incidence, reservoir, transmission method, and clinical symptoms. In Kyrandia, cases of a human haemorrhagic disease have been reported since 1940, yet recently, the reported cases have been increasing in number due to several factors. In October 2005, the Ministry of Health (MOH) reported fatal laboratory-confirmed cases in the State of Shanta in Kyrandia, where a total of 605 cases of outbreak-related illness were reported during that period.

The goal of this case study is to build the capacity of trainees to investigate hemorrhagic disease outbreaks of an unknown origin. This case study is based on real events with some fictitious elements. Details from the original outbreak investigation have been modified to enhance the learning objectives and support the instructional goals. This case study aims to stimulate students to identify the source of a disease outbreak, analyze surveillance data, eliminate the outbreak, and develop strategies to prevent future outbreaks. The case study also aims at training students to evaluate existing prevention strategies, describe newly emerging infections, learn more about known diseases, and appropriately address public concern. This case study is designed for the training of basic level field epidemiology trainees or any other health care workers working in public health-related fields. The case study can be administered in 3-4 hours. Used as adjunct training material, the case study provides the trainees with competencies in analysing available data in order to identify triggering factors for viral haemorrhagic disease outbreak.

Keywords: Haemorrhagic disease**,** outbreak, Kyrandia

How to Use the Case Study

General instructions: This case study should be used as adjunct training material for novice epidemiology trainees to reinforce the concepts taught in prior lectures. The case study is ideally taught by a facilitator in groups of about 20 participants. Participants are to take turns reading the case study, usually a paragraph per student. The facilitator guides the discussion on possible responses to questions. The facilitator may make use of flip charts to illustrate certain points. Additional instructor's notes for facilitation are coupled with each question in the instructor's guide to aid facilitation.

Audience: This case study was developed for novice field epidemiology students. These participants are commonly health care workers working in the county departments of health whose background may be as medical doctors, nurses, environmental health officers or laboratory scientists who work in public health-related fields. Most have a health science or biology background.

Prerequisites: Before using this case study, participants should have received lectures on disease surveillance and outbreak investigation.

Materials needed: Flash drive, flip charts, markers, calculators, computers with MS Excel, Annex 2 of the International Health Regulations 2005.

Level of training and associated public health activity: Novice – Outbreak Investigation

Time required: 2-3 hours

Language: English

Goal of Case Study

The goal of this case study is to build the capacity of trainees to investigate hemorrhagic disease outbreaks of an unknown origin

Learning Objectives

At the conclusion of the teaching session, participants will be able to:

1. Analyse and interpret data generated from a surveillance system in outbreak detection
2. Develop a case definition and discuss how to use it to conduct active case searches
3. Calculate attack rate and case fatality rate
4. Explain the process of notification to WHO
5. Discuss the measures associated with the collection of clinical specimens for the investigation of a suspected disease outbreak
6. Design an action plan for disease control and apply the appropriate measures for prevention and control

Introduction:

A haemorrhagic disease, i.e. a disease accompanied by abnormal bleeding, could manifest itself in any age group from infants to the elderly. The primary disease may involve any organ of the body or the body as a whole. A haemorrhagic disease usually has a severe course which is accompanied with high mortality [1]. A viral haemorrhagic disease outbreak is always an urgent public health event requiring immediate action. In the Eastern Mediterranean Region, a viral haemorrhagic disease was reported in more than 12 countries in the Region, yet most of the outbreaks in the region occured in remote areas with limited or non-existent medical services [2].

Kyrandia is located in the Eastern Mediterranean Region and has a land area of approximately $190{,}84^3$ km^2, and a population of 1.6 million people. The country is divided into 7 states and 22 localities (Figure 1). Kyrandia is primarily a savannah, with the Preim Mountains (460 – 910 m elevation) comprising small, isolated ranges throughout the state. Travel within Kyrandia is difficult and limited, especially during the rainy season. The rainy season lasts from mid-May until October. The population of Kyrandia consists primarily of subsistence farmers, and many families own farm animals including cattle and goats. Several nomadic tribes migrate seasonally across the country.

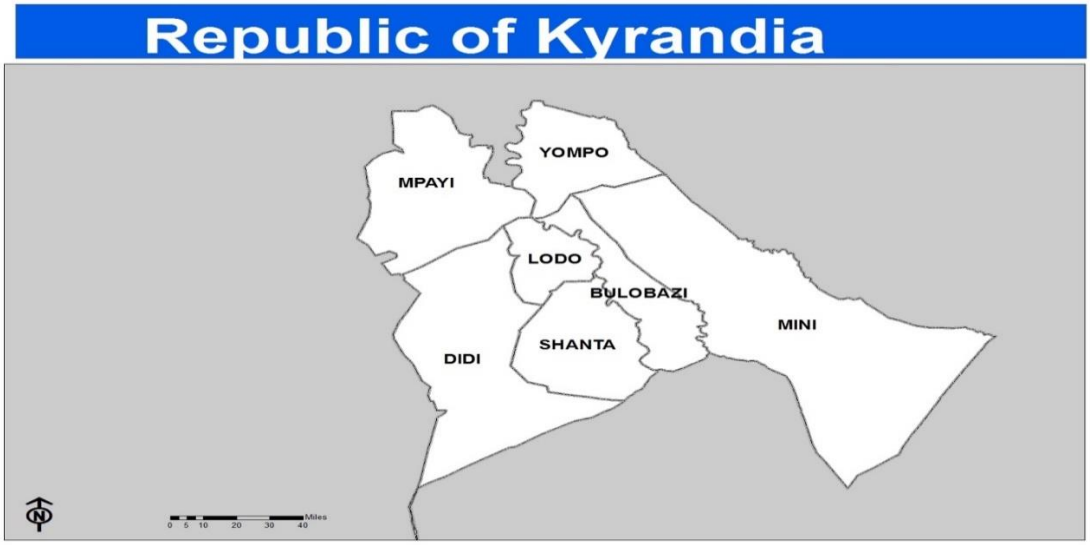

Figure 1: Map of Kyrandia Showing Constituent States, 2005

The health care infrastructure is in Kyrandia is rudimentary or non-existent, and much of the population relies on traditional medical practices. Kyrandia is affected by a heavy burden of vector-borne diseases including malaria, schistosomiasis, dengue, onchocerciasis, and lymphatic filariasis.

Kyrandia has witnessed several outbreaks of zoonotic arbovirus diseases such as Rift-Valley fever, Crimean-Congo haemorrhagic fever, yellow fever, and dengue A large-scale Yellow Fever outbreak occurred in the Preim Mountains in the 1940's infecting over 15,000 people. Yellow fever vaccination has not been introduced into the routine immunization schedule, and before this outbreak, the population of Kyrandia had not been vaccinated against the Yellow Fever virus.

Part 1: Story

1st of October 2005, Federal Ministry of Health: This morning, the Federal Ministry of Health (FMH) notified you, a public health officer, that there are 16 cases of haemorrhagic illness, including 11 fatalities, registered in the state of Shanta since the 28th of September. According to routine surveillance previously carried out in this region, mass haemorrhagic diseases have not been registered in last 5 years.

Part 1 Questions

Question 1. What are the possible causes of this condition?

Question 2. Is this an outbreak? If yes, why?

Question 3. Do you consider this disease to be severe? Justify your answer.

Question 4. What additional information do you need? Which would help you to investigate this public health event?

Part 2: Methods

The next day, you decided to make a call to Shanta State Hospital. *Following is a transcript of the communication between you and Doctor Mohamed Mehdi, Director of the Shanta State Hospital*

You*:* *Hello! Doctor Mohamed Mehdi? I am a public health officer from the Ministry of Health. I would like to ask you several questions about the cases of haemorrhagic fever you observed.*
Dr Mohamed*:* *All right, but let's talk as quickly as possible: there are many cases here, as you know...*
You*:* *What are the main symptoms of the disease?*
Dr Mohamed*:* *Mainly fever and bleeding. I have also observed jaundice in four patients.*
You*:* *Do you consider this disease severe?*
Dr Mohamed*:* *Oh, as I see, it is, many of the admitted patients have died.*
You*:* *Were there any cases of the disease in medical personnel?*
Dr Mohamed*:* *Thank God there weren't. We have no protective equipment except for gloves and masks.*
You*:* *Could you give me any information about age, sex ratio of your patients, and place of their residence?*
Dr Mohamed*:* *I do not remember these numbers; I will send you this info by email.*
You*:* *Did you perform any laboratory investigations to reveal a causative agent?*
Dr Mohamed*:* *No, we don't have such possibilities. We will send 11 blood samples to the National Public Health Laboratory; please, address them directly for results.*

Part 2 Questions

Question 5. What samples should be collected for testing? What etiologic agent should the lab test for?

Question 6. You need to organize transportation of the blood samples for further serological investigations. How must they be packed and declared according the International Air Transport Association (IATA)? *You can use (Annex 1) to answer the this questions*

Question 7. What do you think the biosafety level (BSL), it must be found it the national heath lab to investigate the samples?

Part 3: Results

You contacted the Shanta Hospital and the physician sent you information. Many of the patients were nomads of the Trury tribe (Table 1), and there did not appear to be any clustering of illness within families or transmission to health care workers.

According to the Shanta public health authorities the cases were presented with illness characterized by fever and severe headache and backache. Half of the patients had haemorrhagic signs, including gingival bleeding, epistaxis, hematemesis and melena, and 37.5% of them had jaundice. The Federal Ministry of Health, WHO, and the State Ministry of Health started initial investigations in the Shanta State

Table 1: List of Patients from Shanta Hospital

ID #	Sex	Age	Onset	Residence	District	Fever	Jaundice	Haemorrhage	Death
1	Male	60	05 Sep.	Permanent Resident	Shanta	+	-	+	+
2	Female	41	05 Sep.	Nomad	Shanta	NA	NA	NA	+
3	Female	8	05 Sep.	Permanent Resident	Didi	NA	NA	NA	-
4	Male	31	19 Sep.	Nomad	Shanta	NA	NA	NA	+
5	Female	17	19 Sep.	Nomad	Bulobazi	NA	NA	NA	+
6	Male	13	26 Sep.	Nomad	Shanta	+	+	+	+
7	Female	21	26 Sep.	Nomad	Shanta	+	+	+	-
8	Male	25	26 Sep.	Permanent Resident	Lodo	NA	NA	NA	+
9	Female	47	03 Oct.	Nomad	Shanta	+	-	+	-
10	Female	37	03 Oct.	Permanent Resident	Shanta	NA	NA	NA	+
11	Male	2	03 Oct.	Nomad	Lodo	+	+	-	+
12	Male	5	03 Oct.	Permanent Resident	Mini	+	-	-	+

13	Male	7	03 Oct.	Nomad	Shanta	NA	NA	NA	-
14	Male	33	03 Oct.	Nomad	Shanta	+	-	-	-
15	Male	2	03 Oct.	Permanent Resident	Lodo	+	-	-	+
16	Female	6	03 Oct.	Nomad	Lodo	NA	NA	NA	+
17	Male	21	03 Oct.	Nomad	Mpayi	+	-	-	-
18	Female	7	03 Oct.	Permanent Resident	Mpayi	+	-	-	+

NA – not available (no information available)

Eleven blood samples collected from patients with characteristic symptoms were submitted to the National Public Health Laboratory. Using a dengue virus (DENV) rapid strip test, IgM antibodies against DENV were detected in five (45%) of 11 blood samples.

Part 3 Questions

Question 8. How could you interpret the data obtained from the list? What risk factors do you suspect? (see Table 1)

Question 9. List the steps needed to investigate an outbreak.

Question 10. What is the outbreak case definition to add new cases to a line list throughout the outbreak?

Question 11. What is your strategy to further follow up on this outbreak?

Question 12. Do you think the country should notify WHO about this event? *Use Annex 2 of the International Health Regulations 2005 to answer this questions.*

Part 4: Discussion

During the past 10 days, field teams interviewed village and nomad chiefs, health directors of state and districts ministries, physicians and medical assistants at the Shanta State.

The index case was a 60-year-old male resident of Yondo (Shanta district) who died on the 20th of September. The first case in the nomadic population was reported from the Shanta district with an estimated onset date of September 5, and it occurred in a 41-year-old female who died on

September 23. The index patients had no history of travel in the week before their illness. Sporadic cases of the diseases occurred until early October when the number of reported cases increased rapidly, peaking on the 17th of October.

You received surveillance data from the Federal Ministry of Health sentinel surveillance system. During the period from September 5 (the outbreak's onset) to Octoberc31, the number of cases increased and amounted to 408 cases (see Figure 2, Table 2). Cases of haemorrhagic fever have been reported in States of the South Bulobazi and Didi

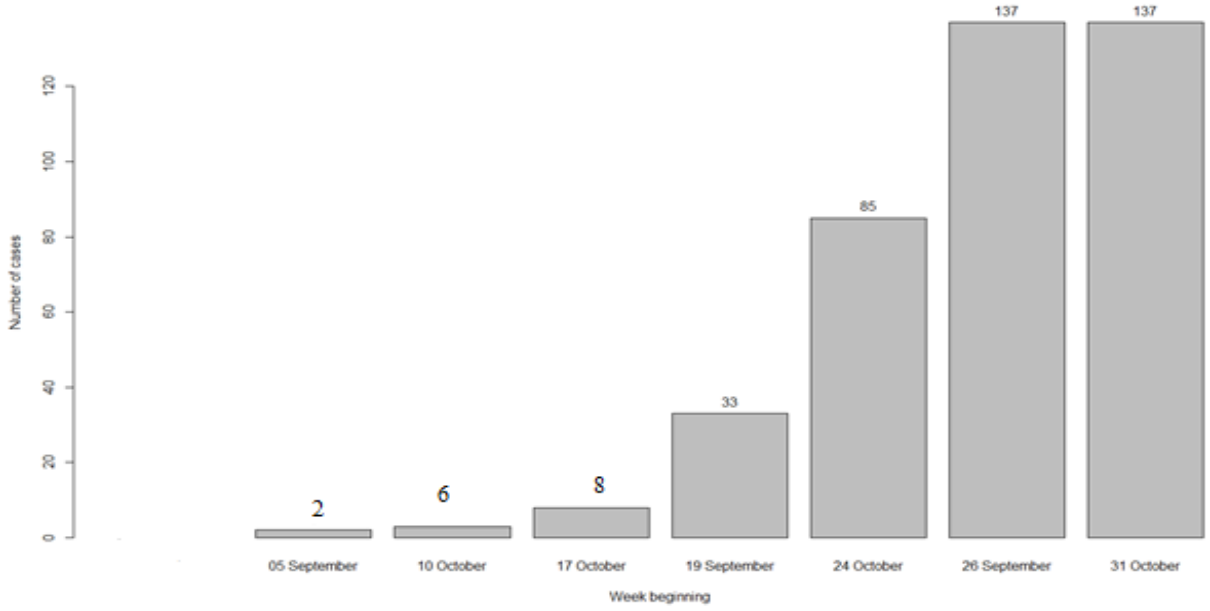

Figure 2. Kyrandia Haemorrhagic Fever Outbreak, Epidemic Curve by Date of Onset

Table 2: Characteristics of Outbreak-related Illness Cases

Characteristic	**n (%)**
Total reported cases	408 (100)
Deaths	292 (71.6)
Sex	
Male	233 (57.1)
Female	175 (42.9)
Age	

< 5	32 (7.8)
5 – 14	95 (23.3)
15 – 29	118 (28.9)
30 – 44	94 (23.0)
> 45	69 (16.9)
Residence	
Nomad	201 (49.3)
Permanent Resident	207 (50.7)

Further serological testing conducted at the Naval Medical Research Unit-3 (NAMRU-3, Cairo, Egypt) found IgM antibodies against the Yellow Fever virus in 13 (34%) of the 38 serum samples, and Chikungunya virus was isolated from two samples at the Centre for Disease Control and Prevention, Fort Collins, CO, USA. In addition, further Clinical information was obtained for 177 patients unvaccinated against Yellow Fever attending clinics in Didi and Lodo, and was used to classify patients into three categories [4] (see Table 3).

Table 3: Classification of 177 Patients with Illness Reported During the Outbreak and Results of their Serological Investigation

Classification	YF	DEN	YF + DEN	CHIK	YF + CHIK	None
Suspected yellow fever	10 (16%)	1 (2%)	1 (2%)	9 (15%)	6 (10%)	35 (56%)
Fever + jaundice + haemorrhage	4 (22%)	0 (0%)	0 (0%)	1 (6%)	3 (17%)	10 (56%)
Fever + jaundice + death (20 of them without any haemorrhage)	6 (14%)	1 (2%)	1 (2%)	8 (18%)	3 (7%)	25 (57%)
Severe illness	0 (0%)	0 (0%)	0 (0%)	3 (14%)	1 (5%)	18 (82%)
Fever + haemorrhage	0 (0%)	0 (0%)	0 (0%)	3 (15%)	0 (0%)	17 (85%)
Fever + jaundice	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (50%)	1 (50%)
Febrile illness	0 (0%)	0 (0%)	0 (0%)	2 (18%)	0 (0%)	6 (82%)

Part 4 Questions

Question 13. What is a new standard case definition? Suggest suspected, probable, and confirmed case definitions for a case for use in this investigation.

Question 14. According to the epidemic curve's shape, what do you assume was the pattern of infection spread in the population (point, intermittent, propagated)?

Part 5: Conclusion

From the 5th of September through the 31st of October, 408 cases of acute febrile illness, many with jaundice or haemorrhage, were reported from Kyrandia.

Results of serological investigation suggested that at least a portion of the outbreak was due to Yellow Fever Virus (YFV). This is evidenced not only by serological results of recent YFV infections in several unvaccinated persons, but also by the high case fatality rate and the clinical syndromes compatible with Yellow Fever.

In addition, the isolation of the Chikungunya virus, the serological evidence of recent Chikungunya infections, and the clinical syndromes compatible with Chikungunya suggest that this virus also contributed to the outbreak.

On the 1st of November, the Federal Ministry of Health officially declared an outbreak of Yellow Fever after which the Yellow Fever case definition mentioned above was adopted.

In response to a request from the Federal Ministry of Health, an international, multidisciplinary team (including yourself) carried out additional epidemiological and entomological investigations to confirm the cause and further describe the outbreak. Cases were reported from 6 States in Kyrandia (see Figure 3).

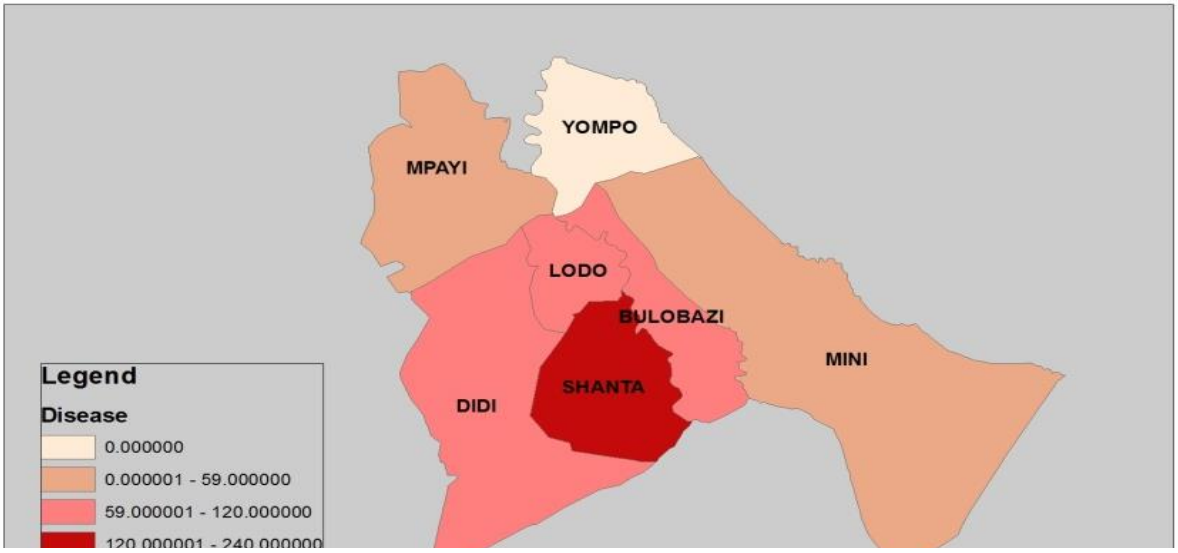

Figure ***3: Haemorrhagic Fever Case Distribution by State, 2005***

Part 5 Questions

Question 15. Look at the map. Discuss the infection spread. What additional investigations do you need to perform?

Question 16. Based on the preliminary findings mentioned above, what control and prevention measures should the investigating team recommend?

Question 17. The basic reproductive rate (R0) for Yellow Fever is about 4. How many people do you expect to be infected from one case if no measures are put in place?

Question 18. You need to write a final outbreak investigation report. What parts should be included in the report? Why is it important to write an outbreak report? Who should receive this outbreak report?

Summary of the Case, Actions Taken, and Recommendations

Vaccination against YFV is the most effective public health intervention to prevent and control epidemics in endemic regions. However, its impact on the control of this particular outbreak was likely limited. Despite achieving high vaccination coverage, the outbreak had largely waned by the time the campaign was organized and launched.

Nevertheless, the vaccination campaign was essential in preventing and limiting future outbreaks in this region. The impact of mosquito control on this outbreak is difficult to determine, and mosquito control has been limited to primarily larger towns while most cases were reported from smaller villages. Mosquito control efforts were conducted in some villages along the Trury migration route and efforts in larger towns might have helped prevent transmission in these areas. Also, mosquito control measures for YF outbreaks have generally had limited efficacy against sylvatic vectors, and control may be useful in limiting virus spread in urban areas until protection afforded by vaccination campaigns can be realised. Control operations were hampered by a number of technical constraints including lack of resources and personnel trained in mosquito control and entomologic assessments of control efficacy.

As with the 1940's outbreak, the end of this outbreak may be attributed to the end of the rainy season and the corresponding elimination of suitable mosquito breeding sites rather than either vector control or the vaccination campaign.

Prompt recognition and control of this particular outbreak was hampered by lengthy delays in recognition of the outbreak and in the time required for shipping and testing of diagnostic samples. Effective and timely responses to future outbreaks depend on improved surveillance and increased laboratory capacity in developing countries. Diagnosis of YF and other arboviral diseases relies on improving medical facilities and health care provision in endemic regions.

Source: The case study is based on real events [3] with some fictional elements. Details from the original outbreak investigation have been modified to enhance learning objectives and support the instructional goal. Persons that are only named "a case" in the scientific literature are sometimes given fictional features.

Annexes

Annex 1: The triple package layers (figure provided by IATA, Montreal, Canada)

Annex 2: International Health Regulations IHR (2005)

Acknowledgements

We wish to acknowledge the Global Partnership Initiated Academia for Controlling Health Threats (GIBACHT) and their funding body, the German Federal Foreign Office, and the Eastern Mediterranean Public Health Network (EMPHNET) for their support in developing this case study

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Resources and reading materials

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