Syndromic surveillance of potentially epidemic infectious diseases: Detection of a measles epidemic in two health centers in Gabon, Central Africa

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Abstract

Measles is a respiratory disease caused by the measles virus (MV) belonging to the *Paramyxovirus* family and the *Morbillivirus* genus. Due to a failure in maintaining immunization coverage in some countries, measles is a re-emerging disease in the human population, especially in Africa. The aim of this study was to describe a measles epidemic in Gabon. At first, a syndromic surveillance was set up. Blood samples from febrile patients with maculopapular rash were taken and sent to the measles reference center in Cameroon for laboratory confirmation. Between March and May 2016, 79 clinically suspected cases were reported including 82.3% (n=65) and 17.7% (n=14) in Oyem and Libreville, respectively. In total, 39.2% (n=31) of children were 11 months-old, 34.2% (n=27) were children aged 1 to 4 years, 11.4% (n=9) were older children from 5 to 9 years, 6.3% (n=5) of children were aged 10 to 15 years and 8.9% (n=7) were 15 years and older. 53.3% (16/30) were laboratory confirmed. This measles outbreak reiterates the importance of maintaining a high level of vaccine coverage in Gabon for vaccine-preventable diseases, as well as the usefulness of a near-real-time surveillance system for the detection of infectious diseases.

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Introduction

Despite remarkable advances in the fields of management and medical research, infectious diseases still represent the second cause of death worldwide, mainly due to the period emergence or re-emergence of them in the human population In the last few years, vaccination has been an essential tool in the fight against infectious diseases and it has greatly reduced the overall burden of infectious diseases according to the World Health Organization (WHO).[1] Several vaccination campaigns have been performed around the world to fight against numerous diseases. Nonetheless, vaccine preventable diseases remain a major public health concern in the world.

Measles is among the infectious diseases which have had an impact on the evolution of human society. It is a highly contagious respiratory infection that is caused by a virus that grows in the cells lining the throat and lungs. This disease is transmitted mainly through air because the virus spreads whenever someone who is infected coughs or sneezes. The Measles Virus (MV) is an enveloped virus with a long non-segmented RNA genome of negative polarity.[2] MV belongs to the *Paramyxovirus* family and the *Morbillivirus* genus. It is characterized by the fact that it exclusively uses a human reservoir.[3] People who catch the disease develop an overall body skin rash and symptoms such as fever, cough, and a runny nose. Without vaccination, measles can induce several complications such as ear infection, pneumonia, and encephalitis. Therefore, this highly contagious disease which mainly affects children could be avoided with vaccine. Measles was responsible for 139,300 deaths in sub-Saharan Africa in 2010. Beside endemic cases, some deaths occurred during epidemics.[4]

In Gabon, many cases of measles have been reported during the past few years.[5] However, the total number of cases of measles reported annually has declined substantially, as is the case worldwide. Nonetheless, despite the availability of vaccines and the existence of public immunization recommendations, epidemics of childhood diseases continue to occur. The aim of this study was to assess the effectiveness of a syndromic surveillance system able of detecting new or re-emerging infections such as measles in our population.

Materials and Methods

Ethical considerations

All work was carried out with the authorization from the Gabonese Ministry of Health (authorization No. 292). The study was conducted in two hospital centers in Gabon, in the cities of Libreville and Oyem. All the samples obtained were only collected in patients who came to the hospital centers for a consultation and were suspected to be infected by the measles virus. National clinical and epidemiological data were manually notified, electronically recorded and transmitted monthly to the Ministry of Health for compilation via the regional epidemiological database.

Study sites

This cross-sectional study was conducted in Oyem at the Regional Hospital Center and in Libreville at the Nzeng-ayong Medical Center (Figure 1). These hospitals participate in the syndromic surveillance network for infectious diseases with epidemic potential (SuSyMIPE).

Case-definition

A suspected case of measles was defined as a fever ≥38°C with a maculopapular rash which extends from the face to the extremities with at least one of the following manifestations: cough, coryza or conjunctivitis. The investigation was car-

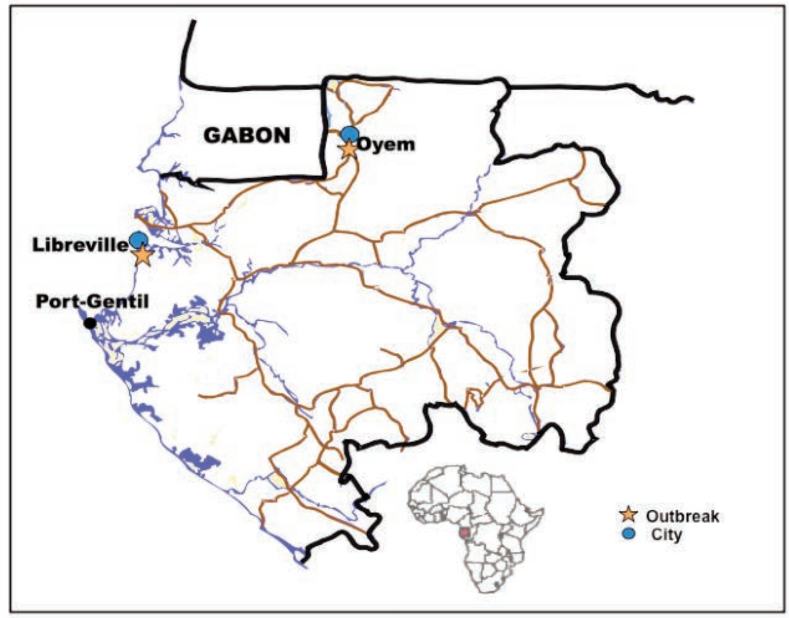

Figure 1. Geographical location of cases reported during the measles outbreak, Libreville-Oyem, March-May 2016.

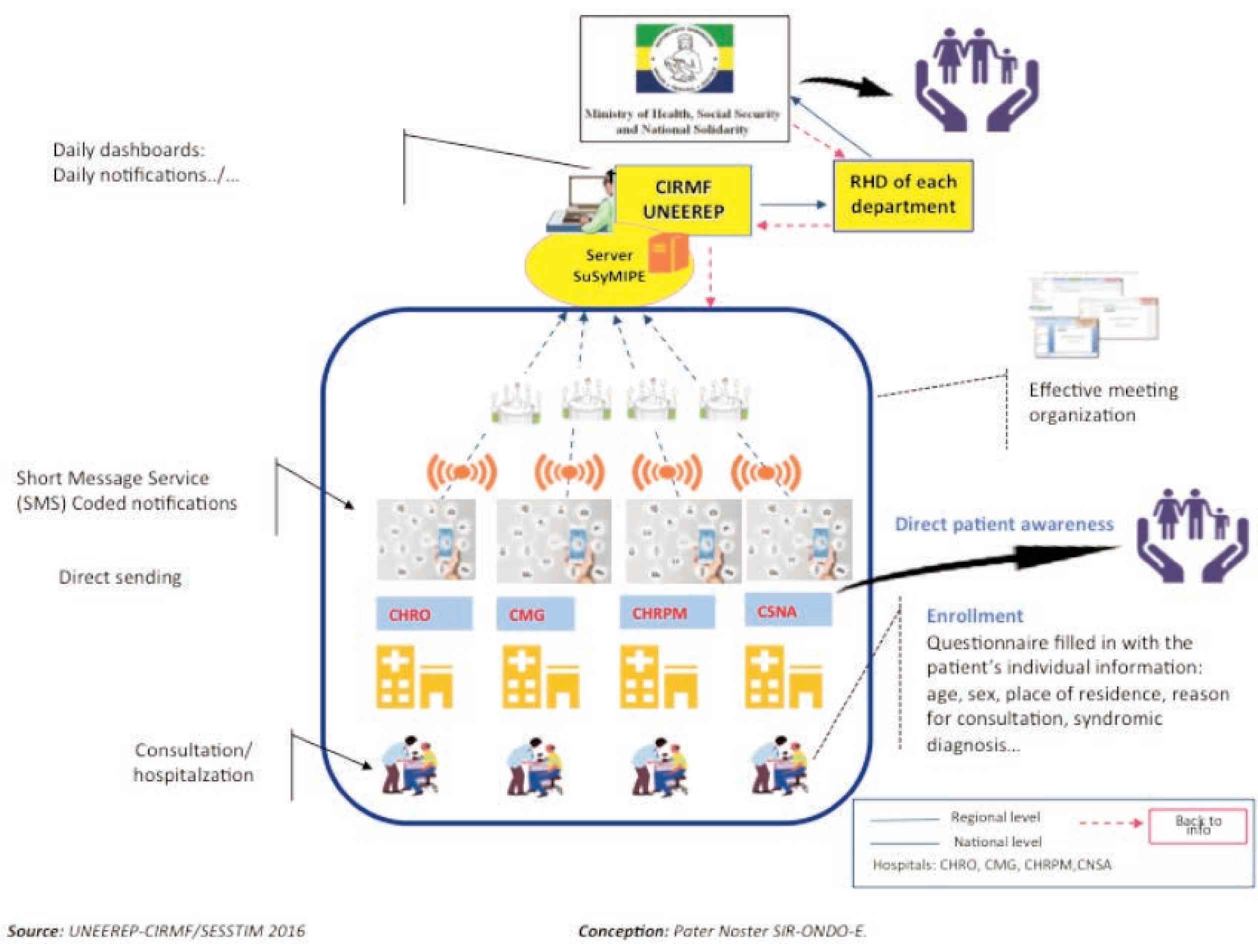

Figure 2. Architecture of the monitoring network for the syndromic surveillance of infectious diseases and potential epidemics.

ried out in the field by the SuSyMIPE network teams who investigated the cases in two of the four health facilities participating in the network in Libreville and Oyem.

Confirmation of cases

Serum samples from suspected patients were confirmed using Real-Time Polymerase Chain Reaction (RT-PCR). RNA was extracted from blood and the measles virus was diagnosed according to the previously described protocol.[6]

National surveillance system

This system presents a pyramidal organization with three levels that coexist without any formal relationship of complementarity: the peripheral, intermediate and central levels. Integrated national surveillance of diseases, including measles, was effective in health facilities in the various health departments of Gabon. Collected samples were sent for analysis at the National Virology Laboratory of the Health Sciences University in Libreville and the Pasteur Institute of Cameroon for the confirmation of different suspected cases.

Outbreak declaration and management

The data of the services participating in the SuSyMIPE Network (Syndromic Surveillance of Potential Epidemic Infectious Diseases) were systematically collected on a standardized questionnaire. The information collected included the patient's name, place of residence, age, sex, date of consultation, date of onset of symptoms, date of onset of rash, vaccination status, and epidemiological relationship with a known case. Immunization status was determined by the history and/or examination of the vaccination record. The syndromic diag-

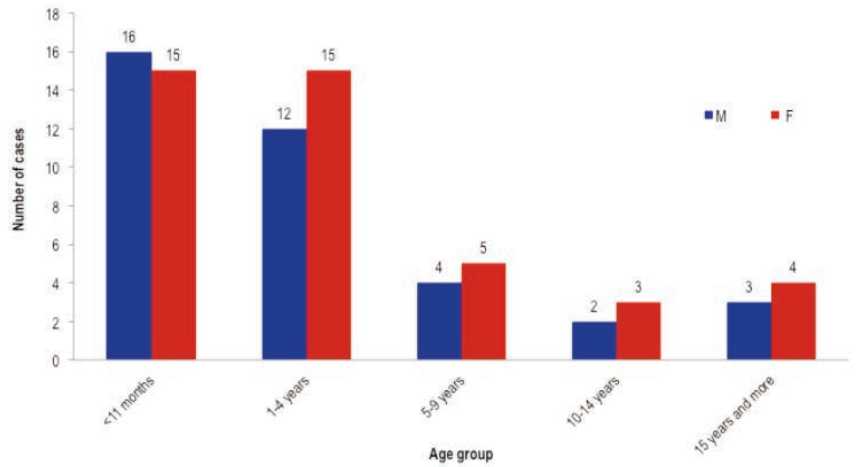

Figure 3. Distribution of measles cases by age, group and sex, Libreville-Oyem, March-May 2016.

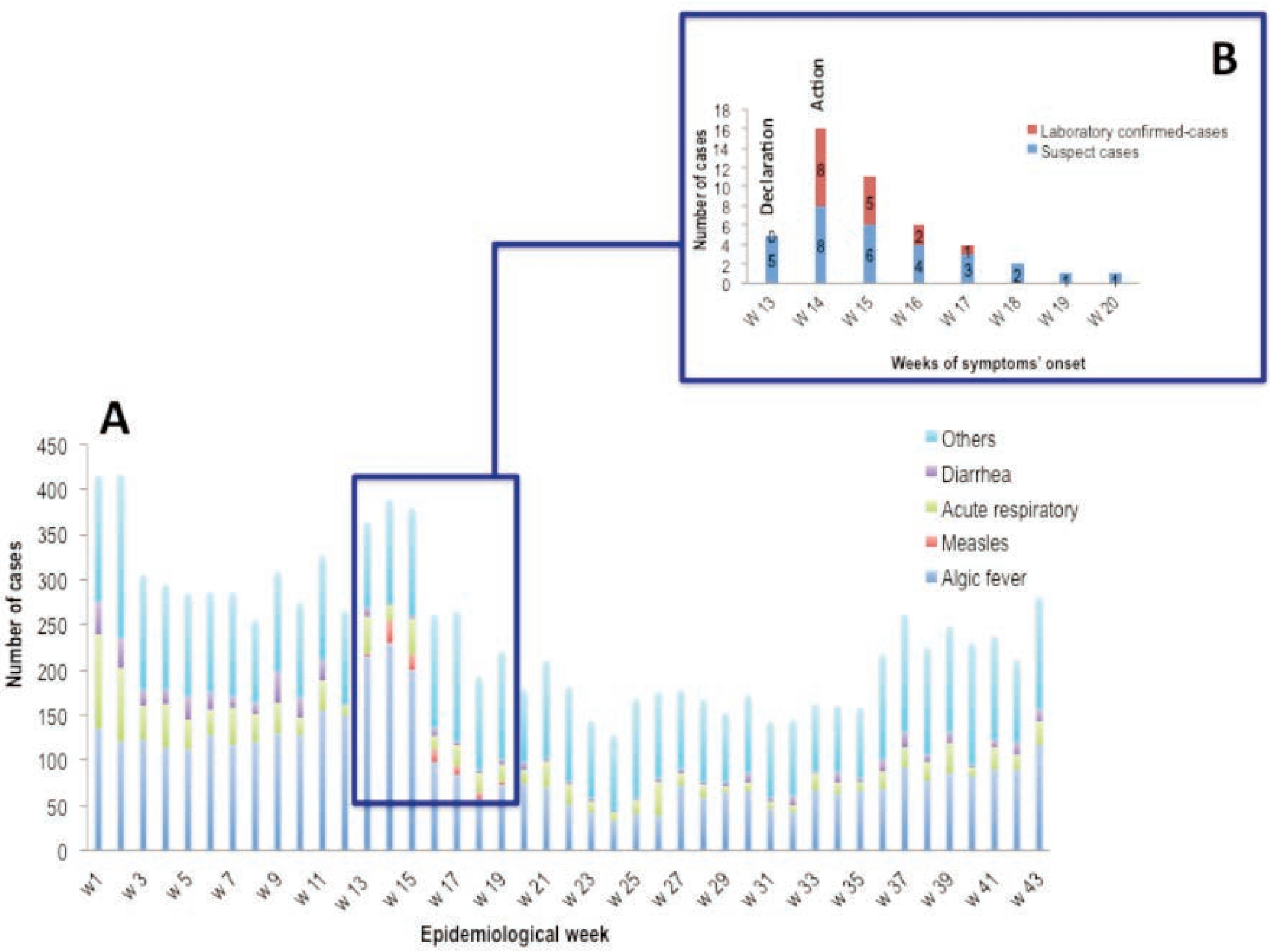

Figure 4. A) Weekly syndromic data notified by all the emergency services. B) Number of measles cases reported per epidemiological week during the Gabonese epidemic: Libreville-Oyem, March-May 2016 (N=79).

noses of the physically examined patients were expressed in codes. At the end of the afternoon, these data were sent by the doctor responsible for the study site to the SuSyMIPE network base, directly via Short Message Service (Figure 2). Daily notifications on all suspected cases were sent to the Regional Health Departments (RHAs) of each department. In case of hospitalization, isolation of the patient was set up until the complete eruption of the rash.

Blood collection

The blood taken from each patient was put in 3 to 5 ml EDTA Vacutainer tubes (VWR International, France). The blood samples along with the investigation sheets, were given to the Nkembo Expanded Program for Vaccination (EPI) for the sampling in Libreville and the great endemics for those of Oyem and they were then channeled to a reference laboratory in Cameroon (Institut Pasteur). In order to complete the data analysis, the data had to be of good quality and transmitted in real time (the same day and on a regular basis).

Statistical analysis

The collected data was registered using an Excel file and analyzed by the SPSS© (Statistical Package for Social Sciences) software version 20. Frequencies, proportions, and age-specific rates were calculated to describe the epidemiology of the outbreak. The statistical significance was defined when a P-value was <0.05.

Results

Outbreak and study population

Between January and March 26th, the means of febrile children seen in study sites varied between 112 and 145 by week. At March 28th, 215 febrile children were registered among them, 10-20% presented maculopapular rash. Between March 28th and May 10th, 79 suspected cases of measles (65 cases in Oyem and 14 in Libreville) were reported by the *SuSyMIPE* network, and in this context the measles epidemic was detected.

The sex ratio M/F of the population was 0.88 and the mean age was 49.37±72.82 months.

Clinical symptoms

Among a total of 79 suspected cases, 32 samples were tested in laboratory. The remaining 47 suspected cases had the same symptoms as the previously confirmed cases. Among the cases reported, 73.4% of them were aged between 0 and 4 years old. In total, 39.2% (n=31) of children were 11 months old, 34.2% (n=27) were children aged 1 to 4 years, 11.4% (n=9) were older children from 5 to 9 years, 6.3% (n=5) of children were aged 10 to 15 years and 8.9% (n=7) were 15 years and older (Figure 3).

The last case was reported at week 19. Of the 79 reported cases, 82.3% (n=65) were from Oyem and 17.7% (n=14) from Libreville. We recorded 53.2% (n=42) of females and 46.8% (n=37) of males (P=0.14). The majority of confirmed cases were in the Nzeng-Ayong district for those in Libreville and three districts in Oyem (Mekom Nkodje, Akouakam 1 and Methui). Vaccination status was known for the 79 reported cases. Of these, only 1.3% (n=1) were vaccinated with a single dose of MCV. Based on the available data for 70 cases, 57% (n=45) were reported within 48 hours of the onset of clinical symptoms.

Confirmation of measles cases

In response to the increase in reported measles cases, active surveillance for measles was initiated in both provinces, using the World Health Organization (WHO) case definition.[6] After one month of monitoring, our system recorded 30 suspected measles cases. Only around 53.3% (n=16/30) of the first suspected cases were laboratory confirmed as infected with the measles virus (Figure 4) but afterwards, all suspected cases were confirmed.

The main symptoms observed following a brutal appearance in the initial phase were fever and skin lesions in all patients. The predominant syndromes in this study were fever, maculopapular rash, cough and/or conjunctivitis. The duration of the symptoms was 3 to 5 days. The mean duration of symptoms in the acute phase was 7 days (range: 1 to 24 days). Hospitalization was required for 38 patients (48.1%) with more pronounced manifestations, and the average length of stay was 2.6 days (1-6 days). No serious forms or deaths were attributable to this measles epidemic (Figure 5).

Discussion

In this study, we investigated the 2016 measles epidemic in two cities in Gabon. This measles epidemic mainly affected children and adults during 6 weeks.

Nearly one third of cases were among children of 0 to 11 months of age, this is certainly due to the relatively low measles antibody levels in this age group and the fact that the majority of these children had not received measles vaccination.

Isolation measures against measles in hospitals were not respected at the beginning of the outbreak, which probably facilitated the transmission of the virus. Vaccine coverage in adults could not be assessed due to the lack of vaccination cards. No complications or deaths due to the measles epidemic were reported in our study.

Infectious diseases are the leading cause of mortality and morbidity in sub-Saharan Africa.[7] Concurrent infections with the chikungunya and dengue viruses occurred during simultaneous epidemics in Gabon in 2007.[8-12] These epidemics, which are not included in the WHO data, are nevertheless described for the most part in various scientific publications. The aim of transferring case reports by SMS is to very quickly detect an unexpected event, syndromic

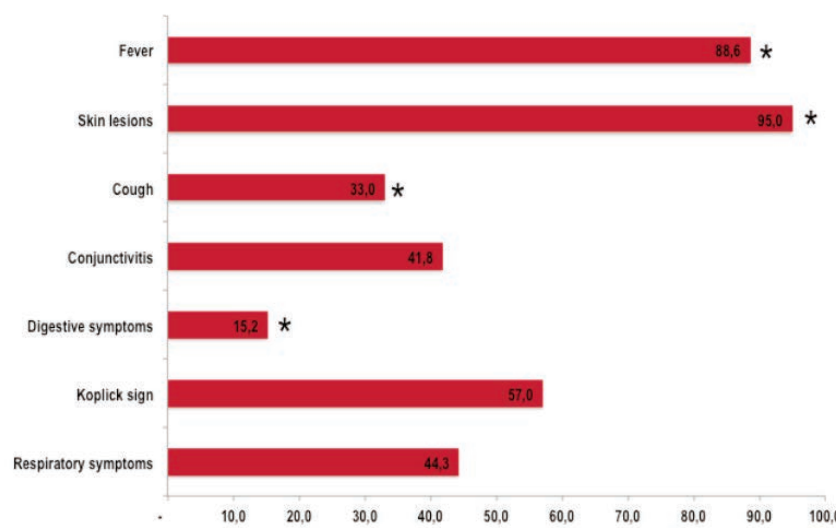

Figure 5. Proportion of symptom follow-up reported during the measles outbreak, Libreville-

regroupings composed of several medical diagnoses relevant in the syndromic surveillance of infectious diseases with epidemic potential in Gabon.

Gabon has in this case experienced a limited non-fatal outbreak of measles unlike other African countries where large measles outbreaks linked with deaths recently occurred, except for Senegal in 2009 and the Central African Republic in 2011.[13-18] In 2010-2011, a new outbreak in the Katanga province of the Democratic Republic of the Congo caused 128,113 measles cases and 1454 deaths.[19,20] Malawi also had a large outbreak in 2010 in a context of high vaccine coverage, which was responsible for 134,039 cases and 304 deaths, numbers comparable to the pre-vaccine era.[21] Another study conducted in South Africa from March 2009 to August 2011 showed more than 18,000 laboratory-confirmed cases of measles.[22]

Infants were primarily affected during the initial phase of the outbreak. After birth, maternal antibodies undergo exponential clearance (half-life of 35 to 40 days)[23] and women who have immunity induced by the vaccine only provide a relatively short period of passive immunity to their young children.[24-27] In closed communities such as schools, measles can be transmitted, and due to repeated exposures, an outbreak can be maintained.[28,29] Because the highest sensitivity to measles is found in unvaccinated children aged 6 to 11 months, a review of the measles vaccine schedule for children in developing countries should be implemented. We found that in addition to children, we had three adults who had been diagnosed with measles with clinical signs similar to those of children and they were confirmed by laboratory test, thus demonstrating that young adults in sub-Saharan Africa and in particular in Gabon can be still susceptible to measles.

The implementation of an infectious disease surveillance system with real-time epidemic potential in Gabon will help to control epidemics. Suspect cases will be reported promptly; however, health care personnel should check the diagnosis in order to increase accuracy and to allow that response measures in the event of an epidemic will be implemented very quickly by health authorities. The delivery of the results was delayed because the biological analysis was done abroad. This study suggests the need for reference laboratory on the national territory (such as a research center) approved by the WHO to render promptly available results.

According with preliminary data, we observed trends that were consistent with seasonal epidemics in the local context, such as the increase of febrile syndrome with maculopapular rash in March. To ensure the efficiency and accuracy of surveillance, sentinel systems require strong communication. The syndromic diagnoses of this study have been coded almost completely and in real time. It has reduced the detection time from 7-10 days to 3-5 days. In addition, SuSyMIPE has adopted mobile (SMS) and web technologies that allow health facilities to inform cases of syndromes under surveillance online using smartphones or laptops. As a result, our system can further facilitate the surveillance of infectious diseases with epidemic potential and reduce surveillance loads. Syndromic surveillance has many advantages, such as an access to large numbers of data in real time, the absence of a specific workload for hospital staffs, the constitution of historical bases to determine the existence of health phenomena which go unnoticed by a retrospective analysis of the data. The experience gained today shows that syndromic surveillance should not be opposed to traditional surveillance and that on the contrary, they are complementary. Despite the challenges in the collecting and sharing of data, the syndromic surveillance system (SuSyMIPE) has significant advantages over the traditional surveillance system. The data reporting procedure was very simple, flexible and financially inexpensive. Even data providers with little computer knowledge can become proficient in a very short time with practice and training.

The limitations of our study are mainly related to the small number of infectious disease detection sites. Power outages in rural areas in Gabon have also increased the difficulties of SMS data communication which limits the development of the syndromic surveillance network. Furthermore, our study was limited for two reasons. First, the estimation of VGM conversion was based on interviews with patients and clinical records. Second, it is difficult to assess measles vaccine effectiveness. All young adults and adults may have received vaccination to measles during their childhood, however, we find it difficult to trace their vaccination history given the lack of vaccination cards. Thus, our estimate regarding coverage cannot be generalized to the entire population.

Conclusions

The analysis of the two-month pilot data described in this document was primarily aimed at demonstrating the feasibility of collecting functional data from syndromic monitoring sites across the network. The model presented here is designed as proof of concept that, in Gabon, a syndromic surveillance system can work. From now on, a thorough evaluation of this system is needed to correct possible errors and ensure that the system meets the standards. Syndromic surveillance should be put into temporal perspective in its use, in the very short term for detection and warning, in the medium term for the creation of historical reference and finally in the long term to constitute historical databases useful to describe the health status of the population. The SuSyMIPE platform can facilitate early detection of infectious disease epidemics by providing near real-time syndromic data collection and automatic detection of aberrations. This is certainly a small-scale study, which has some limitations, but it could easily be extended to entire countries with limited resources.

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