Surveillance for diseases targeted by new vaccines: Progress, challenges and way forward

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Globally, pneumonia and diarrhoea remain major causes of infant mortality. These two diseases, account for 29% of all deaths of children under five years of age and result in the death of 2 million young lives each year worldwide. The integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD) has been endorsed by global partners and national governments, and proposes a cohesive approach to averting preventable pneumonia and diarrhoea.

For a number of years, WHO-AFRO has been coordinating and supporting Member States to implement, strengthen and expand surveillance for diseases targeted by new vaccines as part of implementation of the Global Framework for Immunization, Monitoring, and Surveillance and regional strategy integrated disease surveillance and response (IDSR).1,2 This hospital based sentinel surveillance for paediatric bacterial meningitis (PBM) and rotavirus surveillance, launched in 2001 and 2006 respectively,3,4 was established in the region as part of vaccine-preventable diseases (VPD) surveillance system to meet the following objectives:

- Provide evidence of the Haemophilus influenzae, invasive pneumococcal disease (IPD) and rotavirus disease burden;
- Generate and document Streptococcus pneumoniae and rotavirus strains circulating in the African Region;
- Support advocacy and evidence-based decision-making on the introduction of Hib, pneumococcal conjugate vaccines (PCV) and rotavirus vaccines;
- Evaluate the impact of these vaccines post introduction.

Pneumonia, meningitis and diarrhoeal diseases cause significant childhood mortality worldwide, placing an intolerable burden on families, societies and economies, significantly straining scarce national resources such as hospitals and the health system as a whole.5,6 Hence, it is imperative that disease surveillance systems monitor the multifaceted syndromes associated with these illnesses to guide choice, and timing of application of various interventions including vaccination against disease responsible for major childhood diseases as part of efforts to decrease childhood mortality to accelerate progress towards attaining Millennium Development Goal 4.

Methods and overview of approaches for implementation of sentinel surveillance

WHO recommends national ministries of health in each country initiate and implement high quality sentinel surveillance supported by a surveillance implementation team, including:

- Ministry of health focal point responsible for VPD surveillance;
- Sentinel hospital focal point – should be a paediatrician;
Sentinel hospital laboratory focal point; and
Data manager.

The sentinel site implementation team should have clearly defined roles and responsibilities, including advocating with the hospital administration and coordination of sentinel surveillance at the hospital level on behalf of the ministry of health and the country.

Sentinel surveillance is conducted within the context of childhood vaccination programmes. All children under the age of five years admitted to a sentinel hospital and who meet standardized case definitions as indicated below are recruited and key variables captured using a standard case investigation form.

Case definitions for suspected cases

- **Bacterial meningitis**: any child aged 0–59 months admitted to a sentinel hospital conducting surveillance presenting with a cough or difficulty in breathing and displaying fast breathing when calm, as defined by age (0 to <2 months: 60 breaths/minute or more; 2 to <12 months: 50 breaths/minute or more; 12 to <59 months: 40 breaths/minute or more).
- **Bacterial pneumonia**: any child aged 0–59 months admitted to a sentinel hospital conducting surveillance presenting with a cough or difficulty in breathing and displaying fast breathing when calm, as defined by age (0 to <2 months: 60 breaths/minute or more; 2 to <12 months: 50 breaths/minute or more; 12 to <59 months: 40 breaths/minute or more).
- **Rotavirus acute gastroenteritis**: any child aged 0–59 months admitted for treatment of acute (i.e. ≤14 days) watery gastroenteritis/diarrhoea to a sentinel hospital conducting surveillance. Excluded are children with bloody diarrhoea and children transferred from another hospital.

Use of consistent case definitions is critical; not only does it avoid an over- or under-estimation of cases, but consistency is also necessary to standardize data over time, both within a sentinel site and among different sites. All sentinel site surveillance should include children who meet the case definition for suspected meningitis (Tier 1). Some sentinel site surveillance systems will also include children who meet the case definitions for pneumonia or sepsis (Tier 2). Once fully established, this surveillance system for severe paediatric infections can also be adapted to monitor other vaccine-preventable diseases.

WHO recommends that each country conduct sentinel surveillance using at least one major hospital serving children under five years. The sentinel hospital could be either a national public or private facility, as long as it is considered to be the largest hospital in the region, serving the greatest number of patients under five, and has adequate resources for conducting surveillance for vaccine-preventable diseases. For the sentinel surveillance at least one principal hospital serving the greatest number of children in each country is preferred over national surveillance for the following reasons:

- Ministry of health staff can easily perform active surveillance and supervision of surveillance activities, these are critical elements to ensure an ongoing functional and sustainable surveillance system that produces high quality and reliable data.
- The principal hospital will likely have the best clinical practices and laboratory capacity in the country, and thus identifying children likely to have an illness due to these organisms is easier and less expensive than conducting surveillance throughout the country.
- As long as there is consistency in surveillance practices (including use of correct case definition, collection of CSF specimens and blood cultures, stool samples), and the population served by the hospital remains constant, diarrhoea, bacterial pneumonia and meningitis trends can be monitored over time and comparisons can be made before and after vaccine introduction regarding disease occurrence, serotype or strain of the causative organism, and severity of clinical presentation.
- Rapid and timely diagnostic and confirmatory testing for rotavirus and bacterial pathogens is done either at
the hospital or national laboratories whereas WHO-supported regional reference laboratories provide facilities of laboratory quality control and assurance and also further characterization and serotyping using advanced molecular genetic methods.

Children under five hospitalized with severe diarrhoea are enrolled and stool specimens collected for detection of rotavirus strains using a commercial enzyme immunoassay in the case of rotavirus surveillance. Similarly, cerebrospinal fluid (CSF) and blood is collected from under fives with pneumonia and bacterial meningitis for surveillance for invasive bacterial diseases.

Sentinel surveillance data originate from the sentinel hospital. They are forwarded to the ministry of health who compile data provided by different sentinel sites, clean data to remove errors and share harmonized data with WHO.

Results and progress

Currently, 34 sentinel sites in 34 Member States are conducting sentinel surveillance and reporting data monthly on the three most common causes of bacterial meningitis and pneumonia: *Hemophilus influenza*, *Streptococcus pneumoniae* and *Neisseria meningitides*. A similar network, comprising of 26 sentinel sites in 20 countries are conducting surveillance for rotavirus diarrhoea in under fives in the African Region (Figure 1). The countries involved in rotavirus surveillance monitor hospitalizations due to severe diarrhoea in under fives and also the trends of the circulating rotavirus strains and report to WHO and immunization partners.

The regional sentinel surveillance network includes sentinel surveillance hospitals and laboratories that report characteristics and specified variables of clinical symptoms and rotavirus testing data for children under five hospitalized with acute gastroenteritis to ministries of health and WHO. In addition to managerial oversight, WHO provides technical assistance to countries, as well as financial support to countries to implement these surveillance activities.

Sentinel surveillance for paediatric bacterial meningitis continues to provide useful data to support the introduction of new life-saving pneumococcal conjugate vaccines (PCV). All 47 countries in the region have successfully introduced Hib containing vaccines into EPI. Additionally, 30 countries (Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Congo, Central African Republic, Democratic Republic of the Congo, Ethiopia, Gambia, Mauritania, Ghana, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Niger, Rwanda, Sao Tome and Principe, Senegal, Sierra Leone, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia, Zimbabwe) have introduced pneumococcal conjugate vaccines into national immunization programmes; the two vaccines provide additional interventions to avert substantial mortality and morbidity due to pneumonia, meningitis and other deadly childhood diseases caused by the pneumococcus bacterium and Hib. Notably, take up of rotavirus vaccines started slowly in the African Region, with only one country (South Africa) having introduced rotavirus vaccine into national EPI by 2009. However, with the increased awareness of rotavirus diarrhoea, the availability of rotavirus disease burden data provided by sentinel surveillance and support from WHO and other partners, countries in the region started rolling out the vaccine mid-2012 and currently 22 countries (Angola, Botswana, Burkina Faso, Burundi, Cameroon, Congo, Eritrea, Ethiopia, Gambia, Ghana, Kenya, Madagascar, Malawi, Mali, Rwanda, Sierrra Leone, South Africa, South Sudan, Togo, United Republic of Tanzania, Zambia, Zimbabwe) have introduced it into EPI. Moreover, the remaining countries are expected to introduce rotavirus vaccine in the near future.
Discussion and challenges

Between 2006 and 2013, data reported to WHO-AFRO through sentinel surveillance show approximately 96,000 cases of suspected bacterial meningitis reported in children aged under five, caused by three major bacterial meningitis pathogens, with *Streptococcus pneumoniae* accounting for 20–35%, while Hib is responsible for 1–5% and Nm 2–3%. During the same period, 53,898 children under five were hospitalized for acute diarrhoea in 34 participating hospitals in 20 African countries. Rotavirus accounted for 40.7% of the total diarrhoeal hospitalizations in under fives in the region and approximately 90% of rotavirus diarrhoea occurs in children under two years.

Conducting high quality invasive bacterial diseases surveillance is challenging and also resource intensive and more so if it includes pneumonia and sepsis surveillance with collection of blood specimens for culturing. This is in part due to inherent diagnostic difficulties in identifying the bacteria in specimens taken from patients who had prior antibiotics treatment as well as managing the timely processing of clinical specimens in laboratories.

It is important to note that hospital-based sentinel surveillance focuses on the most severe cases (hospitalized children) of diseases under investigation, and thus the information generated from this system alone may not be extrapolated accurately to quantify the disease burden occurring in the country.

Conclusion and way forward

Robust regional sentinel surveillance has been established building on existing infrastructure for disease surveillance in more than half of the Member States. This sentinel surveillance has contributed high-quality data that have been used to estimate the country or regional specific rotavirus diarrhoeal disease burden in support of introduction of new vaccines. The regional sentinel surveillance network seeks to ensure each country has its own data (i.e. Tier 1 meningitis data) that can be combined with information generated from other sources, for example hospital records and health information management systems, to accurately estimate the country and regional specific disease burden.

The regional long-term vision is to use this surveillance system and abundant data on the circulating rotavirus and pneumococcal strains/serotypes and to build a system for evaluation of vaccination impact and to guide immunization programmes as new vaccines are introduced.

It is important for Member States to increase investment to sustain and further strengthen ongoing sentinel surveillance. There is also need for Member States to accurately document numbers of children vaccinated and vaccine coverage to assess the true value and impact of these new vaccines on the disease burden. Already, the benefits of vaccination with these new vaccines is being demonstrated, for example the introduction of a pneumococcal conjugate vaccine (PCV) in 2009 in South Africa has not only reduced the overall incidence of invasive pneumococcal disease by about two-thirds in infants (the age group vaccinated) and in adults, but has also reduced penicillin-resistant infections in both groups.14 Data from South Africa also point to another benefit of vaccination; stemming a rising tide of antibiotic resistance in the developing world.15 In order to sustain these gains, WHO and partners will intensify advocacy at the global level to further accelerate the introduction of new vaccines and engage key immunization partners to ensure regular and sustainable access to supplies of new vaccines.

References