INTRODUCTION

Measles is an acute exanthematous viral disease, that is extremely contagious and widespread worldwide. It is caused by a RNA virus belonging to the family of Paramyxoviridae, of the genus morbillivirus. Measles virus is transmitted by aerosols, through infected dried droplets secreted during a cough or sneeze, or even when talking. Humans are the only natural hosts and the virus survival in the air, on objects, or on surfaces is inversely proportional to the relative humidity [1]. Morbillivirus is highly infectious and contagious is particularly high in closed environments, where the virus may be detected until two hours after its dispersion by an infected subject. The reproduction rate of the virus (R0 = average number of secondary cases, i.e. subjects that fall ill, after contact with a primary case, in a susceptible population) is high, i.e. R0 = 17-18. The disease is contagious from the prodromal stage (for 4-5 days before the onset of the exanthem) and continues to be active in the acute phase. It considerably decreases in intensity up to 4-5 days after the disappearance of the rash. The virus penetrates the body through the respiratory tract, where a first local replication begins, and then it rapidly spreads to the regional lymphoid organs, where a second and massive replication occurs. After the first phase of viremic replication, a second phase follows, in which the virus, affecting the mononuclear phagocyte system, quickly and massively reaches all the body districts through the lymphocytes.

Despite the classic manifestations of the disease, the clinical diagnosis of measles must necessarily be accompanied by laboratory confirmation [2].
Before the vaccine was available, measles was one of the most frequent infectious diseases of infancy. Although vaccination significantly reduced the incidence, measles still remains one of the main causes of disease (40 million/year in the world) and death (1–2 millions) among the non-vaccinated pediatric population [2]. In Italy, death occurs in 1/5000 cases and it is mainly linked to two determinants: the age and the complications of the disease. Mortality is high under one year of age, low in children, and again high in adolescents and adults [1].

In 2017, the European region of the World Health Organization (WHO) recorded a total of 14,451 cases of measles. The European countries with the highest number of cases were: Romania (5560), Italy (4991), Greece (967), and Germany (929) [3].

Among the cases reported in Italy, 87% were not vaccinated and 8% had received only one dose of vaccine; 35% had at least one complication; 44% was hospitalized; 378 cases of pneumonia, 2 cases of encephalitis and other complications such as stomatitis (730 cases), keratoconjunctivitis (496 cases), and hepatitis (444 cases) have been reported. Among the infected cases, 315 were healthcare workers. The region with the highest incidence rate was Lazio, accounting for 1699 cases (28.8 cases/100,000 inhabitants) [4].

Starting from the early months of 2017, the “Integrated Surveillance System Measles-Rubella” has recorded on the National area a growth beyond the expectation of measles cases in the population. From January 1 to April 2, 2017, a total of 1333 measles cases were notified to Italian LHUs [5].

The Ministry of Health-Office sent the circular “Prevention of communicable diseases and international prophylaxis” (April 4, 2017) to all Regions with the subject: “The epidemiological situation of measles—Operating guidelines for the management of the outbreak”.

The circular stated that the majority of cases occurred in people aged ≥15 years (58% in the age range 15–39 years and 16% in the age range 40–64 years), with a median age of 27 years. Several nosocomial outbreaks and 315 cases have been reported among healthcare professionals.

Therefore, the vaccination against measles (for subjects aged 0 to 16 years), which previously was just “strongly advised”, became mandatory according to the “Decree-Law prevention vaccination”, converted into law by the Parliament on July 31, 2017.

To be effective, the vaccine must necessarily be administered in two doses: one at the 13th–15th month of life and the second at 5–6 years [6].

Vaccination against measles remains strongly recommended among the healthcare staff, that is always at high risk of contracting measles [7].

The trend of measles infections in recent years shows that:

- there is a shift concerning the age of the subjects involved (increasingly infecting adolescents and young adults);
- some of the cases had benefited from a single dose of vaccine (whereas it is necessary to reach a 95% coverage with two doses in order to effectively prevent the propagation of the disease);
- the healthcare staff susceptible to the disease must be identified and educated on the importance, usefulness, and social value of vaccination (each Local Health Unit—LHU—should know the vaccination status of its employees) [3,4].

With regard to health surveillance, measles, being part of class II diseases, must be notified to the LHU by the diagnosing physician by using the “Compulsory complaint card of infectious disease”, as reported in the Ministerial decree of December 15, 1990. In case of measles, susceptible subjects who may get in touch with the index case (contacts) must also be traced.

With regard to the prevention of susceptible subjects, it is necessary to:

1. record the starting date of the symptoms of the index case and the infectious period;
2. identify the case contacts during the infectious period and trace them;
3. establish active surveillance in the communities where the infected subject lives or identify those who have come in contact with him/her during the 14 days preceding the onset of the symptoms;
4. continue the investigation on the contacts of the cases who are subsequently identified.

The vaccine [4] is always and strongly recommended in subjects considered susceptible, i.e. those without vaccination or who have not previously been infected.

A descriptive epidemiological study was carried on in the Viterbo LHU area [8] in order to investigate the extension of the measles outbreak phenomenon and the size of the population involved.
Subsequently, data were compared with those acquired in 2018, in order to check whether the operational response of health surveillance adopted by the Viterbo LHU had proved effective in decreasing or preventing new cases of disease.

MATERIALS AND METHODS

For data acquisition, the Hospital Discharge Forms—HDSs (schede di dimissione ospedaliera—SDO) and the notifications of infectious diseases (NOIDs) were used. Afterwards, the cases of interest notified were selected according to inclusion and exclusion criteria (see below), with the aim of obtaining a reliable picture about the disease distribution in the Viterbo LHU area, Italy, for the year 2017. Data about the year 2017 were then compared with those of 2018, in order to obtain information on the progress of the disease in two consecutive years.

Inclusion criteria were: the diagnosis of measles made in 2017 and the residence in the Province of Viterbo. Patients with suspected diagnosis of measles not confirmed by virological examination and patients hospitalized for measles in 2017, but diagnosed prior to January 1, 2017, were excluded from the study.

The following data were collected: nationality (to distinguish between autochthonous and non-autochthonous cases), sex, year of birth, start date of symptoms, date of disease notification (which allowed to highlight the timeliness of the diagnosis), residence, possible hospitalization, hospital, and ward.

Data obtained were analyzed after creating a database.

The epidemiologic scenario, once defined, was then analyzed through “Windows Access”, “Windows Office”, and “Excel” softwares.

Averages, weighted averages, ratios, ranges, and percentages were calculated. Data about the resident population in the Province of Viterbo were taken from the National Institute of Statistics (Istituto nazionale di statistica—ISTAT) [9].

RESULTS

A total 50 measles cases were identified in 2017 in the population in the area of Viterbo. Of these cases, 43 were notified directly by physicians working in the Viterbo LHU and 7 cases were notified by Physicians of Regional structures not belonging to the Viterbo LHU and extra-Regional structures.

Two cases of patients non-resident in the Province of Viterbo were also included in the study: one was admitted to Belcolle Hospital of Viterbo following the complications of the disease and the other was a healthcare worker of the same hospital.

Ten cases were healthcare professionals and 3 cases were other workers employed in the Viterbo LHU.

Significant variations were detected in the outbreak event in comparison with the epidemics of previous years, i.e. a change in the age distribution of the disease at the local level. In fact, more than 90% of cases were patients aged over 18, while underage subjects accounted just for 4 out of 50 total cases. Just one case was registered over 50 years of age, as this population grew up at a time when vaccination for measles did not exist and thus was infected, presumably, in the pediatric age. There were also few measles cases recorded in foreign patients (only 10% of cases).

Most cases (38 out of 50) were recorded in the age group between 18 and 39 years, clearly shifting the onset of measles from a predominantly pediatric to an adult age disease. Age range covered 55 years, showing a significant widening in the distribution of the disease in the population.

Considering the age groups, the characteristics of the outbreak highlighted by our study showed that the trend of measles in the Viterbo LHU area perfectly matches the trend at the National level.

In the Viterbo LHU only 4 cases were registered from January 1, 2018 to December 31, 2018, and among them no healthcare worker was involved.

The cases among the healthcare workers of this outbreak event were related to a case of measles notified on March 2, 2017 (“index case”, hospitalized), as emerged from the investigation we carried out. The index case was a male subject who carried out his activity on the emergency vehicles and was an employee of a Roman LHU, and probably had contracted the infection while working.

The second case was a female subject, arrived at the Emergency Room of Belcolle Hospital to receive medical treatments. A possible link between these two cases was initially ruled out, considering that both subjects had reported they did not know each other. Afterwards, the woman, until
that moment unaware that the man was infected, reported having had personal contact with the index case, thus revealing the way of contagion.

The third case of illness was the first aid physician who treated the woman, when the diagnosis was not made yet.

The woman was admitted to the hospital and, due to lack of beds in the ward of destination, was temporarily accepted in another ward, where she infected the fourth case, a nurse, and the fifth case, a student of the health professions who was doing the internship there.

The Notification Board of “suspected epidemic event” was drafted on April 5, 2017, following these 5 initial episodes of measles.

New cases had emerged, although sporadically, involving other healthcare professionals and other workers within the hospital. Of these, the last case was an attendant at the hospital canteen, notified on September 3, 2017.

Considering the notification date of the disease between the index case (March 2, 2017) and the last case (September 3, 2017), we concluded that outbreak affected the Belcolle Hospital for 7 months. The modes of transmission were sometimes not clearly identifiable.

The infection involved the most disparate professionals of the hospital, i.e.:

- 10 healthcare professionals, including physicians, nurses, midwives, department nursing coordinators, and students of the health professions;
- 2 non-sanitary employees (excluding the index case) in the LHU: a cleaner and a clerk in the cafeteria (transport of food).

The latter case in particular, thanks to the health surveillance and the measures taken, was promptly identified and did not infect anyone.

Starting from the index case, retracing the chain of contagion and tracking who had been exposed, it was possible to stop the spread of the infection with vaccination and the implementation of preventive measures in susceptible people. In order to respond to the urgent need of combating the spread of disease among healthcare professionals, the Hospital Health Department of the Viterbo LHU set up a “crisis unit” (consisting of several professionals: Hospital Health Management, Department of Prevention, Department of Coordinating Vaccinations, Risk Management, Department of Infectious Diseases, Department of Clinical Diagnostic, Hospital Pharmacy, competent physician) with the task of interacting with the Hospital Health Management by implementing an Operative protocol to stop the contagion.

Therefore, a general survey on the status of health staff vaccinations was carried out and the clinical risk of the population exposed was mapped on the basis of the previous immunization against the disease or vaccination. The search for susceptible subjects was extended to all the staff already employed in LHU, initially also through self-certification, thus obtaining an immediate picture on the vaccination coverage and the previous immunization of employees against the disease. Subsequently, a procedure was undertaken in order to detect the presence of antibodies against measles.

Unimmunized subjects who were exposed and were clinically compatible with vaccination were identified. Afterwards, a preventive vaccination campaign was carried out on the basis of priorities, clinical risk, and compatibility, as assessed on a case-by-case basis. Contacts of healthcare professionals and other infected LHU workers were quarantined at their home, because they were deemed temporarily unfit for work.

The search for the antibodies against measles was included in the occupational health check of healthcare workers of the Viterbo LHU.

**DISCUSSION**

The possible involvement of healthcare professionals in a direct airborne infection (such as measles) should never be underestimated by a healthcare organization, especially when it is unaware of the vaccination and immune status of its employees. Proper monitoring and careful surveillance not only of patients, but also of healthcare professionals themselves, are essential elements in preventing and controlling infections.

Measles has different symptoms in adulthood and pediatric age. In adulthood, frequently the rash (which often occurs atypically) is postponed, and the disease onset is characterized by fever, general malaise, and sore throat: therefore, the infection may go undetected, thus increasing the likelihood of contagion to susceptible subjects.

The late diagnosis and the presence of a susceptible health practitioner in Belcolle
Hospital were the main factors which allowed the measles virus to trigger an outbreak among its employees.

The search for the cases involved among the hospital employees was very tricky. When retracing the chain of infection in case of suspected outbreak event, it is crucial to reconstruct the dynamics of the propagation of the infection and identify the "index case", defined as the first case of disease. Afterwards, the infectious period of the infected subject must be tracked, and all the susceptible subjects (high- and low-risk contacts) who may have come into contact with the index case in that time have to be searched [10].

In Viterbo, for the first time, the search for the antibodies against measles was included in the occupational health check. In the absence of vaccination certification, the antibody titration for the measles virus was detected with serological test.

In this way, the immune status against measles became one of the defining elements of working suitability for health workers of the Viterbo LHU. This was particularly important, especially considering the presence of fragile subjects and delicate context that characterize hospitals.

The operational response we implemented was based on the indications reported in the ministerial circular of April 4, 2017 [8] and in the “National Plan for the Elimination of Measles” [10]:

- actively offering vaccination to those contacts susceptible to measles within 72 hours of exposure and even beyond this interval to detect also the susceptible cases eventually uninfected;
- alerting general practitioners, pediatricians, gynecologists, hospital physicians, and first aid;
- monitoring people that receive measles, mumps, and rubella (MMR) or IgG vaccines as post-exposure prophylaxis for the possible occurrence of signs and symptoms compatible with measles for at least a period corresponding to the disease incubation period;
- offering MMR vaccination to healthcare professionals at the time of hiring;
- checking whether employees are immunized against measles and vaccinating susceptible workers;
- verifying the vaccination coverage of all health professions’ students, in view of their hospital internship;
- maintaining a high level of awareness among the health staff about the possibility of measles transmission in the nosocomial field;
- quarantining at home, during the incubation period, susceptible healthcare workers who have been exposed to the disease;
- quarantining suspected cases that occur in the Emergency Room or other wards;
- searching for contacts at risk;
- strengthening surveillance on hospital cases.

Therefore, the measures taken in this situation have had the aim of:
1. monitoring the current epidemic by interrupting the transmission chain;
2. preventing secondary cases;
3. preventing future epidemic measles events.

CONCLUSION

According to this epidemiological study, the incidence of measles in this local microcosm and at national level perfectly overlap, thus confirming the existing gap from the 95% vaccination coverage target [5].

The operational response implemented by the LHU proved to be effective in blocking the spread of infection. In fact, only 4 cases of measles were diagnosed in 2018 (and among them no healthcare worker was involved) versus 50 cases in the year 2017 in the Viterbo LHU area. Notwithstanding the encouraging progress achieved at local level, measles is still a serious problem in Italy even in 2018, despite a reduction in cases with respect to 2017: in January 1-December 31, 2018 period, 2526 cases of measles were notified in Italy, 47% of which with at least one complication. Overall, 4.6% (115 cases) were healthcare professionals. During that period, there were 8 measles-related deaths: 7 adults aged 25-75 and a 10-month-old child [11].

In this study, we monitored the evolution of what could be considered a "healthcare staff-related outbreak". Therefore, this close monitoring was useful in order to:
- define the problem;
- obtain information with regards to the population of the area;
- identify priorities of action;
- implement “catch-up” campaigns to recover subjects escaped from vaccination;
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For the first time the vaccination coverage against the measles of the actual and future employees of Belcolle Hospital and Viterbo LHU, thus early identifying susceptible subjects in order to offer them the vaccination. The detection of IgG and IgM for measles has been included for the first time in the periodic occupational health check of LHU, in addition to the usual examinations. This research was also extended to the students of the health professions as a requirement for their internship.

The immunization (due to a past infection or vaccination carried out correctly with two doses of vaccine) is checked by the competent physician of the LHU.

An education and information campaign started within the hospital about the efficacy and safety of the MMR vaccine.

We hope that our work can serve as an example or support for other health LHUs, triggering hospitals and Local Health Authorities to implement new operational protocols and actions aimed at preventing problems, such as that of measles, which currently has not found an effective and homogeneous resolution, considering the recurrent outbreaks and spread throughout the national and international area.

**Key points**
- Measles is an acute exanthematous viral disease, that is extremely contagious and widespread worldwide.
- This study traced the distribution of the disease among the staff of the Belcolle Hospital in Viterbo, producing useful information for the development of preventive and control measures.
- Data were collected from the Hospital Discharge Sheets (HDSs) and the notifications of infectious diseases (NOIDs).
- In 2017, 50 cases of measles were detected in the population in Viterbo area, 10 of whom were healthcare professionals and 3 other professional workers employed in the Viterbo LHU.
- In 2018, an education and information campaign about the efficacy and safety of the MMR vaccine was initiated within the Hospital.
- The measles outbreak gave us the opportunity to monitor for the first time the vaccination coverage against the measles among the Hospital employees.

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**Conflicts of interests**
The authors declare they have no competing financial interests concerning the topics of this article.
REFERENCES