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# Hospital-Acquired Measles: A Systematic Review Using the Outbreak Reports and Intervention Studies of Nosocomial Infection (ORION) Statement 

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#### Abstract

Purpose: Despite the recent increased number of nosocomial measles, the outbreak investigation reports are not usually standardized, thus posing unclear understanding of magnitude of its public health burden. We used the Outbreak Reports and Intervention Studies of Nosocomial Infection (ORION) statement, to compare nosocomial outbreaks and synthesize evidence to prevent hospital transmission of measles. Methods: A PubMed, Web of Science, Embase, Scopus, and Cochrane search in English, using the medical subject headings "measles," "nosocomial," "hospital," and "healthcare," was performed. We evaluated the quality of outbreak reports of nosocomial measles infection worldwide using the ORION statement findings and recommendations. Results: We reviewed 24 studies in accordance to the ORION statement. Measles transmission in healthcare settings is a significant burden on the morbidity, mortality, and economy of measles. The healthcare workers' booster vaccination guidelines should be monitored and enhanced during the post-elimination period of measles. The outcomes of infections must be explicit for outbreak reports. Conclusions: This study identified the epidemiological and clinical characteristics of nosocomial measles infections and provided strong evidence for infection control policies in hospitals.


Keywords: Measles; Healthcare; Hospital

## INTRODUCTION

Measles is a highly contagious respiratory infectious disease posing significant disease burden, worldwide. In 2000, an estimated global incidence of 39.9 million children were infected annually, which have caused 777,000 deaths and 28 million disability-adjusted life years, worldwide. ${ }^{1)}$

Following the widespread use of 2-dose measles vaccines, the number of cases has decreased significantly, from 145 cases per million in 2000 to 49 cases per million in 2018; and deaths decreased by $73 \% .{ }^{2}$ ) Despite the success, in countries with established vaccination system,

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No potential conflict of interest relevant to this article was reported.

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measles outbreaks have been reported in hospitals, causing transmission with-in and out of healthcare setting. ${ }^{3)}$ The hospitalized patients, especially infants without vaccination history, are vulnerable to measles at high risk of severe outcomes and mortality. ${ }^{4)}$ Moreover, national measles elimination programs can be severely disrupted by occurrence of nosocomial measles outbreak.

Despite the recent increased number of nosocomial measles, the outbreak investigation reports are not usually standardized, thus posing unclear understanding of magnitude of its public health burden. ${ }^{5}$ Hence, there is a need for a comprehensive review of nosocomial measles outbreaks. The Outbreak Reports and Intervention Studies of Nosocomial Infection (ORION) statement, originally proposed by Stone et al., ${ }^{6}$ ) provides standardized methods for nosocomial outbreak reporting. It is useful to compare nosocomial outbreaks and synthesize evidence to prevent hospital transmission of infectious diseases. ${ }^{7)}$

In this study, we pooled the published data on nosocomial outbreak of measles and used the ORION statement to identify the epidemiological and clinical characteristics of nosocomial measles infections, in aim to guide preventive measures.

## MATERIALS AND METHODS

To analyze outbreak reports of nosocomial measles infection, we performed a literature review and evaluated the quality of outbreak reports of nosocomial measles infection worldwide using the ORION statement.

## 1. Selection criteria, search methods and study selection

We included articles related to nosocomial measles. All publication types from peer-reviewed journals and articles in English were included. Time restriction was not applied. We excluded articles that did not describe nosocomial measles outbreaks. The review was performed by searching the electronic bibliographic databases PubMed, Web of Science, Embase, Scopus, and Cochrane search. The search terms were considered "measles," "nosocomial," "hospital," and "healthcare", and the search terms used for each database are listed in Table 1. Duplicate articles were removed, and the title and abstract were screened. A flow diagram of the screening process is shown in Fig. 1.

Table 1. The search strategy of the patients with hospital-acquired measles

| Databases | Searches | Results |
| :---: | :---: | :---: |
| PubMed | (("Measles"[Mesh]) OR ((measles))) AND ((((((((((Nosocomial) OR ("Hospital Infection*")) OR ("hospital-related")) OR ("hospital related")) OR ("hospital-acquired")) OR ("hospital acquired")) OR ("Healthcare Associated")) OR ("Healthcare-Associated"))OR ("Health Care Associated")) OR ("Cross Infection*")) OR ("Cross Infection"[MeSH Terms])) | 325 |
| Web of Science | TS: (measles) AND TS: ((Nosocomial or ("Hospital Infection*") or ("hospital-related") or ("hospital related") or ("hospital-acquired") or ("hospital acquired") or ("Healthcare Associated") or ("Healthcare-Associated") or ("Health Care Associated") or ("Cross Infection*"))) | 168 |
| Embase | (measles:ti,ab,kw) AND (nosocomial OR 'hospital infection*' OR 'hospital-related' OR 'hospital related' OR 'hospital-acquired' OR 'hospital acquired' OR 'healthcare associated' OR 'healthcare-associated' OR 'health care associated' OR 'cross infection*') | 210 |
| Scopus | ( TITLE-ABS-KEY (measles) AND TITLE-ABS-KEY ( nosocomial OR "Hospital Infection*" OR "hospital-related" OR "hospital related" OR "hospital-acquired" OR "hospital acquired" OR "Healthcare Associated" OR "Healthcare-Associated" OR "Health Care Associated" OR "Cross Infection*" ) | 198 |
| Cochrane | measles in Title Abstract Keyword AND Nosocomial or "Hospital Infection*" or "hospital-related" or "hospital related" or "hospitalacquired" or "hospital acquired" or "Healthcare Associated" or "Healthcare-Associated" or "Health Care Associated" or "Cross Infection*" | 60 |



Fig. 1. Flow diagram of the review process.

## 2. Data collection and quality assessment

The following data were collected: year of publication; country; start date and end date of measles outbreak; number of infected children (aged <15 years; aged <1 year; aged <6 months) and adults; number of clinical or lab-confirmed cases; number of nosocomial cases; number of deaths related to death; number of cases who were vaccinated; number of healthcare workers (HCWs) who spread measles in hospital.

We then evaluated the quality of outbreak reports of nosocomial measles infection worldwide using the ORION statement findings and recommendations. The ORION checklist consists of a 22 -item, and the items and descriptors are self-explanatory concerning the following contents: 1) the title and the abstract; 2) background, type of paper, date, and objectives in the introduction; 3) design, participants, setting, interventions, culturing and typing, infection-related outcomes, economic outcomes, potential threats to internal validity, sample size, and statistical methods in the methods; 4) recruitment, outcomes and estimation, ancillary analyses, and adverse events in results; 5) interpretation, generalizability, and overall evidence in the discussion (supplement). ${ }^{6}$

## RESULTS

We reviewed 24 studies in accordance to the ORION statement. We presented our results based on the sequences of the ORION statements and reviewed each item in the statement.

## 1. Title and abstract: ORION item 1

All 24 studies had abstracts and titles that could fully describe their main results and the description of the paper as an outbreak report. ${ }^{8-31)}$ Two studies did not have an introduction since one of them was a case report and one was a letter to the editor. ${ }^{15,30)}$

## 2. Background: ORION item 2

All studies with introductions had a clearly stated rationale. ${ }^{8-14,16-29,31)}$ The scientific and local backgrounds were presented in all studies, except for one study, ${ }^{21)}$ and a total of 14 studies described existing understanding of measles number of cases. ${ }^{10-33,16,18-20,23,26-28,30)}$

## 3. Type of paper: ORION item 3

Based on the information provided, all studies were outbreak reports and reported one outbreak, except for one study that compared two outbreaks. ${ }^{13)}$

## 4. Dates: ORION item 4

Among the 18 studies, the duration of outbreaks were known and stated by month and year or range of case occurrence. ${ }^{84,17,18,20-26,28-31)}$ In one study, the end date of the outbreak was unknown, although the start day was provided. ${ }^{29)}$

## 5. Objectives: ORION item 5

Twenty-two studies described their main objectives in their introduction sections, ${ }^{8 \cdot 15,17-29,31)}$ and two studies did not provide objectives because their design was a case report and a letter to the editor. ${ }^{16,30)}$ The main objectives were to describe the outbreak, particularly its transmission chains, vaccination status, hospitalizations, complications, nonclassical presentation, control, and management. Eight studies listed specific objectives such as identifying the seroconversion rate, ${ }^{8}$ ) assessing risk factors for measles and its transmission, ${ }^{10,18,24)}$ assessing risk factors for hospitalization, ${ }^{12)}$ assessing possible reasons for misdiagnosis or delayed diagnosis, ${ }^{13)}$ assessing infection prevention and control policies and procedures, ${ }^{19)}$ evaluating vaccine failure, and describing the economic burden. ${ }^{25)}$

## 6. Design: ORION item 6

Retrospective surveillance was done in six studies. ${ }^{9,11,13,14,1,20)}$ Two studies used a surveillance system to obtain data from participants ${ }^{11,24)}$ and one study used PubMed for the literature review to identify the instances of individuals with measles vaccine and the estimated cost in response to measles outbreaks. ${ }^{25)}$ The other 16 studies did not determine the surveillance system design in their methods; however, an investigation was conducted at the time the index case was detected or an outbreak was suspected. ${ }^{8,10,12,15,16,18,19,2123,26-31)}$

## 7. Participants: ORION item 7

Eight studies listed patients as the study participants, ${ }^{10,11,15,24,26,28,30,31)}$ another set of eight studies listed $\mathrm{HCWs}^{9,1618,20,22,23,25)}$ as participants, seven studies listed both patients and HCWs as participants, ${ }^{8,1244,19,27,29)}$ and three studies included families. ${ }^{12,21,28)}$ Demographic information, clinical manifestations, vaccination status, hospitalization, complications, and history of contact were collected from health records, questionnaires, interviews, and surveillance systems in 14 studies. ${ }^{8-11,17-20,24-27,29,31)}$ In the other 10 studies, the data collection method was not described. ${ }^{1246,2123,28,30)}$

Standard case definition of "suspected measles" was any case with fever (at least $37.5^{\circ} \mathrm{C}$ ); maculopapular rash; and either cough, coryza, Koplik's spots, or conjunctivitis. A confirmed measles case was defined as any case that met a definition of a "suspected measles" and that was confirmed by laboratory testing, and this case definition was provided in 14 studies, ${ }^{103,16,18,20,22-24,26,28,29,31)}$ and the other 10 studies did not define the measles cases. ${ }^{8,9,14,15,17,19,21,25,27,30)}$ Laboratory testing results reporting at least one of the following were considered positive: 1) measles virus isolation from a clinical specimen; 2) measles virus
nucleic acid detection from clinical specimens; 3) measles virus-specific antibody response in serum or saliva; and 4) detection of measles virus antigen. ${ }^{11}$

A total of 5 studies provided various definitions of hospital-acquired (nosocomial) measles. ${ }^{11,12,19,22,28)}$ As a review of these definitions, a case was considered nosocomial if contact occurred during hospitalization or a visit to a hospitalized patient; HCWs with measles were also considered hospital-related. ${ }^{11)}$ Community-related cases were excluded. The following case scenarios were considered positive for nosocomial transmission: 1) if infection occurred within the healthcare system (e.g., other patients in the waiting room and staff in reception area ${ }^{122}$; 2) if a person shared the same airspace within 4 days before or after rash onset; or 3) if an individual was in these areas within one hour. ${ }^{22)}$ Another study defined a nosocomial case as a confirmed case if an individual was in contact with another confirmed case in the hospital 7-21 days before the onset of symptoms. ${ }^{28)}$

## 8. Setting: ORION item 8

The types of hospital workers and wards were mentioned in 14 studies. ${ }^{8,9,1188,23,29)}$ Number of beds was reported in five studies. ${ }^{8,17,18,29,30)}$ The presence and implemented activities of the infection control team were mentioned in eight studies. ${ }^{8,9,12,16,17,23,27,29)}$

## 9. Interventions: ORION item 9

Although the aim of the study was not to assess interventions, intervention measures were reviewed in 22 studies ${ }^{8,10-29,31)}$ : outbreak-response vaccination, ${ }^{8,10,14,16,18,20-24,27)}$ work restriction, ${ }^{8,22)}$ personal hygiene ( N 95 mask, hand hygiene), ${ }^{8,14,20,22)}$ isolation and distancing, ${ }^{10,11,14,15,18,22,23,25,26,29)}$ contact tracing, ${ }^{11,1441,21-24,27-29,31)}$ administration of immunoglobulin (Ig), ${ }^{11,14,16,27}$ educational interventions (forum, training), ${ }^{13,14,18,25,277}$ fever screening, ${ }^{20,24)}$ furlough at the first sign of illness, ${ }^{22)}$ and assessing immune status. ${ }^{9,16,18,22,24,29,31)}$

## 10. Culturing and typing: ORION item 10

Laboratory confirmation was reported in 17 studies. Viral RNA using reverse transcription polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assay for measlesspecific IgM and IgG antibodies was performed. ${ }^{816,18,22-24,26,29-31)}$ Among the clinical cases, the percentage of laboratory confirmation of measles ranged between $15 \%$ and $100 \%$ (Table 1). Measles virus subtypes $\mathrm{B} 3^{1113,16,21,22,29)}$ and $\mathrm{D8}^{8,15,17,28)}$ were dominant in the surveys, except for $\mathrm{D} 4,{ }^{27)} \mathrm{H} 1$, and undetermined ${ }^{18}$ in three studies.

## 11. Infection-related outcomes: ORION item 11

The attack rate, which is the proportion of measles cases among the total number of patients at risk of infection during the study period, was measured in six studies ${ }^{8,10,15,18,20,24)}$ and the incidence rates per 100.000 population were measured in three studies to estimate measles occurrence in hospitals and districts. ${ }^{11,24,26)}$

## 12. Economic outcomes: ORION item 12

Four studies described the cost of outpatient visits; hospital stay; antibody and PCR testing; vaccination; working hours for outbreak management; indirect cost from the productivity loss of parents, patients, or both; and the number of health care personnel furlough. ${ }^{13,25)}$ The economic burden was estimated in four studies, and the cost ranged from 79.733\$$724.397 \$^{8,13,17)}$ and in one study, the economic cost was estimated at $19.000 \$$ per one person. ${ }^{25)}$

## 13. Potential threats to internal validity: ORION item 13

Among the 24 studies, 21 were descriptive, with no assessment of causal relationships, and there was no need to describe potential bias and confounders. Four studies were casecontrol studies that aimed to assess the risk factors for measles, and confounders were not reported. ${ }^{10,18,24)}$

## 14. Sample size: ORION item 14

Not applicable.

## 15. Statistical methods: ORION item 15

Studies that were outbreak reports ( $\mathrm{n}=18$ ) used descriptive analyses. Four studies used multivariable regression analysis to assess the risk factors for transmission, ${ }^{10}$ hospitalization ${ }^{12)}$ and infection, ${ }^{18,24)}$ where one was unplanned. ${ }^{12)}$ In one study, the Pearson chi-square test or Fisher exact test was used to compare proportions or rates, and the ranksum test was used to compare medians. ${ }^{18}$ Other study used the Fisher's exact test to compare the proportions in $2 \times 2$ tables, the Freeman-Halton test for tables larger than $2 \times 2$, and the Mann-Whitney-Wilcoxon test for comparing medians. ${ }^{12)}$

## 16. Recruitment: ORION item 16

Participants from 11 studies were recruited from European countries (Austria, Belgium, England, France, Germany, Italy, and the Netherlands) ${ }^{9,1113,1517,21,27,29,30)}$; ten study participants were recruited from Asia (China, Hong Kong, Japan, Mongolia, South Korea, and Singapore) ${ }^{8,14,18-20,23,24,26,28,31)}$; two from North America (USA) ${ }^{22,25)}$; and one from Africa (Uganda). ${ }^{10)}$ Three outbreaks were localized in one unit, ${ }^{15,18,277} 15$ outbreaks occurred in the entire hospital, ${ }^{8,1013,16-18,20-26,28,30,31)}$ two reports were in two hospitals ${ }^{9,299}$ and one report was in three hospitals. ${ }^{19)}$ The other three outbreaks occurred at the district level. Ten studies did not provide the range of patient ages. ${ }^{9,1447,25,26,29-31)}$ The duration of outbreaks ranged from 1 day to 1 year, from the start date to the end date.

## 17. Outcome and estimation: ORION item 17

Table 2 presents the number of children and adult patients at the start of the outbreaks, number of clinical and laboratory-confirmed cases, and number of deaths during the study period. The attack rate of measles, which is the number of case patients divided by the number of target population, was calculated in three studies, and the results were $2.22 \%$ in population aged <25, ${ }^{8}$ ) $32 / 100,000$ in those aged 9 months to 5 years ${ }^{10)}$ and 8.9/100,000 in the total population. ${ }^{24}$ The attack rate in HCWs was estimated in two studies, where the results were $0.95 \%{ }^{8}$ ) and $4.4 / 1,000^{18)}$ among hospitals. The attack rate of laboratory-confirmed cases was not reported in any of the studies.

In all studies, laboratory confirmation was performed among all reported cases. In these studies, the proportion of laboratory-confirmed cases among all patients ranged from $7 \%$ to $100 \% .^{8-31)}$ The proportion of nosocomial laboratory-confirmed cases and nosocomial clinical cases among the total number of patients were unavailable in all studies. The proportion of clinical cases among HCWs was reported in nine studies and ranged between $20 \%$ and $100 \%$. ${ }^{8,1113,17,22,25,29,30)}$ Seropositive results of IgG in HCWs ranged from $56 \%$ to $96 \%$ in four studies. ${ }^{17,24,29)}$

Eight studies reported measles patient vaccination coverage ranging from $0 \%$ to $96 \% .{ }^{8,9,11}$ ${ }^{13,22,28,31)}$ Studies with child participants reported $0 \%$ vaccination coverage; additionally, most

Table 2. Characteristics of nosocomial measles outbreaks

| Ref. | Year published | Country | No. of patients |  | Observed cases |  | Nosocomial cases |  | Measles vaccinated | HCWs who spread measles in hospital | Deaths related to measles |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | Children (<18 yr) | Adults | Clinical | Labconfirmed | Clinical | Labconfirmed |  |  |  |
| Song et al. ${ }^{\text {8) }}$ | 2022 | Korea | - | 26 | - | 26 | - | 26 | 25 | 22 | - |
| Westgeest et al. ${ }^{9}$ ) | 2020 | Netherlands | - | 2 | - | 2 | - | 1 | 0 | 2 | - |
| Biribawa et al. ${ }^{10}$ | 2020 | Uganda | 77 | 4 | 75 | 6 | - |  | - | - | 4 |
| Orsi et al. ${ }^{11)}$ | 2020 | Italy | 13* (<15 yr) | 23 | 2 | 34 | - | - | 2 | 5 | 1 |
| Cornelissen et al. ${ }^{12)}$ | 2020 | Belgium | 137* (<15 yr) | 152 | 107 | 182 |  | 37 | 39 | 36 |  |
| Kohlmaier et al. ${ }^{13)}$ | 2020 | Austria | 11 | 2 |  | 13 | 2 | 9 | 2 | 1 |  |
| Cheng et al. ${ }^{14)}$ | 2019 | Hong Kong |  | 29 |  | 29 |  | 2 | 2 | 2 |  |
| Hubiche et al. ${ }^{15}$ ) | 2019 | France |  | 3 |  | 3 |  | 2 | 2 | - |  |
| Berry et al. ${ }^{16)}$ | 2019 | England |  | 8 |  | 8 |  | 5 | 6 | 5 |  |
| Hiller et al. ${ }^{17)}$ | 2019 | Germany |  | 17 |  | 17 |  | 17 | 2 | 10 |  |
| Fu et al. ${ }^{18)}$ | 2019 | China |  | 11 |  | 11 |  | 11 | 1 | 11 |  |
| Lake et al. ${ }^{19}$ ) | 2018 | Mongolia | $155^{\dagger}$ ( $<6$ mon) | 420 | 681 | 286 | 602 |  | 27 | 55 |  |
| Jia et al. ${ }^{00}$ | 2018 | China |  | 19 | 5 | 14 | 5 | 14 | 2 | 19 |  |
| Porretta et al. ${ }^{21)}$ | 2017 | Italy | 8 | 27 |  | 34 |  | 23 | 3 | 15 |  |
| Gohil et al. ${ }^{22)}$ | 2016 | US ${ }^{\ddagger}$ |  | 22 | 6 | 16 |  | 6 | 4 | 5 |  |
| Zhang et al. ${ }^{23)}$ | 2016 | China | 7 | 53 |  | 60 |  | 60 | 44 | 50 |  |
| Zhang et al. ${ }^{24}$ | 2015 | China | 4 | 41 | 2 | 43 | 2 | 43 | - | - |  |
| Fiebelkorn et al. ${ }^{25}$ | 2015 | US ${ }^{\ddagger}$ |  | 1,822 | 908 | 914 |  | 78 | 19 | 29 |  |
| Wang et al. ${ }^{26)}$ | 2014 | China | 2 | 9 |  | 11 |  | 8 | 1 | 0 |  |
| Baxi et al. ${ }^{27}$ | 2014 | UK | 2 | 2 | 1 | 3 | 1 | 3 | 2 | 1 |  |
| Low et al. ${ }^{28)}$ | 2012 | Singapore | 14 |  |  | 14 |  | 7 | 0 | 0 |  |
| Barbadoro et al. ${ }^{29)}$ | 2012 | Italy | 1 | 3 |  | 4 |  | 4 | 3 | 3 |  |
| Lefebvre et al. ${ }^{30}$ ) | 2011 | France |  | 2 |  | 2 |  | 2 | - | 0 | 1 |
| Nakano et al. ${ }^{31)}$ | 2002 | Japan | 30 |  | 8 | 22 | 8 | 22 | 1 | 0 |  |

Abbreviation: HCW, healthcare worker.
*Aged <15; ${ }^{\dagger}$ Aged < 6 months; ${ }^{\ddagger}$ Children number unknown.
of the participants had not reached the vaccination age at the study time. ${ }^{28)}$ Eight studies reported HCWs' vaccination status ranging from $20 \%$ to $100 \%$. ${ }^{8,12,18,20,21,23,25,29)}$ Owing to the small number of case patients, some studies resulted in a $100 \%$ vaccination status.

## 18. Ancillary analyses: ORION item 18

Six studies performed ancillary analyses, and the results were as follows: the significant risk factors for exposure were hospitalization at the pediatric department, visiting communal water collection points, and measles vaccination history. ${ }^{10)}$ The hospitalizations of measles were significantly shorter for individuals aged 1-14 years, those who were unvaccinated (odds ratio [OR], 6.0; 95\% confidence interval [CI], 2.8-17.1), and those aged >15 years (OR, 2.3; $95 \%$ CI, 1.03-5.24) that were associated with hospitalization. ${ }^{12)}$ Visiting the emergency room 7-21 days before the outbreak and no documentation of vaccination before the outbreak were the risk factors associated with measles. ${ }^{18)}$

## 19. Harms: ORION item 19

Deaths related to measles were reported in only three studies (range, 1-4 patients). ${ }^{10,11,30)}$

## 20. Interpretation: ORION item 20

Studies have reported several transmission chains that can infect people, such as patient to patient, ${ }^{12,13,26,27,30)}$ patients to HCWs, ${ }^{12,13,27,29)}$ HCWs to inpatients, ${ }^{12,27)}$ HCWs to HCWs, ${ }^{, 11,20,21,23,27,29)}$ HCWs to family members, ${ }^{211}$ HCWs to hospital visitors ${ }^{21)}$ and community cases to HCWs. ${ }^{14)}$ One study reported that the emergency room has become a connected "belt" that links patients and the departments. ${ }^{18)}$ Outpatient clinics, hospital entrances, and household transmission ${ }^{13}$ can be the pathways of measles transmission; thus, collecting
laboratory specimens during home health visits rather than visiting healthcare facilities was also a risk for HCWs. ${ }^{25)}$ One study demonstrated that measles was transmitted by an unknown mechanism between two patients. ${ }^{30)}$ Twelve studies did not examine the index case or source of infection because of limited contact tracing. ${ }^{8,10-12,19-21,24,25,27,29,31)}$

## 21. Generalizability: ORION item 21

Regarding age, young individuals ${ }^{8)}$ and adults ${ }^{23)}$ were comparably at higher risk for measles infection. Some studies mentioned that parents who have never contracted measles or been vaccinated against measles during childhood may be at a higher risk of transmission because they visit medical facilities more frequently. ${ }^{26)}$ Most studies have focused on the importance of the vaccination status of patients ${ }^{8,9,11,12,20,22,23,26)}$ and HCWs, and this can be the most common risk factor for measles infection. Assessing the immunization of the population and providing immunity to susceptible populations would be the first step to reduce measles outbreaks. Some studies have reported that, in addition to the non-classical presentations of measles (such as atypical measles, coinfection, suspected drug eruption, bloody diarrhea, or incubation period >21 days), the risk of placing patients with/without measles in nearby or single units ${ }^{19,28)}$ would hamper the isolation of suspected cases. ${ }^{12,13)}$ Misdiagnosis was the second most common risk for the selected studies. ${ }^{13,16,20)}$ Delays in diagnosis and reporting have delayed proper management of the outbreak. ${ }^{20,21)}$ It is critical to conduct rapid case identification with the implementation of precaution measures, ${ }^{28,29)}$ including the use of respiratory protection and an alcohol-based hand rub for patient care to combat the risk of infection; this was mentioned in two studies. ${ }^{22,25,29)}$ No study has discussed the validity and advantages or disadvantages of laboratory tests; however, one study has stated that the RTPCR test may be a sensitive method to confirm a measles infection.

Guidelines on measles vaccination of HCWs are not clearly presented, and national policies are note mandated in many countries. ${ }^{8,9,11,16,18,19,21-24,27-29)}$ Individuals were considered protected against measles if 1) they were born before 1965, ${ }^{10)} 2$ ) vaccinated twice, ${ }^{11,12)}$ or 3) had an measles-specific IgG antibody titer of $>16.50 \mathrm{AU} / \mathrm{mL}$. In many places around the world, measles immunity is not routinely studied. ${ }^{9,23)}$ Poor documentation of measles vaccination ${ }^{16,25,27)}$ and prophylaxis vaccine out-of-pocket are barriers to the cost of measles prevention. ${ }^{12)}$ Measles vaccination limits the risk of complications and the onset of large outbreaks. ${ }^{15)}$ Additionally, clinical signs and exanthema appear to be less severe in patients with two vaccinations compared to those with no vaccination: in a teenage psychiatric unit, two secondary nosocomial cases occurred in teenagers among 24 contact cases, and both secondary cases were twice-vaccinated and had no complications. ${ }^{15)}$

## 22. Overall evidence: ORION item 22

Measles transmission in healthcare settings is a significant burden on the morbidity, mortality, and economy of measles. The HCWs booster vaccination guidelines should be monitored and enhanced during the post-elimination period of measles. The outcomes of infections must be explicit for outbreak reports.

## DISCUSSION

In this study, we used the ORION statement findings and recommendations to identify the epidemiological and clinical characteristics of nosocomial measles infection worldwide and found that some of the critical information may be missed in reporting the nosocomial
measles infection. To improve the prevention of hospital transmission of measles, it is prudent to notice cases using clinical case definition and virologic confirmation.

While individual outbreak reports describe a single occurrence in a specific context, an assimilation of these reports may aid in improving our knowledge of epidemiological changes in measles worldwide. Measles is a highly transmissible virus with its basic reproduction number (R0) of 12-18, yet it's transmission dynamics may vary depending on the population and setting. ${ }^{32)}$ Healthcare facilities are the major sites of measles acquisition, and numerous studies have shown that measles is transmitted from patients to HCWs and from HCWs to patients and colleagues. ${ }^{33)}$ The risk of contracting measles is estimated to be 2to 19-times higher for HCWs than for the general public. ${ }^{17)}$ In the future, discussions should be made on whether nosocomial measles infection is a problem in low-and middle-income countries where measles has not been eradicated, or whether there is a greater concern about nosocomial measles infection through HCWs or caregivers due to waned vaccine immunogenicity in high-income countries where measles has been eradicated.

In conclusion, this study identified the epidemiological and clinical characteristics of nosocomial measles infections and provided stronger evidence for infection control policies to mitigate measles outbreaks in hospitals.

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## 요약

최근 의료기관 관련 홍역 유행 사례가 보고되고 있지만, 유행 역학조사 보고서가 표준화되어 있지 않아 질병부담의 크 기를 이해하는 데 어려움이 있다. 본 연구에서는 의료기관 관련 감염을 측정하기 위해 개발된 Outbreak Reports and Intervention Studies of Nosocomial Infection (ORION) 조사도구를 사용하여 병원 내에서의 홍역 발생의 크기 를 측정하고자 하였다. 본 연구에서는 PubMed, Web of Science, Embase, Scopus 및 Cochrane에서 "measles," "nosocomial," "hospital," 및 "healthcare" 등의 주제어를 사용하여 검색을 수행하였다. 총 24건의 의료기관 관련 홍역 유행 역학조사 연구를 ORION 도구를 활용하여 검토했다. 연구 결과 전 세계적으로 의료기관 내에서의 홍역 전파 는 발병률, 사망률 및 경제적으로 중대한 부담을 주고 있는 것을 확인하였다. 의료기관 관련 홍역을 예방하기 위해 의 사 및 간호사 등 의료 종사자들의 예방접종 지침이 준수되어야 할 것이며, 특히 표준화된 유행 역학조사 보고서의 활용 이 필요하다.

