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Differences in the clinical presentation and the frequency of complications between elderly and non-elderly scrub typhus patients

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ABSTRACT

Age can affect the clinical features and severity of infectious disorders, such as scrub typhus. We performed this study to examine differences between elderly and non-elderly scrub typhus patients, and to identify risk factors predictive of disease outcomes. This retrospective study included patients admitted to a tertiary hospital with scrub typhus between 2001 and 2011. A total of 615 patients were enrolled in this study, 328 of which were >65 years of age. Of the elderly patients, 46.0% (151/328) experienced at least one complication compared to only 23.0% (66/287) in younger patients. A linear trend was observed between age and complication rates ($p = 0.002$). The most common complication in elderly patients was acute kidney injury (75, 22.9%). Treatment failure was reported in 10 elderly patients (3.0%) compared to one non-elderly patient (0.3%). Mental confusion and dyspnea of clinical manifestations at admission were common in elderly patients. Frequency of fever, rash, and eschar were similar in both groups. The following four factors were significantly associated with severe scrub typhus in elderly patients: (1) white blood cell (WBC) counts > 10,000/mm^3 (OR = 2.569, CI = 1.298–5.086), (2) MDRD GFR < 60 mL/min (OR = 3.525, CI = 1.864–6.667), (3) albumin ≤ 3.0 g/dL (OR = 4.976, CI = 2.664–9.294), and (4) acute physiology and chronic health evaluation II (APACHE II) score > 10 points (OR = 3.304, CI = 1.793–60.87). Complications and mortality were more common in elderly patients, often associated with delays in diagnosis and treatment.

1. Introduction

Scrub typhus is a mite-borne bacterial infection of humans caused by *Orientia tsutsugamushi* prevalent in Asia, Northern Australia, and the Indian subcontinent (Jensenius, Fournier, & Raoult, 2004). With early diagnosis and management, most patients with scrub typhus are able to recover without complications. However, some patients develop serious and sometimes fatal complications (Park et al., 2000; Thap et al., 2002), particularly the elderly who experience a greater degree of morbidity and mortality associated with scrub typhus (Kim, Kim, Choi, & Yun, 2010). Complications of scrub typhus include interstitial pneumonia, acute renal failure, myocarditis, meningoencephalitis, gastrointestinal bleeding, acute hearing loss, and multiple organ failure. However, changes caused by infection in the elderly are subtle, leading to a variety of nonspecific symptoms (Norman, 2000). This often leads to delayed diagnosis and treatment of elderly patients, which may account for the increased complication rate seen in these patients.

Studies of the clinical characteristics of complicated scrub typhus have reported abnormal laboratory findings and risk factors (Hu et al., 2005; Kim et al., 2010; Ogawa et al., 2002; Park et al., 2011). However, no studies have assessed differences in the clinical manifestations and frequency of complications between elderly and non-elderly scrub typhus patients. A better understanding of initial presenting symptoms and frequency of complications in elderly scrub typhus patients will facilitate development of improved disease management strategies. When considered alongside the growing elderly population, increased outdoor activity and agricultural exposure in disease-endemic areas is expected to result in increased scrub typhus among the elderly.

We therefore aimed to identify differences in the complication frequency between elderly and non-elderly people, along with clinical predictors of complications in elderly scrub typhus patients.

2. Materials and methods

2.1. Subjects

This study was approved by the Institutional Review Board of Chonnam National University Hospital in Gwang-ju, Republic of

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Korea. A waiver of consent was granted, given the retrospective nature of the project.

This study included a retrospective review of adult patients (age ≥ 16 years) with scrub typhus who were admitted to Chonnam National University Hospital from 2001 to 2011. A diagnosis of scrub typhus was made based on typical clinical manifestations and the results of a serologic test. Serologic testing was performed using a passive hemagglutination assay (PHA) to detect *O. tsutsugamushi* antigen. A positive result was defined as a titre of ≥1:80 in a single serum sample or by a fourfold or greater increase in the follow-up titre. The PHA was performed using Genedia Tsutsu PHA II test kits (GreenCross SangA, Yongin, Republic of Korea).

Patients with scrub typhus were divided into two groups: with and without complications. The medical records were reviewed for information on age, gender, underlying disease, incubation period, symptoms, physical and laboratory findings at the time of admission, and clinical course.

2.2. Definitions

We defined the elderly as 65 years of age or older people.

Complicated scrub typhus was defined by the following conditions (Kim et al., 2010; Park et al., 2011): (1) shock, which was defined by a systolic blood pressure less than 90 mmHg or a fall in systolic blood pressure of >40 mmHg; (2) acute kidney injury, defined as a >twofold increase in serum creatinine or a decrease in glomerular filtration rate (GFR) of >50% from baseline; GFR was estimated based upon the modification of diet in renal disease (MDRD) equation (Ricci, Cruz, & Ronco, 2011); (3) pneumonia with parenchymal lung lesions on chest radiograph and cough or dyspnea; (4) acute respiratory distress syndrome (ARDS), defined by the ratio of arterial partial oxygen tension as a fraction of inspired oxygen below 200 mmHg in the presence of bilateral infiltrates on chest radiograph; (5) meningoencephalitis with neurologic symptoms and evidence of infection of the central nervous system based on imaging studies or cerebrospinal fluid counts >5 leukocytes/mm^3 (Jeong et al., 2007; Kim et al., 2010; Pai et al., 1997); (6) gastrointestinal bleeding; and (7) cholecystitis, defined by the presence of Murphy's sign and radiological evidence of gall bladder inflammation. Mortality was defined as scrub typhus-related if no other definite cause of death or hopeless discharge was observed.

2.3. Statistical analysis

The Kormogorov–Smirnov goodness-of-fit test was used to determine the distribution of each set of data for normality before subsequent analysis. Categorical variables were expressed as percentages of counts, and continuous variables were expressed as means ± standard deviation (SD) or medians and interquartile range (IQR). Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. Continuous variables were compared using Student's *t*-test or Mann–Whitney *U*-test, as appropriate. Logistic regression analysis was carried out, including variables with $p < 0.10$ in univariate analysis. All tests of significance were two-tailed, and *p* values ≤ 0.05 were deemed to indicate statistical significance. Statistical analyses of the data were performed using the SPSS statistics software (version 19.0; SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Baseline characteristics of patients and frequency of complicated scrub typhus

A total of 771 patients were diagnosed with scrub typhus during the study period. Of these, 615 were admitted and 217 (35.2%) had complicated scrub typhus at presentation. The mean age was 63 years (range, 18–96 years); 264 patients (42.9%) were male. The most common age group was 60–69 (194 patients; 32%); the second most common group was 70–79 (175 patients; 28%) (Fig. 1). Three hundred and twenty-eight patients (53.3%) were 65 years of age or older, ranging from 46% to 67% annually.

Of the elderly patients, 46.0% (151/328) had at least one complication, compared to 23.0% (66/287) in younger patients. A linear trend was observed between age and complication rates ($p = 0.002$). Risk multiplied 1.682-fold for each 10-year increase in age. The most common complication in elderly patients was acute kidney injury (75; 22.9%) followed by pneumonia (70; 21.3%), septic shock (46; 14%) and meningoencephalitis (31; 9.5%) (Table 1); in non-elderly patients, pneumonia was most common. Ten elderly patients either died (5), or were hopelessly discharged (5) during the course of this study, compared to only one death in non-elderly patients. The most common causes of mortality were septic shock (6/10) and pneumonia (4/10).

3.2. Clinical manifestations and laboratory findings at admission: the elderly vs. non-elderly

Table 2 shows the demographic data, initial manifestations, and laboratory findings at admission. Underlying disease was more common among elderly patients. Infection through occupational contact such as farming was more common in elderly patients, while casual contact, such as during a picnic, was more common in the non-elderly. No differences were seen regarding time from symptom onset to antibiotics therapy, nor were any differences observed in the frequencies of fever, rash, or eschar. However, mental confusion and dyspnea were significantly more common in the elderly ($p < 0.001$), as were leukocytosis, lower renal function, hypoalbuminemia, and high C-reactive protein (CRP). APACHE II scores were also higher among elderly patients. The differences of antibody titre and portion diagnosed as rising titre or single titre between the elderly and non-elderly were not significant (data not shown).

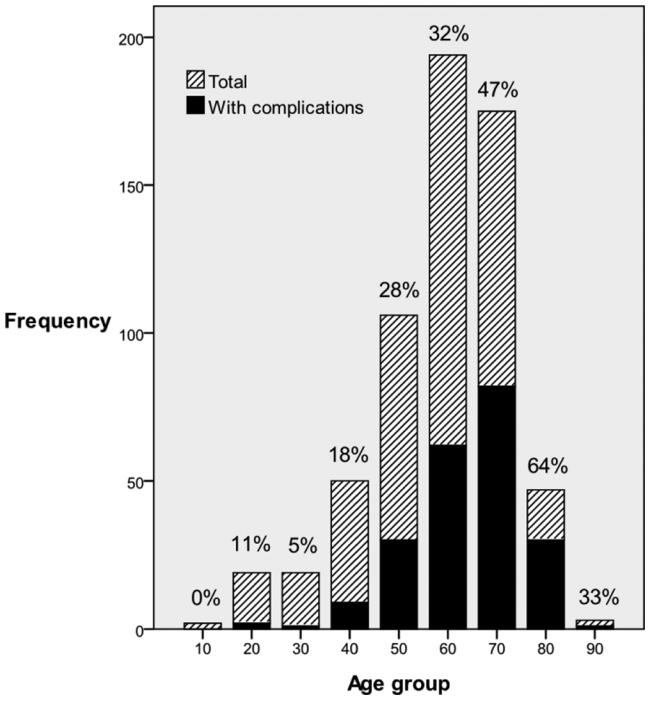

Fig. 1. Numbers of total and complicated scrub typhus patients by age group.