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Severe Fever With Thrombocytopenia Syndrome in Korea: Assessing the Impact of Hospital Patient Volume on Care Quality and Policy Implications

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ABSTRACT

Background: The case fatality rate of severe fever with thrombocytopenia syndrome (SFTS) in South Korea remains high. We aimed to assess whether hospital patient volume affects the quality of care and clinical outcomes, to provide policy-relevant insights for improving SFTS management.

Methods: We retrospectively analyzed all SFTS patients reported to the Korea Disease Control and Prevention Agency (KDCA) from 2016 to 2021. Detailed clinical variables were collected from patients treated at 28 participating hospitals. SFTS management was compared according to hospital patient volume. The infectious disease physicians at the study hospitals were surveyed about their unmet needs in SFTS care.

Results: A total of 1,328 SFTS patients from 163 hospitals were reported during the study period. Of these, 60.7% (99/163) treated fewer than one patient per year. The distribution of patients was uneven across the country, with the highest annual incidence of 1.91 cases per 100,000 population in Gangwon province. From 657 patients across 28 study hospitals, five high-volume hospitals were compared with 12 low-volume hospitals to evaluate differences between the two extremes of hospital volume. High-volume hospitals had a shorter median turn-around time for formal results compared to low-volume hospitals (4 days [interquartile range, IQR 2–6] vs. 7 days [IQR 4–13], $P < 0.001$). Among three testing institutions, the turn-around time for formal results was shortest for in-house testing, followed by the Health and Environment Research Institutes, and then KDCA (3 days [IQR 1.5–4] vs. 5 days [IQR 3–7] vs. 18.5 days [IQR 12–22.25], all post hoc $P \leq 0.007$). The case fatality rate was not significantly different between the groups (16.9%, 42/248 vs. 13.8%, 17/123; $P = 0.440$). The survey showed that among 27 responders, the most commonly reported difficulty in SFTS care was delayed turn-around time of diagnostic tests (85.2%).

Conclusion: SFTS cases occurred sporadically and rarely across the country, and the level of clinical expertise in managing SFTS varied between hospitals depending on patient volume. However, the case fatality rate showed no significant difference. Regional centralization of SFTS patients may be helpful in terms of improving quality of care and facilitating clinical trials for experimental therapeutics.

Keywords: SFTS; Severe Fever With Thrombocytopenia Syndrome; National Policy; Korea

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Author Contributions
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INTRODUCTION

Severe fever with thrombocytopenia syndrome (SFTS) is a newly emerging infectious disease primarily reported in China, Korea, and Japan with a small number of cases in neighboring countries.[1,2] After the first report in China,[3] the first case in South Korea was reported in 2013.[4] We reported the clinical characteristics of SFTS during the early phase of the epidemic in Korea,[5] and have recently updated our findings on the severe nature of its clinical features.[6] SFTS is a reportable infectious disease managed by the government not only in Korea but also in China and Japan.[7,8] The case fatality rate of SFTS from 2016 to 2021 was 16.8% (223/1,328) in Korea,[6] which was much higher than the 7.6% (39/515) in Japan during the same period,[9] and also higher than previous reports from China, which ranged from 10.5 to 16.2%.[2,10] Given SFTS's rarity, rapid progression, and high fatality, national policies are urgently needed to improve outcomes.

In this study, we aimed to describe the current status of SFTS care in South Korea and examine whether the volume of patients treated at a hospital influences care quality and outcomes, thereby providing policy-relevant factors that may help improve SFTS management.

METHODS

Study subjects and design

All SFTS patients reported to the Korea Disease Control and Prevention Agency (KDCA) from January 2016 to December 2021 were included, as SFTS is legally mandated to be reported. To collect detailed clinical data on individual patients, participating hospitals were selected based on regional distribution, patient volume, and the presence of infectious disease physicians. These 28 participating hospitals formed the Korea SFTS Clinical Network, listed in the Acknowledgments section. We used epidemiological data from KDCA and detailed clinical data from patients at the 28 participating hospitals.

Only cases diagnosed with SFTS via positive conventional or real-time reverse transcription polymerase chain reaction (RT-PCR) assay were included. Since the government replaced conventional RT-PCR with real-time RT-PCR in early 2016, most subjects were diagnosed using real-time RT-PCR. Patients diagnosed with enzyme-linked immunosorbent assay or indeterminate RT-PCR results were excluded.

The aim of this study was to describe the characteristics of SFTS care in South Korea and to evaluate whether patient volume influences the quality of diagnosis and treatment. It was assumed that there would be differences in the quality of care based on the hospital's experience, as measured by the number of patients treated. In the analysis of KDCA data for 1,328 patients from 163 hospitals, we compared the top 10 hospitals, ranked by the number of patients treated, with the bottom 99 hospitals, each treating fewer than one patient per year. In the analysis of data from 28 participating hospitals with 657 patients, we compared the top five hospitals and the bottom 12 hospitals based on the number of patients treated to evaluate the differences at both ends of the spectrum. The top five hospitals were selected so that the median number of patients treated during the study period would be 50. Since three hospitals were tied for the 10th lowest when the hospitals were ranked by the number of patients treated in ascending order, we included the bottom 12 hospitals for comparison.

Additionally, a survey was conducted among infectious disease physicians at participating hospitals to assess their satisfaction and needs in managing SFTS cases.

Data collection and definitions

From the KDCA data, basic information was obtained, including demographics, diagnosing hospital, RT-PCR results, residential area, mortality status, and dates for symptom onset, diagnosis, and death. The official resident registry from the Korean Statistical Information Service was used to estimate the annual SFTS incidence per 100,000 population (https://kosis.kr/eng/). Detailed clinical data from participating hospitals included demographic variables, RT-PCR results, turn-around time of test results, underlying diseases, clinical manifestations, and laboratory findings at admission, treatments, and mortality status. Survey questions addressed topics such as turn-around time of diagnostic tests, availability of medical staff or treatment resources, and all available data were presented in **Supplementary Data 1**.

In KDCA data, the date of diagnosis refers to the date recorded by the clinician on the SFTS case report form, which may include dates of clinical diagnoses made prior to laboratory confirmation. A formal result was the official report provided on a certificate, while an informal result was an advance reporting by phone or text message. National administrative provinces were grouped into six geographic regions (**Fig. 1A**): Seoul/Gyeonggi,

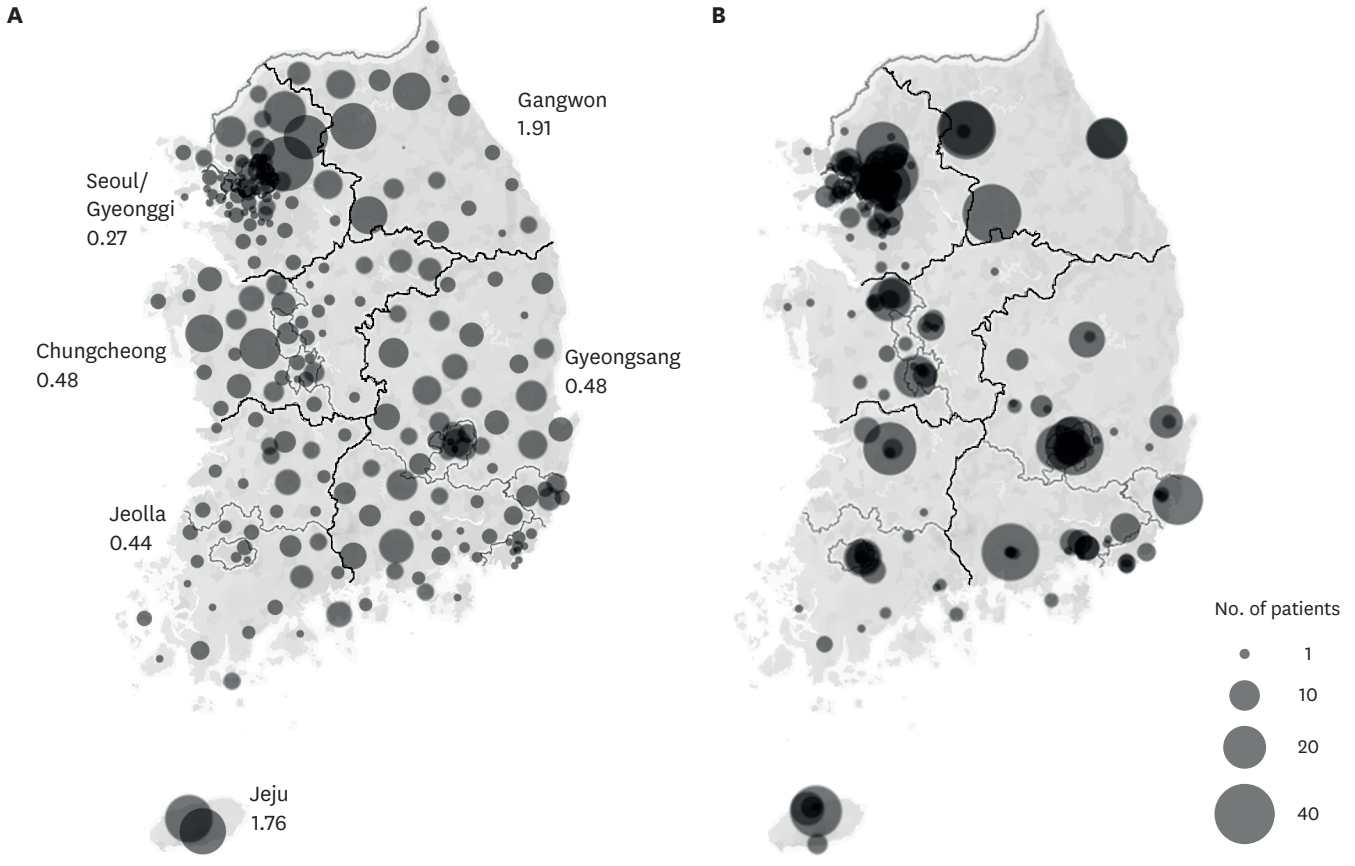


Fig. 1. Geographical distribution of 1,328 patients with severe fever with thrombocytopenia syndrome in South Korea, 2016–2021. (**A**) The distribution of patients by residential area. (**B**) The distribution of patients by initially diagnosed hospitals. Gangwon is a largely hilly region in South Korea. The number below each province indicates annual incidence per 100,000 population, and the size of gray circles represents the number of patients.

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Gangwon, Chungcheong, Gyeongsang, Jeolla, and Jeju. Medical institution types were classified according to the Medical Service Act of Korea.[11] KDCA is affiliated with the central government, while the Health and Environment Research Institutes (HERIs) are regional governmental agencies, responsible for diagnostic tests for various rare infectious diseases; both are public institutions. In-house testing at each hospital was performed using real-time RT-PCR assays. Death due to hemodynamic instability in the absence of major bleeding or bacteremia was classified as refractory shock.

Statistical analysis

Categorical variables were compared using Pearson's χ^2 test when fewer than 20% of cells had expected counts below five; otherwise, Fisher's exact test was used. Continuous variables were compared using the Mann-Whitney *U* test or Student's *t*-test for two groups, and the Kruskal-Wallis test for three groups. Normality was assessed by the Kolmogorov-Smirnov test; non-normal data were analyzed with the Mann-Whitney *U* test, normal data with Student's *t*-test. Post hoc tests used the Mann-Whitney *U* test with Bonferroni correction. $P < 0.05$ was considered significant. Statistical analyses were conducted with SPSS version 25.0 (IBM Corp, Armonk, NY, USA). **Fig. 1** was created using Tableau Software version 2023.3 (Tableau Software, Washington, D.C., USA), using OpenStreetMap as the base map (https://www.openstreetmap.org/#map=7/35.853/126.705).

Ethics statement

This study was approved by the Institutional Review Board (IRB) of Boramae Medical Center (IRB No. 10-2022-66). The requirement for informed written consent was waived because of the retrospective nature and minimal risk of the study. Personal identifiers were removed before data processing, and the study complied with the tenets of the Declaration of Helsinki.

RESULTS

Nationwide incidence of SFTS in Korea

A total of 1,328 SFTS patients were reported from 163 hospitals nationwide during the study period of 2016–2021, with an overall case fatality rate of 16.8% (223/1,328). The geographical distribution by residential area of SFTS patients is presented in **Fig. 1A**. SFTS patients were reported across the country, and the annual incidence per 100,000 population was highest in Gangwon (1.91), followed by Jeju (1.76), Chungcheong and Gyeongsang (both 0.48), Jeolla (0.44), and Seoul/Gyeonggi (0.27). **Fig. 1B** shows the geographical distribution of diagnosing hospitals. Out of 163 hospitals, 99 treated fewer than one patient per year, and only eight treated more than 40 patients during the study period. The distribution of patients by initially diagnosing hospitals was more concentrated in urban regions within the provinces, compared with the distribution based on patients' residence.

Comparison of hospitals based on SFTS patient volume using KDCA national data

Among the 1,328 SFTS patients from the KDCA data, we compared the top 10 hospitals based on the number of patients treated with the bottom 99 hospitals, each of which treated fewer than one patient per year (**Table 1**). The top 10 hospitals comprised five general hospitals and five tertiary hospitals, whereas the bottom 99 hospitals included two public health clinics, nine hospitals, 78 general hospitals, and 10 tertiary hospitals. The analysis included 460 patients from high-volume hospitals and 210 from low-volume hospitals. The median

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Table 1. Comparison between high- and low-volume hospitals based on the volume of SFTS patients among all hospitals reporting SFTS patients during 2016-2021 in South Korea

Variables	Patients included in the volume-based analysis (n = 670)	High-volume hospitals[a] (n = 460)	Low-volume hospitals[a] (n = 210)	*P* value
Age, yr	67 (58–77)[b]	67 (58–77)	68 (59–76)	0.623
Sex, female	338 (50.4)	230 (50.0)	108 (51.4)	0.732
Fatal case	109 (16.3)	71 (15.4)	38 (18.1)	0.387
Duration from symptom onset to death, days	6 (4–13)	6 (3–13)	7 (5–15)	0.194
Duration from symptom onset to diagnosis, days[c]	3 (0–6)	2 (0–5)	4 (1–8)	< 0.001

SFTS = severe fever with thrombocytopenia syndrome.
[a]High-volume hospitals were defined as the top 10 hospitals based on the number of patients treated, while low-volume hospitals were the bottom 99 hospitals that treated fewer than one patient per year.
[b]The result is the median value, the value in parentheses is the percentage, and the range is the interquartile range.
[c]The date of diagnosis refers to the date recorded by the clinician on the SFTS case report form, which may include dates of clinical diagnosis made prior to laboratory confirmation.

number of patients treated per hospital was 46 (interquartile range [IQR] 41–51) in high-volume hospitals and 2 (IQR 1–3) in low-volume hospitals. Among 670 patients, the median age was 67 years (IQR 58–77), and 50.4% (338/670) were female. The overall case fatality rate was 16.3% (109/670), with no significant difference between groups (15.4%, 71/460 vs. 18.1%, 38/210; $P = 0.387$). The median time to diagnosis after symptom onset was significantly shorter in high-volume hospitals compared to low-volume hospitals (2 days [IQR 0–5] vs. 4 days [IQR 1–8], $P < 0.001$).

Diagnosis and treatment of SFTS patients according to patient volume

In the analysis of 657 patients from 28 participating hospitals, we compared the top five hospitals, which treated 248 patients, with the bottom 12 hospitals, which treated 123 patients (**Table 2**). The median number of patients treated per hospital was 50 (IQR 48–53) in high-volume hospitals and 8 (IQR 6–11) in low-volume hospitals. Among these 371 patients, the median age was 68 years (IQR 58.5–76.5) and 51.2% (190/371) were female. The overall case fatality rate was 15.9% (59/371). The most common cause of death was unspecified multiorgan failure (62.7%, 37/59), followed by refractory shock (27.1%, 16/59), bacterial sepsis (6.8%, 4/59), bleeding (1.7%, 1/59), and respiratory failure (1.7%, 1/59).

Table 2. Diagnosis and treatment of SFTS patients based on patient volume among 28 participating hospitals

Variables	Patients included in the volume-based analysis (n = 371)	High-volume hospitals[a] (n = 248)	Low-volume hospitals[a] (n = 123)	*P* value
Age, yr	68 (58.5–76.5)[b]	68 (58.75–77)	68 (58.5–74.5)	0.205
Sex, female	190 (51.2)	124 (50.0)	66 (53.7)	0.507
Fatal case	59 (15.9)	42 (16.9)	17 (13.8)	0.440
Pre-visit symptom duration, days	5 (3–7)	4 (3–6)	5 (3–7)	0.007
Hospitalization period, days	9 (7–13)	9 (7–13)	10 (7–14)	0.286
Duration from symptom onset to death, days	9 (7–15.5)	8 (7–16)	11 (9–13)	0.250
Underlying diseases				
None	160 (43.1)	111 (44.8)	49 (39.8)	0.368
Hypertension	149 (40.2)	104 (41.9)	45 (36.6)	0.322
Diabetes mellitus	78 (21.0)	53 (21.4)	25 (20.3)	0.816
Cerebrovascular disease	15 (4.0)	10 (4.0)	5 (4.1)	> 0.999
Congestive heart failure	9 (2.4)	6 (2.4)	3 (2.4)	> 0.999
Chronic liver disease	10 (2.7)	7 (2.8)	3 (2.4)	> 0.999
Chronic kidney disease	6 (1.6)	4 (1.6)	2 (1.6)	> 0.999
Bronchial asthma	4 (1.1)	1 (0.4)	3 (2.4)	0.108
Chronic obstructive pulmonary disease	4 (1.1)	3 (1.2)	1 (0.8)	> 0.999
Solid malignancy	9 (2.4)	4 (1.6)	5 (4.1)	0.165
Hematologic malignancy	1 (0.3)	1 (0.4)	-	> 0.999

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Table 2. (Continued) Diagnosis and treatment of SFTS patients based on patient volume among 28 participating hospitals

Variables	Patients included in the volume-based analysis (n = 371)	High-volume hospitals[a] (n = 248)	Low-volume hospitals[a] (n = 123)	*P* value
Clinical manifestations at admission				
Fever	250 (67.4)	160 (64.5)	90 (73.2)	0.094
Diarrhea	120 (32.3)	85 (34.3)	35 (28.5)	0.259
Nausea	109 (29.4)	68 (27.4)	41 (33.3)	0.239
Vomiting	65 (17.5)	43 (17.3)	22 (17.9)	0.896
Altered mental status[c]	58 (15.6)	35 (14.1)	23 (18.7)	0.252
Seizure	4 (1.1)	1 (0.4)	3 (2.4)	0.108
Gross hematuria	7 (1.9)	3 (1.2)	4 (3.3)	0.226
Gastrointestinal bleeding	5 (1.3)	5 (2.0)	-	0.175
Hemoptysis	3 (0.8)	2 (0.8)	1 (0.8)	> 0.999
Laboratory findings at admission[d]				
Lymphocytes, cells/mm^3	476 (319–727)	452 (314–707)	497 (347–773)	0.617
Hemoglobin, g/dL	13.4 (12.4–14.8)	13.5 (12.4–15.0)	13.4 (12.4–14.5)	0.797
Platelets, ×1,000/mm^3	62 (45–88)	62 (46–88)	62 (44–89)	0.601
Aspartate aminotransferase, IU/L	161 (68–335)	155 (61–332)	165 (88–335)	0.281
Alanine aminotransferase, IU/L	39 (35–135)	68 (34–140)	71 (38–128)	0.486
Creatinine > 1.2 mg/dL	81 (22.0)	60 (24.2)	21 (17.5)	0.146
Prothrombin time > 1.1 INR	100 (28.3)	80 (33.5)	20 (17.5)	0.002
aPTT > 40 sec	205 (58.4)	129 (54.2)	76 (67.3)	0.020
Diagnosis of SFTS				
Time to sample collection after admission, days	0 (0–1)	0 (0–1)	0 (0–1)	0.987
Report of informal results	212 (57.1)	145 (58.5)	67 (54.5)	0.464
Report of formal results	369 (99.5)	248 (100)	121 (98.4)	0.109
Turn-around time of informal results, days	4 (2–6)	3 (2–5)	4 (2–7)	0.098
Turn-around time of formal results, days	5 (3–8)	4 (2–6)	7 (4–13)	< 0.001
Type of RT-PCR testing institution				
Health and Environment Research Institute	326 (87.9)	247 (99.6)	79 (64.2)	< 0.001
Report of informal results	181 (55.5)	144 (58.3)	37 (46.8)	0.074
Report of formal results	326 (100)	247 (100)	79 (100)	-
Turn-around time of informal results, days	4 (2–6)	3 (2–5)	5 (3–7)	0.056
Turn-around time of formal results, days	5 (3–7)	4 (2–6)	7 (3.5–10)	< 0.001
Korea Disease Control and Prevention Agency	30 (8.1)	1 (0.4)	29 (23.6)	< 0.001
Report of informal results	16 (53.3)	1 (100)	15 (51.7)	> 0.999
Report of formal results	28 (93.3)	1 (100)	27 (93.1)	> 0.999
Turn-around time of informal results, days	5 (3.75–7.5)	2	5 (4–8)	0.375
Turn-around time of formal results, days	18.5 (12–22.25)	2	19 (12.5–22.5)	0.143
In-house testing by each hospital	15 (4.0)	–	15 (12.2)	< 0.001
Report of informal results	15 (100)	–	15 (100)	-
Report of results	15 (100)	–	15 (100)	-
Turn-around time of informal results, days	2 (1.5–4)	–	2 (1.5–4)	-
Turn-around time of formal results, days	3 (1.5–4)	–	3 (1.5–4)	-
Treatment of SFTS				
Isolation in single room	151 (40.7)	117 (47.2)	34 (27.6)	< 0.001
Intensive care unit admission	94 (25.3)	67 (27.0)	27 (22.0)	0.291
Mechanical ventilation	60 (16.2)	43 (17.3)	17 (13.8)	0.386
Continuous renal replacement therapy	40 (10.8)	27 (10.9)	13 (10.6)	0.926
Plasma exchange	64 (17.3)	51 (20.6)	13 (10.6)	0.016
Steroid	65 (17.5)	52 (21.0)	13 (10.6)	0.013
Ribavirin	51 (13.7)	40 (16.1)	11 (8.9)	0.058
Intravenous immunoglobulin	61 (16.4)	44 (17.7)	17 (13.8)	0.337

SFTS = severe fever with thrombocytopenia syndrome, INR = international normalized ratio, aPTT = activated prothrombin time, RT-PCR = reverse transcription polymerase chain reaction.
[a]High-volume hospitals were defined as the top five hospitals based on the number of patients treated, while low-volume hospitals were the bottom 12 hospitals.
[b]The result is the median value, the value in parentheses is the percentage, and the range is the interquartile range.
[c]Altered mental status included confusion, drowsiness, stupor, semicomatose state and comatose state.
[d]Laboratory findings were evaluated among available data.

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The pre-visit symptom duration was shorter in high-volume hospitals compared to low-volume hospitals (4 days [IQR 3–6] vs. 5 days [IQR 3–7], $P = 0.007$). At the time of admission, prolonged prothrombin time (33.5%, 80/248 vs. 17.5%, 20/123; $P = 0.002$) and activated partial thromboplastin time (54.2%, 129/248 vs. 67.3%, 76/123; $P = 0.020$) were more frequently observed in the high-volume hospital group. There were no other significant differences in underlying diseases, clinical manifestations, or other laboratory findings between the two groups.

The median time from admission to diagnostic sample collection was 0 days (IQR 0–1) in both groups ($P = 0.987$). The overall median turn-around time for informal and formal results was 4 days (IQR 2–6) and 5 days (IQR 3–8), respectively. HERIs of local governments accounted for a larger proportion of tests in high-volume hospitals, with 99.6% (247/248), compared to 64.2% (79/123) in low-volume hospitals ($P < 0.001$). In contrast, the KDCA of the central government (0.4%, 1/248 vs. 23.6%, 29/123; $P < 0.001$) and in-house testing by each hospital (0% vs. 12.2%, 15/123; $P < 0.001$) accounted for a larger proportion of tests in low-volume hospitals than in high-volume hospitals.

In comparison between the testing institutions, the turn-around time for informal results was shorter for in-house testing compared to KDCA (2 days [IQR 1.5–4] vs. 5 days [IQR 3.75–7.5], post hoc $P = 0.011$). There were no significant differences in turn-around time for informal results between HERIs and either KDCA or in-house testing. For formal results, in-house testing had the shortest turn-around time, followed by the HERIs, and then KDCA (3 days [IQR 1.5–4] vs. 5 days [IQR 3–7] vs. 18.5 days [IQR 12–22.25], all post hoc $P \leq 0.007$). We also assessed whether there were differences in turn-around time within the same testing institution according to the patient volume (**Table 2**). In HERIs, high-volume hospitals had a shorter median turn-around time for formal results compared to low-volume hospitals (4 days [IQR 2–6] vs. 7 days [IQR 3.5–10], $P < 0.001$).

The percentage of patients isolated in a single room was higher in high-volume hospitals compared to low-volume hospitals (47.2%, 117/248 vs. 27.6%, 34/123; $P < 0.001$). The use of plasma exchange (20.6%, 51/248 vs. 10.6%, 13/123; $P = 0.016$) and steroids (21.0%, 52/248 vs. 10.6%, 13/123; $P = 0.013$) was also more common in patients treated at high-volume hospitals than in those treated at low-volume hospitals.

The survey for unmet need in SFTS care

Among 28 infectious disease physicians at the study hospitals, 27 responded to a survey (**Fig. 2**). The main challenges reported were delayed turn-around times for diagnostic tests (85.2%, 23/27) and overly stringent insurance regulations for experimental treatments (77.8%, 21/27). In addition, 77.8% (21/27) of respondents expressed a desire for the introduction of favipiravir. Regarding resources, 63.0% (17/27) of physicians indicated a need for dedicated medical staff, 55.6% (15/27) for isolation rooms, and 11.1% (3/27) for ICU beds.

DISCUSSION

Our study showed that although SFTS incidence was low, cases occurred nationwide. Due to the scattered nature of cases, 163 hospitals were involved in the initial diagnosis. Of these, 60.7% (99/163) treated fewer than one patient annually, and only eight hospitals treated over 40 patients during the six-year study period. Our comparative analysis between hospitals at

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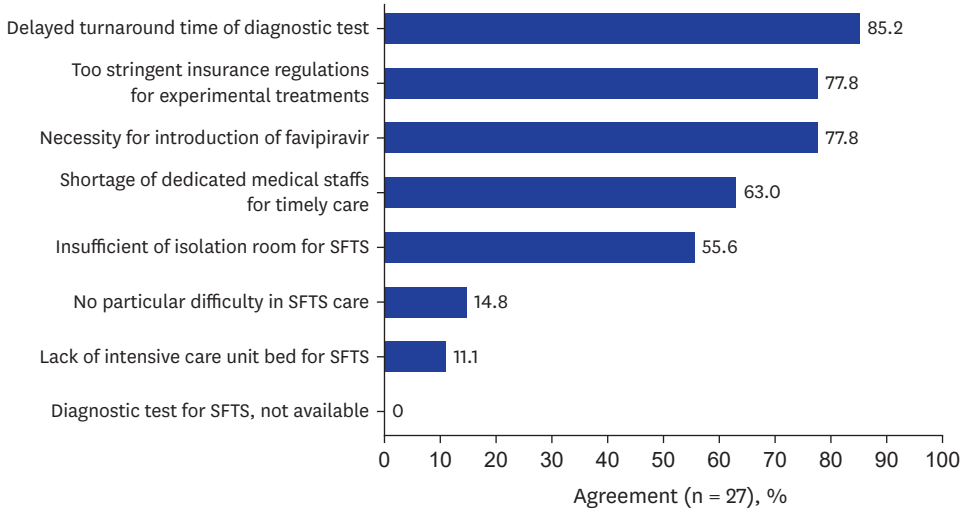


Fig. 2. Survey on difficulties in managing SFTS case by 27 infectious disease physicians at participating hospitals.
SFTS = severe fever with thrombocytopenia syndrome.

both extremes of patient volume showed that high-volume hospitals had shorter diagnostic turn-around times and a higher percentage of isolated cases, indicating greater expertise. However, case fatality rates did not significantly differ between groups.

Among the three testing institutions, the median turn-around time for formal results from in-house testing was significantly shorter at 3 days (IQR 1.5–4), compared to the HERIs (5 days [IQR 3–7], post hoc $P < 0.001$) and KDCA (18.5 days [IQR 12–22.25], post hoc $P = 0.007$). However, only two hospitals in the low-volume group operated their own laboratories for SFTS confirmation. Supporting the implementation of in-house testing at high-volume hospitals could expedite SFTS diagnosis. Furthermore, policy support for in-house testing hospitals to serve as backup centers when HERIs are unavailable, such as on weekends, could help further reduce diagnostic turn-around time.

In the comparison between groups, high-volume hospitals had a shorter median turn-around time for formal results when tested in HERIs, compared to low-volume hospitals (4 days [IQR 2–6] vs. 7 days [IQR 3.5–10], $P < 0.001$). This may reflect stronger links between high-volume hospitals and these agencies for sample transfer and reporting. Our findings suggest that strengthening collaboration with HERIs through targeted education for healthcare providers and improvements in the test referral and result reporting process could help expedite diagnosis. High-volume hospitals had a higher percentage of patients isolated in single rooms (47.2%, 117/248 vs. 27.6%, 34/123; $P < 0.001$) and undergoing plasma exchange (20.6%, 51/248 vs. 10.6%, 13/123; $P = 0.016$) compared to low-volume hospitals.

Although high-volume hospitals had shorter diagnostic turn-around times and more frequent plasma exchange, mortality did not differ significantly. Coagulopathy was more common in high-volume hospitals, suggesting greater disease severity and complicating conclusions about the effect of supportive care on clinical outcomes. Our previous analysis found that fatal outcomes were associated with fever, altered mentality, and laboratory abnormalities including elevated liver enzymes, creatinine, and coagulopathy.[6] The main causes of death—unspecified multiorgan failure (50.5%) and refractory shock (40.6%)—reflect severe systemic

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deterioration. These findings highlight the limitations of current supportive therapies and the need for novel antivirals and therapeutics to overcome the current clinical standstill.

Some antivirals, such as favipiravir and ribavirin, have shown effectiveness in selected groups,[1,12] while intravenous immune globulin showed mixed results,[1] and plasma exchange may be considered in severe cases.[13] In our study, plasma exchange or ribavirin was more frequently administered to patients with congestive heart failure and chronic obstructive pulmonary disease, and patients presented with altered mental status, more profound lymphopenia, and elevated liver enzymes (**Supplementary Table 1**). Although well-designed clinical trials are essential to address the uncertainty surrounding antivirals and therapeutics, the rapid progression and high fatality rate of SFTS pose challenges to traditional trial designs. Clinical trials for SFTS remain limited (clinicaltrials.gov), the novel therapeutics, along with alternative trial strategies, may be necessary to effectively evaluate interventions.

Several factors may account for the higher fatality rate of SFTS in Korea compared to China and Japan. The differences in average age of patients—a well-recognized risk factor for mortality—and circulating viral genotypes may contribute to outcome disparities.[2,7-10,14] From a public health policy perspective, unlike the geographic clustering in China and Japan, Korea's cases are more sporadic and widely spread, complicating resource allocation.[7,8] Additionally, China and Japan conduct active surveillance with frequent reports, while Korea relies on passive surveillance with annual reporting, which may lead to under-detection and higher fatality. Serologic studies have suggested SFTS prevalence in South Korea ranges from 0.2% to 4.1%, much higher than reported cases.[15-18] Although the overall seroprevalence remains low, active surveillance targeting high-risk groups or peak transmission periods could facilitate earlier detection and improve outcomes.

Our findings suggest that implementing in-house testing—the fastest diagnostic method—at high-volume centers and strengthening collaboration with HERIs could expedite SFTS diagnosis. Infectious disease physicians cited delayed turn-around time of diagnostic results and limited availability of specialists and facilities as key challenges. From a policy-making perspective, designating dedicated infectious disease hospitals could be beneficial for improving the management of rare and fatal diseases like SFTS. Such hospitals would centralize scattered cases, enable faster diagnosis, optimize resource use, and support systematic evaluation of experimental therapeutics. Our results support the designation of regional infectious disease hospitals by Korean government, initiated in 2016, as a potential solution to fulfill these roles.[19]

SFTS incidence varied regionally, with higher rates in Gangwon and Jeju provinces. These differences are influenced by factors such as geography (altitude, climate), which affects vector habitats; occupational exposure from agriculture and forestry; and host-related factors like regional population aging. Gangwon is largely mountainous, with a relatively higher proportion of residents involved in forestry compared to other regions. Jeju, a volcanic island with rolling hills and grasslands, has a large number of residents engaged in agriculture and livestock grazing. Given the multifactorial nature of SFTS transmission, further research is needed to clarify the roles of environmental, occupational, and host-related factors.

This study has several limitations. First, generalizability may be limited, as turn-around times and surveys were based on data from 28 hospitals. However, these hospitals accounted for 49.5% (657/1328) of all SFTS cases during the study period, which likely reflects nationwide

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trends. Second, the criteria for group classification were set arbitrarily. Third, differences in disease severity between groups may have influenced the results, although case fatality rates did not differ significantly. Fourth, quality control of in-house testing at individual hospitals was not assessed, as the KDCA validated the results and the number of cases was small. Nonetheless, potential limitations of tests conducted outside the reference laboratories, though likely minimal, should be interpreted with caution. Lastly, the retrospective nature of the study may reduce the precision of the findings.

In conclusion, our study provides an updated overview of the SFTS care in Korea from 2016 to 2021, revealing sporadic nationwide incidence and disparities in care quality based on patient volume, despite no significant differences in fatality rates. Centralizing scattered patients in regional hub hospitals may improve the quality of care and support clinical trials for new therapeutics.

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SUPPLEMENTARY MATERIALS

Supplementary Data 1

Challenges Faced by Clinicians in the Management of SFTS

Supplementary Table 1

Comparison of clinical characteristics between patients treated with plasma exchange or ribavirin with those who were not at 28 participating hospitals

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