



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Impact of COVID-19 on pregnant women in South Korea: Focusing on prevalence, severity, and clinical outcomes



So Hee Kim^{a,1}, Yeonmi Choi^{b,1}, Dokyoung Lee^b, Hyejin Lee^c, Ji Hoi Kim^a, Eun Saem Choi^a, Young Mi Jung^a, Jinwoo Lee^d, Pyoeng Gyun Choe^e, Ji Yoon Lee^b, Youngme Do^b, Chan-Wook Park^a, Joong Shin Park^a, Jong Kwan Jun^a, Seung Mi Lee^{a,2}, Jin Yong Lee^{b,f,g,*,2}

^a Department of Obstetrics and Gynecology, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, South Korea

^b HIRA Research Institute, Health Insurance Review and Assessment Service, 60 Hyeoksin-ro, Wonju-si, Gangwon-do 26465, South Korea

^c Department of Family Medicine, Seoul National University Bundang Hospital, 82 Gumi-ro, 173 Beon-gil, Bundang-gu, Seongnam-si, Gyeonggi-do 13620, South Korea

^d Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, South Korea

^e Department of Internal Medicine, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, South Korea

^f Public Healthcare Center, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, South Korea

^g Department of Health Policy and Management, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, South Korea

ARTICLE INFO

Article history:

Received 4 November 2021

Received in revised form 22 December 2021

Accepted 6 January 2022

Keywords:

SARS-CoV-2

COVID-19

Prevalence

Severity

Pregnancy

ABSTRACT

Background: In the era of coronavirus disease 2019 (COVID-19) pandemic, there is a paucity of information regarding actual prevalence of COVID-19 in pregnant women compared to non-pregnant women. The purpose of this study was to investigate the prevalence of COVID-19 infection and clinical outcome in pregnant women and non-pregnant women.

Methods: This is a nationwide cross-sectional study in South Korea between January 2020 and February 2021 using the claim database. The primary outcome was the prevalence of COVID-19 in pregnant women, and the secondary outcome was the occurrence of severe COVID-19 illness among infected patients. Severity of COVID-19 was classified into four categories according to WHO ordinal scale.

Results: The prevalence of COVID-19 infection was lower in pregnant women than non-pregnant women aged 20–44 (0.02% vs. 0.14%, $p < 0.0001$). However, among COVID-19 positive women at age 20–44, pregnant women was at higher risk of oxygen therapy after hospitalization (score 4 in WHO ordinal scale: 6.4% vs. 1.6%, $p < 0.05$). There were no deaths or hospitalized severe disease in pregnant women with COVID-19, although the majority of them (96.2%) were admitted to hospital. On the other hand, 42.3% of non-pregnant women at 20–44 age were admitted to hospital and 0.04% of them died and 0.1% had hospitalized severe disease.

Conclusions: The prevalence of COVID-19 infection in pregnant women was lower than non-pregnant women in Korea, resulting in relatively small cases of fatality. It has implications that public health policy, such as an effective response to COVID-19 and a powerful preemptive strategy for pregnant women, can lower risk of COVID-19 infection and better clinical outcomes in pregnant women with COVID-19.

© 2022 The Authors. Published by Elsevier Ltd on behalf of King Saud Bin Abdulaziz University for Health Sciences.

CC_BY_NC_ND_4.0

* Corresponding author at: Public Healthcare Center, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, South Korea.

E-mail address: jylee2000@gmail.com (J.Y. Lee).

¹ So Hee Kim and Yeonmi Choi contributed equally to this paper.

² Seung Mi Lee and Jin Yong Lee contributed equally to this paper.

Introduction

We are living the era of coronavirus disease 2019 (COVID-19) pandemic since 2019. According to WHO Coronavirus (COVID-19) Dashboard, as of 1 September 2021, there have been 217,558,771 coronavirus infected cases of COVID-19 and 527,942 new cases were reported to WHO [1]. Pregnant women are no exception to COVID-19 infection. According to WHO collaborating centre for global women's

health’s analysis, the prevalence of COVID-19 in pregnant women was 10% among the participants who admitted for any reasons [2].

Because of physiologic changes in both respiratory and immune systems, it is well known that pregnant women are susceptible [3] and prone to develop severe respiratory infection [4]. With enlarged uterus as pregnancy progressed, diaphragm is elevated, and angle of rib cage is increased [5]. With anatomical adaptation, tidal volume and minute oxygen uptake increase and functional residual capacity and total pulmonary resistance decreases. This physiological change of pregnant women body can decrease the capacity of decompensation for pregnant women with some pulmonary complications [6].

It has been reported that the clinical course of the COVID-19 infection in pregnant women is worse than non-pregnant women with slower recovery [7]. Some reported that the severe COVID-19 infection rate in pregnant women was 70% higher than non-pregnant women of the same age [8]. In 2020, Morbidity and Mortality Weekly Report published by US Department of Health and Human Services/Centers for Disease Control and Prevention reported that pregnant women with coronavirus disease 2019 (COVID-19) might be at increased risk for severe illness compared with non-pregnant women [9].

Until now, there is a paucity of information regarding the actual prevalence of COVID-19 infection in pregnant women compared to non-pregnant women. Previous studies from United States, United Kingdom, and other countries throughout the world reported relatively higher prevalence of COVID-19 among pregnant women (ranged from 1.3%–30.74% [10,11]). However, the studies focused only on pregnant women, limiting comparability of actual prevalence between pregnant and non-pregnant women. In South Korea, National Health Insurance Service (NHIS) is a single healthcare insurer, enabling accurate nationwide estimation of disease prevalence.

This study was designed to investigate whether the prevalence and clinical outcome of COVID-19 infection in pregnant women differed from those in non-pregnant women. We compared the following outcomes between pregnant and non-pregnant (1) the prevalence of COVID-19 infection in the entire population of South Korea and women aged 20–44, and (2) the prevalence of severe or fatal COVID-19. In addition, we analyzed the hospitalization rate to determine the healthcare utilization patterns of COVID-19 infected pregnant women.

Material and methods

Data sources and study design

This is nationwide cross-sectional study using claims data provided by the Health Insurance Review and Assessment Service (HIRA). Under the universal health coverage, HIRA database contains medical use, diagnosis and treatment history for COVID-19 patients and pregnant women. Two cohorts were constructed. Cohort 1 was designed to compare prevalence of COVID-19 infection and occurrence of severe COVID-19 illness in pregnant women to the risks in non-pregnant women among COVID-19 patients. Cohort 2 was constructed to compare risks of obstetric complication in pregnant women with COVID-19 to the risks in pregnant women without COVID-19.

Study population

COVID-19 patients and pregnant women were defined based on the International Classification of Disease-10th Revision and Fee-for-service billing codes in South Korea (Appendix Table). For cohort 1, COVID-19 patients were defined as those who were diagnosed with and treated for COVID-10 (U07.1) from January 2020 to February 2021 (Fig. 1). The total number of COVID-19 patients was 75,805, and we divided female COVID-19 patients (n = 39,874) into pregnant women group (n = 78) and non-pregnant women group (all ages: n = 39,796 and 20–44 age: n = 11,463). For cohort 2, we selected pregnant women whose pregnancy was terminated by delivery between January 2020 and February 2021 (n = 313,716). Pregnant women with COVID-19 were defined as those which were infected COVID-19 during pregnancy. There were 73 pregnant women with COVID-19 and 313,643 pregnant women without COVID-19.

Data collection

Sex, age insurance type, region, underlying disease, sites for treatment, length of stay, severity of COVID-19 infection were extracted from the claim data for cohort 1. Insurances were divided into National Health Insurance (NHI) beneficiaries and Medical aid (MA) recipients. Regions were classified into the Seoul metropolitan area, Daegu and Gyeongsangbuk province, and other areas, according to the COVID-19 epidemic areas in South Korea. Underlying diseases includes hypertension, congestive heart failure, cerebrovascular disease, liver disease, renal

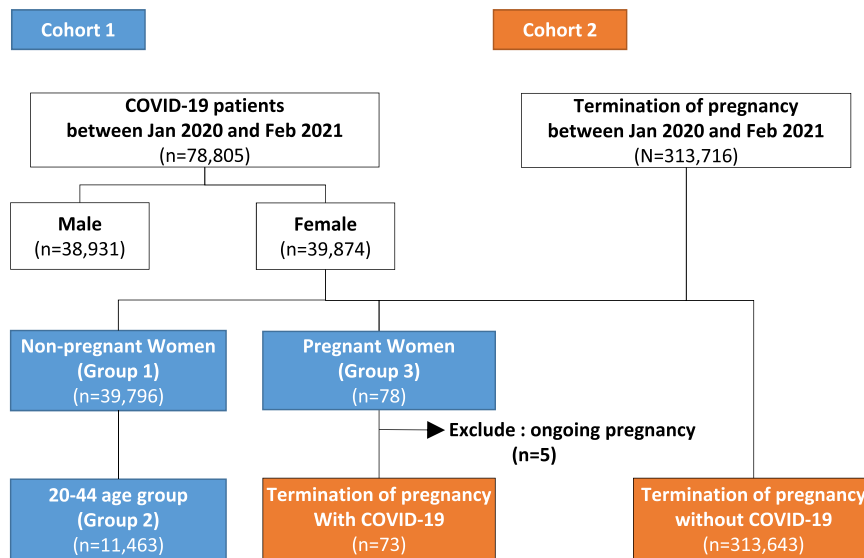


Fig. 1. Study cohort flow chart, COVID-19, coronavirus disease 2019.

disease, chronic pulmonary disease, defined by ICD-10 codes (Appendix Table). Sites for treatment were classified into in-hospital admission and community treatment center where asymptomatic or mild COVID-19 patients were monitored. Length of stay was calculated by difference between the start date and the end date of the treatment related to COVID-19 infection. Severity of COVID-19 infection was classified into ambulatory state (scale 1), hospitalized mild disease (scale 3–4), hospitalized severe disease (scale 5–7) and dead (scale 8) using the WHO's ordinal scale [12]. We defined patients in ambulatory state as those who were treated in community treatment centers. Among WHO ordinal scale, limitation of activities (scale 2) were not able to be determined. For cohort 2, maternal obstetric complication included preeclampsia, eclampsia, gestational hypertension, gestational diabetes mellitus, placenta previa, abruptio placentae, obstructed labor, preterm delivery, acute pyelonephritis, perineal laceration, obstetric hemorrhage, and fetal stress, defined by ICD-10 codes (Appendix Table).

Statistical analysis

Frequency analyses were conducted to identify baseline characteristics, severity of COVID-19 infection, and maternal obstetric complication. The prevalence was calculated by dividing the number of COVID-19 patients by whole number of NHI beneficiaries including medical aid recipients. Chi-square tests, Fisher's exact tests and t-tests were performed to assess the difference between pregnant women with COVID-19 and other groups. All statistical tests were two sided and a $p < 0.05$ value was considered a statistically significant value. SAS Enterprise guide 7.1 was used for all analyses.

Results

Characteristics of pregnant / non-pregnant women with COVID-19

During the study period, there were 39,874 female with COVID-19 (all ages: $n = 39,796$ and 20–44 age: $n = 11,463$) and 78 pregnant women with COVID-19. All pregnant women with COVID-19 were at the age of 20–44. Compared to non-pregnant women at 20–44 age

and the general population, pregnant women with COVID-19 were less likely to be MA recipients and have underlying diseases, and more likely to live in Daegu and Gyeongsangbuk province. There was no significant difference in baseline characteristics between pregnant women and non-pregnant women at 20–44 age (Table 1).

Prevalence of COVID-19 infection in pregnant / non-pregnant women

Among a total of 52,870,968 people in South Korea, 75,805 (0.14%) were diagnosed as COVID-19 between January 2020 and February 2021. The prevalence of COVID-19 infection was lower in pregnant women (0.02%) than non-pregnant women at all ages (0.15%) and non-pregnant women aged 20–44 (0.14%) ($p < 0.001$). (Fig. 2).

Severity of COVID-19 in pregnant / non-pregnant women

The majority of pregnant women with COVID-19 (96.2%) were admitted to hospital. On the other hand, 42.3% of non-pregnant women with COVID-19 at 20–44 age were admitted to hospital. Mean length of stay in pregnant women with COVID-19 was shorter (11.7 days \pm 6.4 days) than non-pregnant women of all-ages (mean 14.6 days \pm 9.9 days) and non-pregnant women aged 20–44 with COVID-19 (13.6 days \pm 9.2 days) ($p < 0.001$).

Among COVID-19 infected women, scale 3 (No oxygen therapy, 89.7% vs. 40.5%, $p < 0.001$) and scale 4 (Oxygen by mask or nasal prongs, 6.4% vs. 1.6%, $p < 0.05$) were significantly higher in pregnant women than non-pregnant women aged 20–44 (Table 2). There were no deaths or hospitalized severe disease (scale 5–8) in pregnant women with COVID-19, whereas 0.04% of non-pregnant women at 20–44 age died and 0.1% of them had severe COVID-19 illness.

Obstetrical complications

Then we compared maternal obstetric complication in cohort 2. Compared with pregnant women without COVID-19, the pregnant women with COVID-19 were more likely to be undergo cesarean

Table 1
Baseline characteristics of study participants.

	General population (n = 52,870,968)		COVID-19 patients (n = 75,805)		Female COVID-19 patients (n = 39,874)				p-value ^a (2 vs 3)	p-value ^a (1 vs 3)	
					Non-pregnant		Pregnant women (Group 3) (n = 78)				
	n	%	n	%	All ages (Group 1) (n = 39,796)	20–44 age (Group 2) (n = 11,463)	n	%			
Age											
0–19	8822,808	16.7	7768	10.3	3463	8.7	< 0.001
20–44	18,223,124	34.5	23,726	31.3	11,463	28.8	11,463	100	78	100	
45–64	17,344,828	32.8	27,583	36.4	15,350	38.6	
65–74	4,907,575	9.3	9,495	12.5	4,968	12.5	
≥ 75	3,572,633	6.8	7,233	9.5	4,552	11.4	
Type of insurance											
Health insurance	51,344,938	97.1	71,968	94.9	37,872	95.2	11,250	98.1	77	98.7	1.00
Medical aid	1,526,030	2.9	3,837	5.1	1,924	4.8	213	1.9	1	1.3	0.47
Region											
Seoul Metropolitan area	26,724,640	50.5	48,149	63.5	24,756	62.2	7,234	63.1	44	56.4	0.46
Daegu and Gyeongsangbuk province	5,111,575	9.7	10,892	14.4	6,294	15.8	2,019	17.6	16	20.5	
Other areas	21,034,753	39.8	16,764	22.1	8,746	22.0	2,210	19.3	18	23.1	
Underlying diseases											
Hypertension	8,827,026	16.7	14,703	19.4	7,560	19.0	188	1.6	0.64
Congestive heart failure	601,805	1.1	1,103	1.5	619	1.6	12	0.1	1.00
Cerebrovascular disease	1,552,554	2.9	3,147	4.2	1,682	4.2	46	0.4	1.00
Liver disease	2,875,594	5.4	4,853	6.4	2,382	6.0	373	3.3	4	5.1	0.33
Renal disease	406,357	0.8	757	1.0	286	0.7	16	0.1	1.00
Chronic Pulmonary disease	4,409,873	8.3	8,796	11.6	4,927	12.4	1,136	9.9	4	5.1	0.16

COVID-19, coronavirus disease 2019

^a Chi-square tests and Fisher's exact tests were performed to assess the difference in proportion among female COVID-19 patients

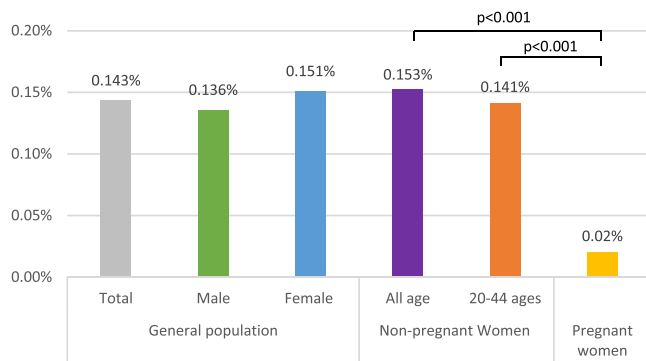


Fig. 2. Prevalence of COVID-19.

section (78.1% vs 54.7%, $p < 0.001$). Majority of pregnant women delivered live birth in both groups, and the prevalence of obstetrical complications, such as preeclampsia, eclampsia, gestational hypertension, gestational diabetes mellitus, placenta previa, abruptio palcentae, obstructed labor, preterm delivery, acute pyelonephritis, perineal laceration, and fetal distress showed no statistically significant difference between two groups, except lower risk of obstetric hemorrhage in pregnant women with COVID-19 (Table 3).

Discussion

The results of this study, which analyzed the prevalence of COVID-19 in pregnant women and clinical outcome through the HIRA database in South Korea, showed that 1) The prevalence of COVID-19 infection was lower in pregnant women than non-pregnant women; 2) Among COVID-19 infected women at age 20–44, pregnant women was at higher risk of oxygen therapy after hospitalization. However, there were no cases of hospitalized severe disease or death in pregnant women with COVID-19.

Table 2

Severity of COVID-19 infection in pregnant / non-pregnant women.

	COVID-19 patients (n = 75,805)		Female COVID-19 patients (n = 39,874)							
			Non-pregnant				Pregnant women (Group 3) (n = 78)		p-value ^a (2 vs 3)	p-value ^a (1 vs 3)
	n	%	All ages (Group 1) (n = 39,796)		20–44 age (Group 2) (n = 11,463)		n	%		
Sites for treatment^b										
In-hospital admission	44,837	59.2	23,843	59.9	4844	42.3	75	96.2	< 0.001	< 0.001
Community treatment center	36,370	48.0	18,643	46.9	7442	64.9	4	5.1	< 0.001	< 0.001
Length of stay	14.3	9.7	14.6	9.9	13.6	9.2	11.7	6.4	< 0.001	< 0.001
Severity(WHO ordinal scale)^c										
Ambulatory state										
1: Non hospitalized	30,960	40.8	15,949	40.1	6617	57.7	3	3.9	< 0.001	< 0.001
Hospitalized mild disease										
3: No oxygen therapy	34,231	45.2	18,635	46.8	4644	40.5	70	89.7	< 0.001	< 0.001
4: Oxygen by mask or nasal prongs	7334	9.7	3705	9.3	181	1.6	5	6.4	< 0.05	0.56
Hospitalized severe disease										
5: Non-invasive ventilation or high-flow oxygen	1148	1.5	441	1.1	15	0.1	1.00	1.00
6: Intubation and mechanical Ventilation	340	0.5	140	0.4	1	0.01	1.00	1.00
7: Ventilation+additional organ support (CRRT, ECMO)	78	0.1	31	0.1	1.00
Dead										
8: Death	1714	2.3	895	2.3	5	0.04	1.00	0.43

COVID-19, coronavirus disease 2019

CRRT, Continuous Renal Replacement Therapy, ECMO: Extracorporeal membrane oxygenation

^a Chi-square tests and Fisher's exact tests and t-test were performed.

^b COVID-19 patients might have been treated both in hospitals and community treatment centers or in either of the sites.

^c Scale was assigned to a patient according to the most severe condition during a treatment period.

Previous studies reported relatively higher prevalence of COVID-19 infection among pregnant women all over the world, ranging 1.3%–30.74% [10,11]. In one study from the United States, tests of all pregnant women who admitted to two New-York based delivery hospitals confirmed 15.6% of COVID-19 infection, including 1.9% of symptomatic pregnant women and 13.7% of asymptomatic COVID-19 infection [13]. This prevalence was supposed to be much higher than the prevalence in general population, which was 0.16% in New York City [14], although these results are derived from different center and different periods. In another study from a large delivery hospital in United Kingdom also reported higher prevalence of COVID-19 infection (one out of 10 pregnant women) [15] and other reported the range of 1.3%–30.74% [10,11] of COVID-19 infection among pregnant women in various countries.

The result from previous studies is different from the result of the current study, as we showed relatively lower incidence of COVID-19 in pregnant women (0.02%). The higher prevalence in pregnant women from previous studies might be partially because of higher chance of nosocomial infection during frequent antenatal visits. The nosocomial infection of COVID-19 was reported in range of 3.7%–44% [16,17] among COVID-19 patients depending on the hospital reported. In spite of social distancing policies, pregnant women are tended to be exposed to people in hospital and might increase the risk of transmission as they regularly visit hospitals for antenatal care including fetal surveillance. However, the nosocomial infection risk is thought to be lower in South Korea than in other countries. The recent two-week nosocomial infection announced by South Korea Centers for Disease Control and Prevention(KCDC) was relatively low at about 1% (as of September 3, 2021) [18] among newly diagnosed COVID-19 infection.

It was reported that clinical outcome and disease severity of COVID-19 infected pregnant women were not significantly different from those of non-pregnant women in early study [19]. However, recent studies reported that pregnant women were at higher risk of severe COVID-19 illness than non-pregnant women, such as maternal death, intubation, and intensive care unit admissions

Table 3
Pregnancy outcome / obstetrical complications of pregnant women with / without COVID-19.

	Pregnant women with COVID-19 (n = 73)		Pregnant women without COVID-19 (n = 313,643)		p-value ^a
	n	%	n	%	
Result of childbirth					1.00
Live birth	73	100	312,888	99.8	
Stillbirth	0	0	755	0.2	
Type of delivery					< 0.001
Cesarean section	57	78.1	171,470	54.7	
Vaginal delivery	16	21.9	142,173	45.3	
Obstetrical complications					
Preeclampsia	1	1.4	5677	1.8	1.0
Eclampsia	0	..	162	0.1	1.0
Gestational hypertension	4	5.5	10,100	3.2	0.27
Gestational diabetes mellitus	13	17.8	57,643	18.4	1.0
Placenta previa	5	6.9	9721	3.1	0.08
Abruptio placentae	0	..	1505	0.5	1.0
Obstructed labor	6	8.2	35,380	11.3	0.41
Preterm delivery	4	5.5	7252	2.3	0.09
Acute pyelonephritis	17	23.3	78,734	25.1	0.72
Perineal laceration	1	1.4	12,397	4.0	0.37
Obstetric hemorrhage	4	5.5	47,051	15.0	0.02
Fetal stress	3	4.1	16,430	5.2	1.0

COVID-19, coronavirus disease 2019

^a Chi-square tests and Fisher's exact tests were performed

[9,20,21]. According to the results of our study, the severity of COVID-19 was higher in pregnant women like previous studies. However, there were no cases of death or hospitalized severe diseases in pregnant women with COVID-19, probably because of small number of cases of COVID-19 in pregnant women. Lower prevalence of COVID-19 infection and low proportion of death or hospitalized severe diseases of COVID-19 illness among pregnant women in South Korea might be explained by effective response to COVID-19 and strong preemptive strategy for pregnant women. From the early stage of outbreak, South Korea has employed a 3 T (Testing-Tracking-Treatment) strategy to prevent and combat the spread of COVID-19. Early detection of COVID-19 through massive diagnostic testing, contact tracing and treatment of confirmed cases were effective response package [22,23]. As a result, South Korea avoided a large COVID-19 outbreak and prevented collapse of health care system.

Furthermore, South Korea adopted more protective approach for high risk groups including pregnant women, the elderly and vulnerable people than for other population. All of COVID-19 patients are treated in community treatment centers or hospitals according to the patient's condition. Asymptomatic or mild COVID-19 patients were assigned to community treatment centers, and moderate or severe patients were treated in hospitals. The recommended treatments for COVID-19 infected pregnant women is not much different from those for general population [24,25]. After confirmation of COVID-19 infection, assessment about pregnancy trimester [26], maternal condition, symptoms and severity of the disease is needed. Based on the assessment, physicians can decide treatments and medications such as oxygen supply therapy, steroids, tocilizumab, and remdesivir [25]. The low molecular weight heparin (LMWH) for venous thromboembolism (VTE) prevention of pregnant women may be the difference. Despite the similar recommended treatments, hospitalization was the first option to be considered for pregnant women with COVID-19 regardless of severity of infection according to government's guideline [23,27]. The current study also showed that 96.2% of pregnant women with COVID-19 were monitored and treated more intensively and cautiously in the hospitals. The

effective response to COVID-19 and the powerful preemptive strategy for pregnant women with COVID-19 contributed to lower risk of COVID-19 infection and better clinical outcomes in pregnant women with COVID-19 in South Korea.

Previous studies showed that the COVID-19 infected pregnant women had higher risk of obstetrical complications such as cesarean section rate, preterm birth, and NICU admission rate [21,28]. This findings suggested that the obstetrical outcome could be affected by the severity of COVID-19 infection [29]. In the current study, rate of cesarean section of pregnant women with COVID-19 was higher than pregnant women without COVID-19 infection. Several studies showed high cesarean section rate in pregnant women with COVID-19 (93% in China [19], 90.2% in Italy [30]). Although there is no evidence about cesarean section in COVID-19 infected pregnant women can result in better obstetric outcomes such as vertical transmission than vaginal delivery [31], the reason for higher cesarean section rate in pregnant women with COVID-19 is thought to be due to anxiety or fear about new infectious diseases [30,32]. In other obstetrical complications had no significant difference, which is not consistent with findings of other studies [21]. However, pregnant women with COVID-19 showed less obstetrical hemorrhage than pregnant women without COVID-19. Several studies reported changes of coagulation state and elevated risk of thromboembolic events in pregnant women with COVID-19 [33,34]. This might be the reason for less obstetrical hemorrhage in pregnant women with COVID-19 in spite of higher rates of cesarean section, which is known to have higher blood loss than vaginal delivery.

There was no clear evidence regarding effects of vaccination during pregnancy in early study [35]. However, recent studies reported that the effectiveness of COVID-19 vaccination for pregnant women was similar to that of general population, and the risk of COVID-19 infection was significantly lower in pregnant women who were vaccinated when compared with those not vaccinated [36,37]. A mass vaccination program was launched in late February 2021 in South Korea. Vaccination for residents aged 49 and under started in August 2021, and vaccination for pregnant women was started in October 2021. Therefore, effect of vaccination was limited in our study which analyzed the data up to February 2021. Further research would be necessary to study effects of vaccination on pregnant women herself and fetus.

The current study had strength and limitation. The major strength of this study is analyzing the nationally representative data. The HIRA database used in this study contains information on all claims including any diagnosis, treatments and procedures for approximately 52 million Koreans. Analyzing nationwide database enabled accurate estimation and direct comparison of prevalence of COVID-19 infection in women according to pregnancy status. Limitation of this study is lack of clinical information in the claim data. To address this issue, WHO's ordinal scale for clinical improvement, which categorized patient states based on the treatments, was used to analyze the severity of COVID-19 infection. Also, we used fee-for-service billing codes in South Korea to identify the actual treatments given to patients.

Conclusions

In conclusion, the prevalence of COVID-19 infection among pregnant women in South Korea was lower than that of non-pregnant women. There were no COVID-19 related deaths or hospitalized severe disease in pregnant women with COVID-19. They also had a higher rate of cesarean section than pregnant women without COVID-19, but they did not show higher prevalence of obstetric complication. It has implications that even though pregnant women with COVID-19 are considered as vulnerable population, the risk of pregnant women itself can be reduced by public health policy such as effective response to COVID-19 and a powerful preemptive strategy for pregnant women.

Contributors

Jin Yong Lee and Seung Mi Lee conceptualized the study. The study and the methodology were conceived by all authors. Yeonmi Choi and Dokyoung Lee led the data analysis and So Hee Kim, Hyejin Lee, Ji Hoi Kim, Eun Saem Choi, Young Mi Jung, Ji Yoon Lee, Youngme Do, Jinwoo Lee, Pyoeng Gyun Choe, Chan-Wook Park, Joong Shin Park, Jong Kwan Jun, Seung Mi Lee, and Jin Yong Lee interpreted data. All authors conducted the formal analysis. Yeonmi Choi, Dokyoung Lee, So Hee Kim, Hyejin Lee, Seung Mi Lee validated the results. All authors collaborated on writing the paper. Seung Mi Lee, So Hee Kim, Yeonmi Choi and Dokyoung Lee discussed and commented on draft versions; Seung Mi Lee, Jin Yong Lee, Hyejin Lee, Ji Hoi Kim, Eun Saem Choi, Young Mi Jung, Ji Yoon Lee, Youngme Do, Jinwoo Lee, Pyoeng Gyun Choe, Chan-Wook Park, Joong Shin Park, and Jong Kwan Jun provided intellectual contributions and critically revised the manuscript. All authors approved the final version.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical statement

This study was approved by Institutional review board of the Health Insurance Review and Assessment Service (2021-099-001).

Declaration of interests

The authors declare that there are no conflicts of interests.

Data Availability

All data used in this study are publicly available after obtaining permission for use from the Health Insurance Review and Assessment Service (HIRA). The corresponding author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported. No important aspects of the study have been omitted, and all discrepancies from the study as planned have been explained.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.jiph.2022.01.004](https://doi.org/10.1016/j.jiph.2022.01.004).

References

- [1] WHO Coronavirus (COVID-19) Dashboard. (<https://covid19.who.int/>); [Accessed 12 September 2021].
- [2] Who collaborating centre. Prevalence of COVID-19 in pregnant and postnatal women. (<https://www.birmingham.ac.uk/research/who-collaborating-centre/pregcov/about/prevalence.aspx>); [Accessed 12 September 2021].
- [3] Liu H, Wang LL, Zhao SJ, Kwak-Kim J, Mor G, Liao AH. Why are pregnant women susceptible to COVID-19? an immunological viewpoint. *J Reprod Immunol* 2020;139:103122. <https://doi.org/10.1016/j.jri.2020.103122>
- [4] Laibl V, Sheffield J. The management of respiratory infections during pregnancy. *Immunol Allergy Clin North Am* 2006;26(viii):155–72. <https://doi.org/10.1016/j.ia.2005.11.003>
- [5] Chen M, Zeng J, Liu X, Sun G, Gao Y, Liao J, et al. Changes in physiology and immune system during pregnancy and coronavirus infection: a review. *Eur J Obstet Gynecol Reprod Biol* 2020;255:124–8. <https://doi.org/10.1016/j.ejogrb.2020.10.035>
- [6] Jensen D, Wolfe LA, Slatkowska L, Webb KA, Davies GA, O'Donnell DE. Effects of human pregnancy on the ventilatory chemoreflex response to carbon dioxide. *Am J Physiol Regul Integr Comp Physiol* 2005;288:R1369–75. <https://doi.org/10.1152/ajpregu.00862.2004>
- [7] Liu F, Liu H, Hou L, Li J, Zheng H, Chi R, et al. Clinico-radiological features and outcomes in pregnant women with COVID-19 pneumonia compared with age-matched non-pregnant women. *Infect Drug Resist* 2020;13:2845–54. <https://doi.org/10.2147/IDR.S264541>
- [8] Lokken EM, Taylor GG, Huebner EM, Vanderhoeven J, Hendrickson S, Coler B, et al. Higher severe acute respiratory syndrome coronavirus 2 infection rate in pregnant patients. *Am J Obstet Gynecol* 2021;225(75):e1–16. <https://doi.org/10.1016/j.ajog.2021.02.011>
- [9] Zambrano LD, Ellington S, Strid P, Galang RR, Oduyabo T, Tong VT, et al. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22–October 3, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1641–7. <https://doi.org/10.15585/mmwr.mm6944e3>
- [10] Ko JY, DeSisto CL, Simeone RM, Ellington S, Galang RR, Oduyabo T, et al. Adverse pregnancy outcomes, maternal complications, and severe illness among US delivery hospitalizations with and without a coronavirus disease 2019 (COVID-19) diagnosis. *Clin Infect Dis* 2021;73:S24–31. <https://doi.org/10.1093/cid/ciab344>
- [11] Hernández-Cruz RG, Sánchez-Cobo D, Acevedo-Gallegos S, Helguera-Repetto AC, Rodríguez-Bosch MR, Ramírez-Santes VH, et al. Clinical characteristics and risk factors for SARS-CoV-2 infection in pregnant women attending a third level reference center in Mexico City. *J Matern Fetal Neonatal Med* 2021:1–5. <https://doi.org/10.1080/14767058.2021.1902500>
- [12] WHO R&D blueprint novel coronavirus COVID-19 therapeutic trial synopsis. World Health Organization Geneva: World Health Organization 2020.
- [13] Sutton D, Fuchs K, D'Alton M, Goffman D. Universal screening for SARS-CoV-2 in women admitted for delivery. *New Engl J Med* 2020;382:2163–4. <https://doi.org/10.1056/NEJMc2009316>
- [14] NYC Department of Health and Mental Hygiene. Coronavirus Disease 2019 (COVID-19) Daily Data Summary. (<https://www1.nyc.gov/>); [Accessed 12 June 2020].
- [15] Cosma S, Borella F, Carosso A, Sciarone A, Casato J, Corcione S, et al. The "scar" of a pandemic: Cumulative incidence of COVID-19 during the first trimester of pregnancy. *J Med Virol* 2021;93:537–40. <https://doi.org/10.1002/jmv.26267>
- [16] Zhou Q, Gao YL, Wang XM, Liu R, Du PP, Wang XQ, et al. Nosocomial infections among patients with COVID-19, SARS and MERS: a rapid review and meta-analysis. *Ann Transl Med* 2020;8. ARTN62910.21037/atm-20-3324.
- [17] Jabarpour M, Dehghan M, Afsharipour G, Hajjipour Abaee E, Mangolian Shahrbabaki P, Ahmadijad M, et al. The Impact of COVID-19 outbreak on nosocomial infection rate: a case of Iran. *Can J Infect Dis Med Microbiol* 2021;2021:6650920. <https://doi.org/10.1155/2021/6650920>
- [18] Central disease Control headquarters. Cases in Korea. (http://ncov.mohw.go.kr/en/bdBoardList.do?brdId=16&brdGubun=161&dataGubun=&ncvContSeq=&contSeq=&board_id=); [accessed 10 September 2021].
- [19] Chen L, Li Q, Zheng D, Jiang H, Wei Y, Zou L, et al. Clinical characteristics of pregnant women with covid-19 in Wuhan, China. *New Engl J Med* 2020;382:100. <https://doi.org/10.1056/NEJMc2009226>
- [20] Martinez-Portilla RJ, Sotiriadis A, Chatzakis C, Torres-Torres J, Espino Y Sosa S, Sandoval-Mandujano K, et al. Pregnant women with SARS-CoV-2 infection are at higher risk of death and pneumonia: propensity score matched analysis of a nationwide prospective cohort (COV19Mx). *Ultrasound Obstet Gynecol* 2021;57:224–31. <https://doi.org/10.1002/uog.23575>
- [21] Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* 2020;370:3320. <https://doi.org/10.1136/bmj.m3320>
- [22] Na BJ, Park Y, Huh IS, Kang CR, Lee J, Lee JY. Seventy-two Hours. Targeting time from first COVID-19 symptom onset to hospitalization. *J Korean Med Sci* 2020;35:192. <https://doi.org/10.3346/jkms.2020.35.e192>
- [23] Lee H, Lee JR, Jung H, Lee JY. Power of universal health coverage in the era of COVID-19: a nationwide observational study. *Lancet Reg Health West Pac* 2021;7:100088. <https://doi.org/10.1016/j.lanwpc.2020.100088>
- [24] Bhimraj A, Morgan RL, Shumaker AH, Lavergne V, Baden L, Cheng VC, et al. Infectious diseases society of America guidelines on the treatment and management of patients with COVID-19. *Clin Infect Dis* 2020. <https://doi.org/10.1093/cid/ciaa478>
- [25] Coronavirus (COVID-19) infection and pregnancy. London; Royal College of Obstetricians & Gynaecologists. 2021.
- [26] Sahin D, Tanacan A, Erol SA, Yucler Yetiskin FD, Besimoglu B, Ozden Tokalioglu E, et al. Management of pregnant women with COVID-19: a tertiary pandemic center experience on 1416 cases. *J Med Virol* 2021:1–11. <https://doi.org/10.1002/jmv.27423>
- [27] Guidelines for operation of COVID-19 Residential Treatment Center. Sejong: Ministry of Health and Welfare; 2021.
- [28] Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. *CMAJ* 2021;193:E540–8. <https://doi.org/10.1503/cmaj.202604>
- [29] Vouga M, Favre G, Martinez-Perez O, Pomar L, Acebal LF, Abascal-Saiz A, et al. Maternal outcomes and risk factors for COVID-19 severity among pregnant women. *Sci Rep* 2021;11:13898. ARTN1389810.1038/s41598-021-92357-y.
- [30] Della Gatta AN, Rizzo R, Pilu G, Simonazzi G. Coronavirus disease 2019 during pregnancy: a systematic review of reported cases. *Am J Obstet Gynecol* 2020;223:36–41. <https://doi.org/10.1016/j.ajog.2020.04.013>
- [31] Cai J, Tang M, Gao Y, Zhang H, Yang Y, Zhang D, et al. Cesarean section or vaginal delivery to prevent possible vertical transmission from a pregnant mother confirmed with COVID-19 to a neonate: a systematic review. *Front Med* 2021;8:634949. <https://doi.org/10.3389/fmed.2021.634949>
- [32] Zhang J, Zhang Y, Ma Y, Ke Y, Huo S, He L, et al. The associated factors of cesarean section during COVID-19 pandemic: a cross-sectional study in nine cities of China. *Environ Health Prev Med* 2020;25:60. <https://doi.org/10.1186/s12199-020-00899-w>

- [33] Kadir RA, Kobayashi T, Iba T, Erez O, Thachil J, Kazi S, et al. COVID-19 coagulopathy in pregnancy: critical review, preliminary recommendations, and ISTH registry-Communication from the ISTH SSC for Women's Health. *J Thromb Haemost* 2020;18:3086–98. <https://doi.org/10.1111/jth.15072>
- [34] Barnes GD, Burnett A, Allen A, Blumenstein M, Clark NP, Cuker A, et al. Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum. *J Thromb Thrombolysis* 2020;50:72–81. <https://doi.org/10.1007/s11239-020-02138-z>
- [35] Rasmussen SA, Jamieson DJ. Pregnancy, postpartum care, and COVID-19 Vaccination in 2021. *JAMA* 2021;325:1099–100. <https://doi.org/10.1001/jama.2021.1683>
- [36] Inbal Goldshtein DN, David MSteinberg, Rotem Ran S, Gorfine Malka, Chodick Gabriel, Segal. Yaakov. Association between BNT162b2 vaccination and incidence of SARS-CoV-2 infection in pregnant women. *JAMA* 2021;326:728–35. <https://doi.org/10.1001/jama.2021.11035>
- [37] Dagan N, Barda N, Biron-Shental T, Makov-Assif M, Key C, Kohane IS, et al. Effectiveness of the BNT162b2 mRNA COVID-19 vaccine in pregnancy. *1693-5 Nat Med* 2021;27:1693–5. <https://doi.org/10.1038/s41591-021-01490-8>