



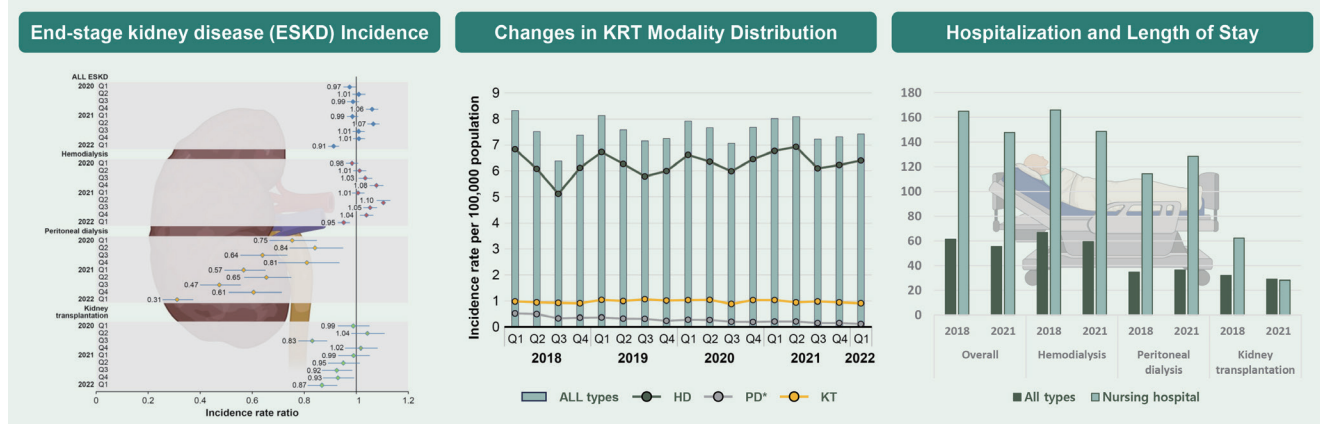
Kidney replacement therapy trends in end-stage kidney disease patients in South Korea during the COVID-19 pandemic

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Our study aimed to assess changes in kidney replacement therapy (KRT) trends and healthcare access for these patients during the pandemic.



Conclusion

Our findings indicate no significant changes in ESKD incidence in South Korea during the pandemic.

Background/Aims: The corona virus disease 2019 posed a major risk for end-stage kidney disease (ESKD) cases. Our study aimed to assess changes in kidney replacement therapy (KRT) trends and healthcare access for these patients during the pandemic.**Methods:** We retrospectively analyzed nationwide data from July 2017 to June 2022 to assess changes in KRT and ESKD incidence. KRT modalities included peritoneal dialysis (PD), hemodialysis (HD), and kidney transplantation (KT). We utilized the interrupted time series (ITS) method to compare changes in KRT modality before and after the incidence of the COVID-19 pandemic.**Results:** ESKD incidence remained stable from 2018 to April 2022. The ITS analysis confirmed that the pandemic did not significantly impact overall KRT incidence. PD cases decreased (5.7% to 1.3%), while HD cases increased (81.6% to 85%), and

KT recipient remained relatively stable (12.7% to 17.3%). The hospitalization and hospital stay decreased in nursing hospital (165.01 days to 147.77 days) and general hospital (61.34 days to 55.58 days) during the pandemic, however, remained unchanged for PD and KT.

Conclusions: Our findings indicate no significant changes in ESKD incidence in South Korea during the pandemic. However, there were shifts in modality distribution, with decreased PD and increased HD cases. Notably, HD cases showed a significant reduction in hospital admissions and length of stay. The healthcare system demonstrated stability during the pandemic, with minimal disruptions in ESKD care.

Keywords: COVID-19; Dialysis; Kidney transplantation; Hemodialysis; Peritoneal dialysis

INTRODUCTION

The corona virus disease 2019 (COVID-19) was first recognized in December 2019 in Wuhan, China [1]. Owing to the surge in COVID-19 infections worldwide, many hospitals were forced to go into emergency mode, and this has prevented them from treating chronically ill patients and performing various procedures and surgeries in a timely manner. In this context, the significance of kidney replacement therapy (KRT) cannot be overstated. KRT is essential for sustaining life and must be provided at appropriate times. However, the COVID-19 pandemic has necessitated the adoption of changes in the methods and timing of administering KRT to patients.

Individuals with chronic kidney disease, especially those in the advanced stages, such as end-stage kidney disease (ESKD), have weakened immune systems and are at a higher risk of infection, including viral infections like COVID-19 [2]. Notably, patients undergoing KRT, including maintenance dialysis or kidney transplant (KT) cases, are particularly vulnerable to COVID-19 [3-5]. Patients in need of KRT, particularly those undergoing hemodialysis (HD) and attending the dialysis center three times a week, face an elevated risk of contracting COVID-19 owing to their heightened exposure to healthcare facilities. Although several studies have reported on this concern [6], there is a scarcity of domestic research on this issue, necessitating an in-depth exploration.

We aimed to analyze data from the nationwide claims data in Korea to investigate the differences in ESKD incidence and changes in KRT modalities during the COVID-19 pandemic and compare these to the previous period. This study sought to determine whether COVID-19 has affected the incidence, choice of modality, and length of stay (LOS) of patients with ESKD, and whether this varied by hospital

system. The acquisition of comprehensive epidemiological data on this concern would be instrumental in developing response strategies for the management of patients with ESKD in the face of future pandemics or similar infectious disease outbreaks.

METHODS

Study design

This retrospective cohort study used South Korean nationwide data from July 2017 to June 2022 to analyze changes in the incidence of ESKD and the delivery of KRT during the COVID-19 pandemic. Specifically, we investigated whether there were differences in incidence rates during the COVID-19 period compared to the pre-pandemic period in 2019, utilizing the incidence rate ratio (IRR) and interrupted time series (ITS) analysis. This study was approved by the Institutional Review Board of Ajou University (IRB approval number: AJOUIRB-EX-2022-564) and all procedures were performed in accordance with the Declaration of Helsinki.

Data source

This study examined health insurance claims data from the Health Insurance Review and Assessment (HIRA) service, covering the period of July 2017 to June 2022 (dataset: M20230103001). This dataset is national in scope because South Korea operates a universal coverage health insurance system with a 97% enrollment rate. This nationwide, real-world HIRA dataset comprises anonymized basic characteristics of individuals, including age and sex, as well as information on medical treatments and healthcare institutions [7]. To calculate the incidence rate per population, we obtained disease-free population data from Statistics Korea.

The monthly and mid-year population values from the Statistics Korea dataset were used to determine the at-risk population [8].

Study population

The study population included incident patients with ESKD, identified from the International Classification of Diseases, Tenth Revision (ICD-10th) codes as well as procedure codes of insurance claims data. ESKD patients were categorized based on the KRT modality and age groups. Considering the KRT modality, patients were classified as undergoing HD, peritoneal dialysis (PD), or KT recipients. For HD and PD, patients who had at least one outpatient visit with ICD code 'N18' and had KRT procedure codes for 3 months or more were defined as ESKD patients. For KT recipients, those with at least one outpatient visit with an 'N18' code and KT procedure codes were considered ESKD patients. The procedure codes were O7020, O7021, and O9991 for HD; O7076 and O7077 for PD; and R3280 for KT [9].

Patients who underwent dialysis after KT were included in the dialysis group. For patients who received both HD and PD, the analysis was based on the most recent dialysis modality used. In terms of age, participants were grouped into five categories: under 18, 18–44, 45–64, 65–74, and 75 years and above. To confirm that the ESKD cases were new, individuals with no KRT-related claims in the one-year period preceding their first KRT claim were defined as incident cases.

Definition of variables

Since the incidence rates fluctuated from month to month, we computed the quarterly incidence rates, expressing them as both crude rates and age-standardized rates per 100,000 individuals [10]. The incidence rate was calculated by dividing the number of incident ESKD cases in a specific year by the at-risk disease-free population and then multiplying by 100,000. IRRs were calculated to compare the incidence rate in the post-COVID-19 period with that in the corresponding quarter of 2019.

To assess the changes related to hospitalization during the COVID-19 period, we analyzed the annual number of admission and LOS. In this context, the term admission encompasses hospitalizations for all medical conditions, and the number of admissions per patients was calculated by dividing the total annual number of admissions by the number of individuals admitted. LOS was calculated by dividing

the total number of days a person spent in the hospital over the year by the annual number of individuals admitted to that specific type of hospital. If an individual was admitted to both a nursing and a general hospital, we calculated the number of admissions and LOS separately for each type of hospital.

Statistical analyses

Summary statistics were used to delineate the characteristics of patients with newly diagnosed ESKD. ANOVA was used to assess year-to-year changes in continuous variables, and the chi-square test was used for categorical variables. The same statistical analysis approach was applied to both categorical and continuous variables for LOS and number of admissions. Poisson regression models were used to calculate the incidence rate and its corresponding 95% confidence interval (CI), whereas autoregression was conducted to test for significant secular trends in the incidence rate for each KRT modality and age group.

We used ITS linear regression to investigate impact of COVID-19 pandemic on KRT incidence. ITS analysis is a quasi-experimental research methodology, allowing for the assessment of immediate and long-term effect following specific interventions [11]. On ITS, the dependent variable, incidence, was calculated as monthly incidence per 100,000 population. ITS analyses were conducted for different subgroups, considering KRT modality and age groups. Observations were collected from January 2018 to April 2022, comprising 52 monthly incidence data points. Both immediate level changes and trend changes in monthly incidence were observed before and after the intervention. In our analysis, March 1, 2020, was considered as the starting point of the COVID-19 pandemic, which is the intervention. Although the coronavirus initially outbreaks domestically in January 2020, the national crisis alert was raised on February 23, 2020. Considering the lag period, our analysis adjusted for the impact of the Covid-19 pandemic starting from March, 2020. The segmented regression equation for ITS analysis is as follows:

$$y_t = \beta_0 + \beta_1 T + \beta_2 X_t + \beta_3 TX_t + \beta_4 Z.$$

Here, y_t represents the monthly incidence. T is the number of months since the beginning of observation, X_t is a categorical variable with 0 before the intervention and 1 after the intervention. TX_t is an interaction term indicating the number of months after the intervention. β_0 is the mean monthly incidence during the pre-pandemic period (the

regression intercept). β_1 represents the monthly trend change in incidence before the pandemic, and β_2 is the level change in incidence immediately after the COVID-19 outbreak. β_3 denotes the change in monthly incidence trend after the COVID-19 outbreak, and $\beta_1 + \beta_3$ represents the

overall time trend after the COVID-19 pandemic. Z is a vector of dummy variables representing the month of the year.

All statistical analyses were performed using SAS 9.4 software (SAS Institute, Inc., Cary, NC, USA), and *p* values less than 0.05 were considered statistically significant.

Table 1. Characteristics of adult patients with newly diagnosed ESKD

Variable	2018	2019	2020	2021	2022 ^{a)}	<i>p</i> value
Incident case	15,338	15,610	15,718	15,833	5,494	
Age (yr)	63.3 ± 14.4	63.3 ± 15.1	64.0 ± 14.9	64.7 ± 14.8	63.8 ± 15.1	< 0.001
Sex						0.3039
Male	9,273 (60.5)	9,462 (60.6)	9,595 (61.0)	9,686 (61.2)	3,402 (61.9)	
Female	6,065 (39.5)	6,148 (39.4)	6,123 (39.0)	6,147 (38.8)	2,092 (38.1)	
Insurance						0.0171
NHI	13,256 (86.4)	13,473 (86.3)	13,561 (86.3)	13,688 (86.5)	4,823 (87.8)	
MA	2,013 (13.1)	2,035 (13.0)	2,076 (13.2)	2,059 (13.0)	654 (11.9)	
VA	69 (0.4)	102 (0.7)	81 (0.5)	86 (0.5)	17 (0.3)	
DM	10,803 (70.4)	11,165 (71.5)	11,385 (72.4)	11,401 (72.0)	3,799 (69.1)	
Types of KRT						< 0.001
HD	12,509 (81.6)	12,845 (82.3)	13,174 (83.8)	13,454 (85.0)	4,473 (81.4)	
Catheter utilization at initiation of HD	7,961 (63.6)	8,038 (62.6)	8,066 (61.2)	7,886 (58.6)	2,477 (55.4)	
Peritoneal dialysis	881 (5.7)	633 (4.1)	480 (3.1)	362 (2.3)	71 (1.3)	
KT	1,948 (12.7)	2,132 (13.7)	2,064 (13.1)	2,017 (12.7)	950 (17.3)	
Preemptive KT	990 (50.8)	1,010 (47.4)	970 (47.0)	963 (47.7)	424 (44.6)	
CCI score	5.8 ± 2.3	5.6 ± 2.3	5.6 ± 2.3	5.5 ± 2.3	5.4 ± 2.3	< 0.001
Myocardial infarction	1,159 (7.6)	1,120 (7.2)	1,109 (7.1)	1,036 (6.5)	340 (6.2)	< 0.001
Congestive heart failure	5,162 (33.7)	4,837 (31.0)	5,022 (32.0)	5,141 (32.5)	1,733 (31.5)	< 0.001
Peripheral vascular disease	3,132 (20.4)	3,237 (20.7)	3,397 (21.6)	3,567 (22.5)	1,279 (23.3)	< 0.001
Cerebrovascular disease	3,819 (24.9)	3,828 (24.5)	3,951 (25.1)	3,900 (24.6)	1,182 (21.5)	< 0.001
Chronic pulmonary disease	6,940 (45.2)	6,575 (42.1)	6,189 (39.4)	5,084 (32.1)	1,704 (31.0)	< 0.001
Rheumatic disease	680 (4.4)	654 (4.2)	695 (4.4)	705 (4.5)	220 (4.0)	0.494
Peptic ulcer	5,151 (33.6)	4,789 (30.7)	4,772 (30.4)	4,506 (28.5)	1,581 (28.8)	< 0.001
Liver disease	1,404 (9.2)	1,411 (9.0)	1,462 (9.3)	1,570 (9.9)	476 (8.7)	0.022
Diabetes mellitus	9,588 (62.5)	9,467 (60.6)	9,271 (59.0)	9,220 (58.2)	3,148 (57.3)	< 0.001
DM complication	8,056 (52.5)	7,723 (49.5)	7,843 (49.9)	7,769 (49.1)	2,643 (48.1)	< 0.001
Paraplegia	562 (3.7)	445 (2.9)	467 (3.0)	423 (2.7)	104 (1.9)	< 0.001
Kidney disease	14,971 (97.6)	15,051 (96.4)	15,204 (96.7)	15,345 (96.9)	5,372 (97.8)	< 0.001
Cancer	1,832 (11.9)	1,964 (12.6)	1,988 (12.6)	2,169 (13.7)	623 (11.3)	< 0.001
Metastatic tumor	229 (1.5)	193 (1.2)	201 (1.3)	218 (1.4)	69 (1.3)	0.2987
Severe liver disease	325 (2.1)	317 (2.0)	284 (1.8)	297 (1.9)	94 (1.7)	0.1594

Values are presented as number only, mean ± standard deviation, or number (%).

ESKD, end-stage kidney disease; NHI, National Health Insurance; MA, medical aid; VA, veterans; DM, diabetes mellitus; KRT, kidney replacement therapy; HD, hemodialysis; KT, kidney transplantation; CCI, Charlson Comorbidity Index.

^{a)}Data for 2022 only include records up to April.

RESULTS

From 2018 to April 2022, the annual incident cases of ESKD in South Korea remained stable, ranging from 15,338 to 15,833 per year, with no significant differences in the absolute numbers before or after the pandemic. However, there were significant shift in the distribution of KRT modalities among the patients with incident ESKD. The percentage of patients with PD decreased from 5.7% in 2018 to 1.3% by 2022. The proportion of HD patients undergoing HD increased from 81.6% to 85.0%, but the number of patients using catheters at the initiation of HD decreased from 63.6% to 55.4%. The proportion of KT recipients remained relatively stable, ranging from 12.7% to 17.3%. However, the preemptive KT percentage decreased from 50.8% to 44.6% (Table 1).

When examining the characteristics of incident ESKD patients, age, sex, insurance type, or other factors not significantly changed before and after the pandemic. The average age ranged from 63.3 to 64.7 years over the five-year study period, with a male predominance of over 60%. An important observation we made involved the remarkably high proportion of medical aid beneficiaries, ranging from 11.9% to 13.2%. In South Korea, medical aid beneficiaries constitute only 3% of the population [12], making this ratio notably high among patients with ESKD. Approximately 70% of the patients had diabetes, and one in three patients had conditions such as congestive heart failure or peptic ulcers. When assessing comorbid conditions within the year preceding

the ESKD diagnosis, the Charlson Comorbidity Index (CCI) score [13] ranged between 5.4 and 5.8 points (Table 1).

Quarterly incidence rate by KRT modality and age

From the first quarter of 2018 to the first quarter of 2022, the incidence rate of ESKD ranged between 6.38 and 8.33 per 100,000. Annual trends showed higher incidence rates in the first and second quarters than in the third and fourth quarters; however, no secular trends were observed. Regarding KRT modality, HD had the highest quarterly incidence rate, followed by KT and PD. HD showed quarterly incidence rates ranging from 5.12 to 6.93, while KT ranged from 0.88 to 1.06. PD had quarterly incidence rates ranging from 0.11 to 0.52, with a noticeable decreasing secular trend from 2018 to 2022 (Fig. 1A).

When examining the age-standardized quarterly incidence rate by age group, the older age groups exhibited higher incidence rates. The overall age-standardized quarterly incidence rate for the entire population was 7.53 per 100,000 persons. Among those aged 45 and older, a notably higher quarterly incidence rate was observed. The age-standardized quarterly incidence rates for the age groups of 45–64, 65–74, and 75 and older were 8.95, 19.57, and 30.92 per 100,000 persons, respectively. Significantly decreasing secular trends were observed in the 45–64 and 65–74 age groups. The age-standardized quarterly incidence rates for the age groups under 18 and 19–44 were 0.21 and 2.12 per 100,000 persons, respectively (Fig. 1B).

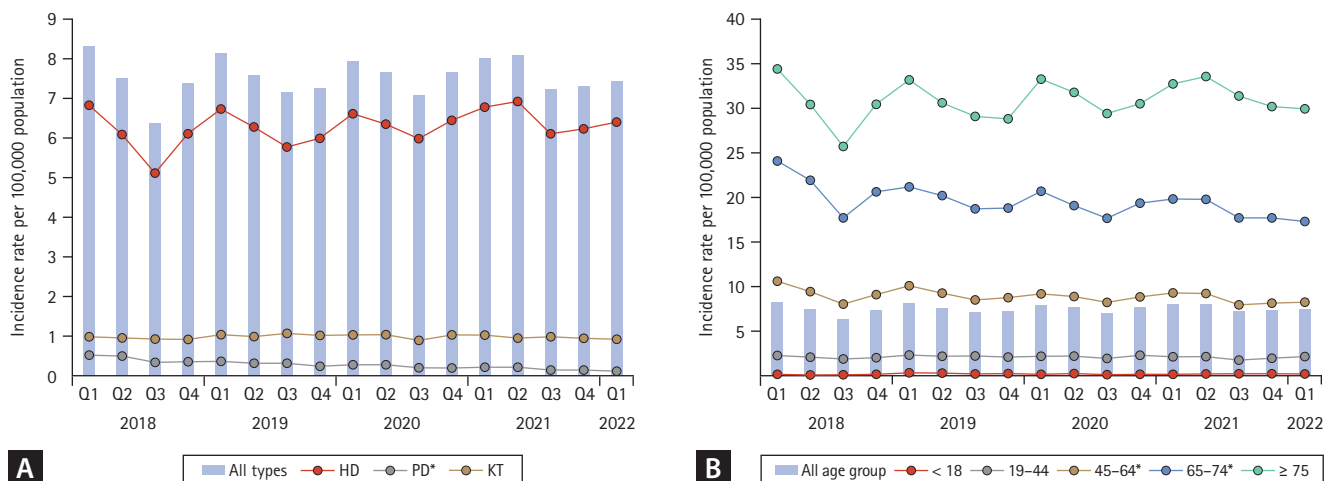


Figure 1. ESKD incident rate by KRT modality and age. (A) Incidence rate of ESKD per 100,000 population by KRT modality. (B) Age-standardized incidence rate per 100,000 population. ESKD, end-stage kidney disease; KRT, kidney replacement therapy; HD, hemodialysis; PD, peritoneal dialysis; KT, kidney transplantation. *Statistically significant trends.

IRR by KRT modality and age

A comparison of the pre- and post-pandemic periods showed that the overall ESKD incidence did not exhibit a noticeable increase or decrease in the IRR. There were no observable quarterly trends and the overall incidence of ESKD remained unchanged. When examined by the KRT modality, PD consistently had an IRR of 1 or less in all quarters com-

pared to 2019, whereas HD mostly had an IRR greater than 1. The incidence of KT had values of one or more in the second and fourth quarters of 2020; however, it showed a decreasing trend over time (Fig. 2A).

In terms of age-specific IRR, most age groups, excluding the 75 years and older age group, showed an IRR of 1 or less in most quarters. The 45–74 age groups consistently

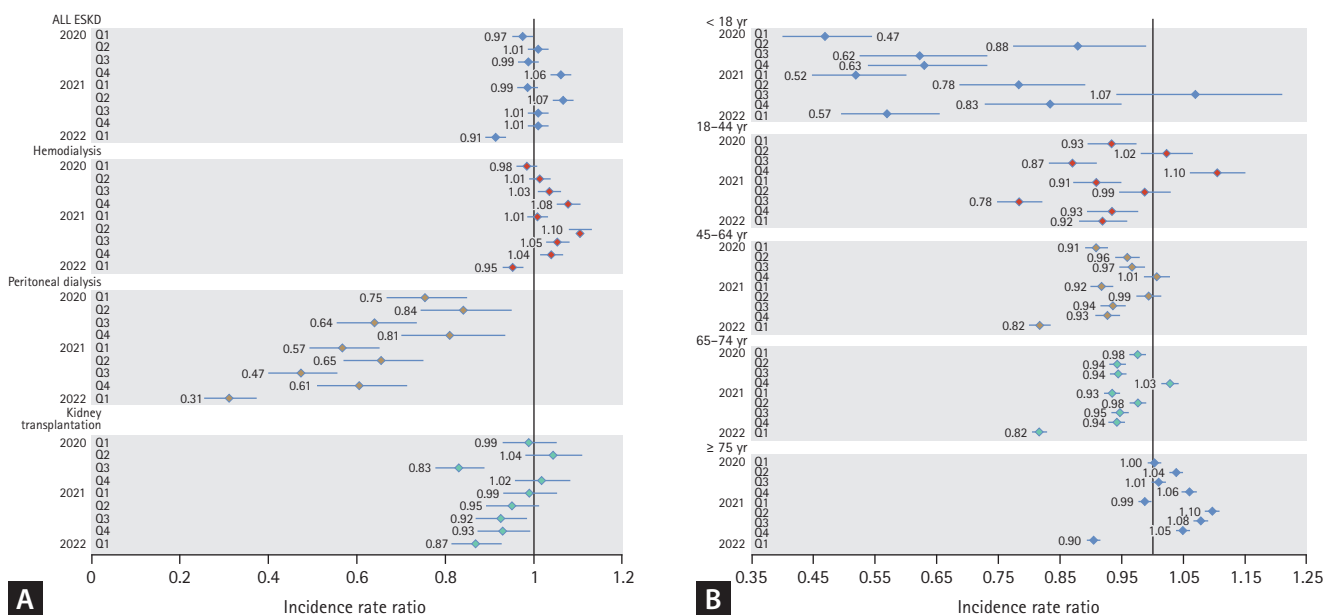


Figure 2. Incident rate ratios by KRT modalities and age group. (A) Incident rate ratios for ESKD and its KRT modalities compared to the corresponding quarter in 2019. (B) Incident rate ratios by age group for ESKD compared to the corresponding quarter in 2019. KRT, kidney replacement therapy; ESKD, end-stage kidney disease.

Table 2. Changes in trends and levels before and after the COVID-19 pandemic: an interrupted time series results

Group	Mean incidence (intercept)	Change in trend before COVID-19 pandemic (95% CI)	Change in level after COVID-19 outbreak (95% CI)	Change in trend after COVID-19 outbreak (95% CI)
All KRT	2.50	-0.001 (-0.004 to 0.003)	0.083 (0.008 to 0.157)	-0.001 (-0.006 to 0.003)
Types of KRT				
HD	2.03	0.001 (-0.002 to 0.004)	0.061 (-0.010 to 0.132)	0.001 (-0.003 to 0.005)
PD	0.17	-0.004 ^a (-0.004 to -0.003)	0.020 (0.010 to 0.030)	0.001 ^a (0.001 to 0.002)
KT	0.31	0.001 (0.000 to 0.002)	0.007 (-0.013 to 0.028)	-0.003 ^a (-0.005 to -0.002)
Age group (yr)				
< 18	0.05	0.002 ^a (0.001 to 0.002)	-0.020 (-0.036 to -0.004)	-0.002 (-0.003 to -0.001)
18–44	0.70	0.001 (-0.001 to 0.003)	0.004 (-0.040 to 0.048)	-0.004 (-0.006 to -0.001)
45–64	3.19	-0.001 ^a (-0.014 to -0.005)	0.063 (-0.039 to 0.165)	0.000 (-0.006 to 0.006)
65–74	7.35	-0.042 ^a (-0.057 to -0.027)	0.265 (-0.057 to 0.058)	0.017 (-0.004 to 0.039)
≥ 75	10.28	-0.012 (-0.028 to 0.004)	0.606 (0.252 to 0.959)	0.005 (-0.015 to 0.026)

CI, confidence interval; KRT, kidney replacement therapy; HD, hemodialysis; PD, peritoneal dialysis; KT, kidney transplantation.

^a)Denotes *p* value < 0.005.

Table 3. Changes in annual number of admissions and LOS among incident ESKD patients during the COVID-19 pandemic

Type of hospital	Overall					Hemodialysis					Peritoneal dialysis					Kidney transplantation					
	2018	2019	2020	2021 ^{e)}	2021 ^{e)}	2018	2019	2020	2021 ^{e)}	2021 ^{e)}	2018	2019	2020	2021 ^{e)}	2021 ^{e)}	2018	2019	2020	2021 ^{e)}	2021 ^{e)}	
All types	15,338	15,610	15,718	9,019	7,884	12,509	12,845	13,174	7,884	772	575	421	204	1,860	2,070	1,967	975				
Admission ^{a,b,c)}	2.67 (2.07)	2.65 (2.11)	2.50 (1.98)	2.52 (2.00)	2.56 (2.04)	2.74 (2.12)	2.70 (2.15)	2.54 (2.02)	2.56 (2.04)	2.43 (1.70)	2.69 (1.86)	2.48 (1.75)	2.67 (1.73)	2.25 (1.74)	2.28 (1.89)	2.24 (1.66)	2.10 (1.62)				
LOS ^{a,b)}	61.34 (83.24)	60.11 (82.55)	57.53 (80.67)	55.58 (78.16)	59.38 (82.31)	66.67 (88.23)	64.93 (87.59)	61.66 (85.19)	59.38 (82.31)	34.78 (50.16)	35.75 (45.33)	33.34 (47.63)	36.52 (52.81)	32.04 (30.50)	33.27 (33.42)	32.15 (31.17)	28.95 (23.46)				
Nursing hospital	2,717	2,831	2,768	1,531	1,510	2,665	2,776	2,727	1,510	40	35	24	16	12	20	17	9				
Admission ^{a,b)}	1.77 (1.13)	1.69 (1.11)	1.60 (1.01)	1.76 (1.19)	1.72 (1.18)	1.77 (1.13)	1.69 (1.10)	1.60 (1.01)	1.72 (1.18)	2.08 (1.61)	1.83 (0.98)	1.42 (0.72)	1.94 (1.65)	1.25 (0.62)	1.25 (0.55)	1.71 (1.57)	2.11 (1.36)				
LOS ^{a,b)}	165.01 (125.8)	160.28 (127.0)	154.95 (126.9)	147.77 (122.4)	148.69 (122.4)	165.98 (125.8)	161.88 (94.4)	156.15 (127.0)	148.69 (122.4)	132.55 (114.3)	94.37 (108.3)	91.46 (105.4)	121.25 (128.5)	58.58 (62.3)	53.55 (52.5)	52.00 (78.7)	41.00 (28.2)				
General hospital	13,986	14,260	14,182	7,488	6,334	11,406	11,670	11,835	6,334	732	540	397	188	1,848	2,050	1,950	966				
Admission ^{a,b,c,d)}	2.84 (2.16)	2.84 (2.21)	2.68 (2.07)	2.68 (2.09)	2.76 (2.15)	2.97 (2.23)	2.94 (2.26)	2.75 (2.14)	2.76 (2.15)	2.45 (1.70)	2.74 (1.89)	2.54 (1.77)	2.73 (1.73)	2.26 (1.74)	2.29 (1.89)	2.24 (1.66)	2.10 (1.62)				
LOS ^{a,b,d)}	41.20 (52.03)	40.22 (50.80)	38.52 (49.21)	36.68 (46.80)	38.09 (49.62)	43.46 (55.27)	41.86 (53.76)	39.89 (51.83)	38.09 (49.62)	29.44 (37.48)	31.96 (34.79)	29.83 (39.30)	29.31 (32.20)	31.87 (30.14)	33.07 (33.14)	31.97 (30.42)	28.83 (23.40)				

Values are presented as mean (standard deviation).

LOS, length of stay; ESKD, end-stage kidney disease; N, number of patients.

^{a)}Denotes statistical significance in the overall ESKD patient population.

^{b)}Denotes the statistical significance of the hemodialysis group of patients with ESKD.

^{c)}Denotes statistical significance in the peritoneal group of patients with ESKD.

^{d)}Denotes the statistical significance of kidney transplantation of ESKD patients with ESKD.

^{e)}Data for 2022 include records up to June.

exhibited values of 1 or less, except for the fourth quarter of 2020. Similarly, the 18–44 age group had IRR values of 1 or less, except for the second and fourth quarters of 2020. The age group under 18 years, owing to its low incidence rate, showed wide CIs, but aside from the fourth quarter of 2021, it consistently exhibited IRR values of 1 or less. In contrast, the age group of 75 years or older that had the highest age-standardized incidence rate compared to other age groups, showed values of 1 or more in most quarters, excluding the first quarter of 2021 and the first quarter of 2022 (Fig. 2B).

ITS to assess impact of the COVID-19 pandemic

Overall, ITS analysis provided confirmed that the COVID-19 outbreak had not statistically significant immediate or long-term effects on the overall incidence of KRT. Specifically, there were no significant month-to-month changes in the incidence of all KRT before (baseline trend: -0.001 ; $p = 0.81$) and after the outbreak (trend change: -0.001 ; $p = 0.77$). Notably, only the incidence of PD showed a significant trend change. It exhibited a decreasing trend pre-COVID (baseline trend: -0.004 ; $p < 0.001$), which lessened post-outbreak (trend change: 0.001 ; $p = 0.04$). The incidence of KT showed a significant decreasing trend after the COVID outbreak (trend change: 0.001 ; $p = 0.02$), while HD incidences remained stable throughout (Table 2).

When analyzed by age groups, the 45–64 group showed a significant decrease in incidence pre-COVID (baseline trend: -0.001 ; $p = 0.04$), with a more pronounced decrease in the 65–74 group (baseline trend: -0.042 ; $p = 0.01$). For those aged 18 and below, there was a significant increase pre-pandemic (baseline trend: 0.002 ; $p = 0.03$). Other age groups did not exhibit significant trend changes, and no age group showed significant month-to-month changes post-COVID. Furthermore, there were no immediate level change effects observed in any KRT modality or age group following the COVID outbreak (Table 2).

Hospitalization and LOS

We examined the annual number of admission and the LOS in patients with ESKD from 2018 to 2021. Although there were no significant differences in the incidence rates of ESKD, there were significant changes in the number of admissions and LOS over time. The annual number of hospitalizations in 2018 and 2019 was 2.67 and 2.65, re-

spectively. In contrast, it decreased slightly to 2.50 in 2020 and 2.52 in 2021. This trend was also observed in general hospitals, where the number of hospitalizations decreased from 2.84 in both 2018 and 2019 to 2.68 in both 2020 and 2021. Nursing hospitals, on the other hand, showed a lower number of admissions compared to general hospitals, but with longer hospital stays. The number of admissions to nursing hospitals decreased from 1.77 in 2018 to 1.60 in 2020, but increased to 1.76 in 2021. The LOS decreased continuously for all patients with ESKD from 2018 to 2021. In nursing hospitals, LOS decreased from 165.01 days in 2018 to 147.77 days in 2021, while in general hospitals, it decreased significantly from 61.34 days in 2018 to 55.58 days in 2021 (Table 3).

In HD patients, there was a significant reduction in the number of admissions and LOS after the COVID-19 pandemic, similar to the trends observed in the overall incidence of ESKD. As patients undergoing HD constitute the majority of the overall ESKD incidence, the parameters such as the number of admissions and LOS in HD cases were similar to those for the overall ESKD cases. Patients undergoing HD had a slightly higher number of admissions, approximately 0.05 admissions more than the overall ESKD cases, and their LOS was approximately 5 days longer. In both nursing and general hospitals, the LOS of patients undergoing HD decreased over time, and the number of admissions showed a similar pattern of increase and decrease, as was observed for ESKD cases overall (Table 3).

In contrast, patients undergoing PD did not show significant trends in annual number of admissions and LOS, and there were no significant differences. Compared to overall patients with ESKD, there was no difference in the number of admissions for PD cases, but the LOS was nearly half as long. While no distinct trends were observed for any hospital type during the COVID-19 period, nursing hospitals showed a sudden increase in both the number of admissions and LOS in 2021. KT recipients had the lowest annual number of admissions and LOS among all modality types, and no significant differences were observed across the years (Table 3).

DISCUSSION

This study aimed to investigate the incidence of ESKD, modalities of KRT, and changes in healthcare access for ESKD patients in South Korea during COVID-19 pandemic.

Initially, our findings revealed that the absolute number of annual incident cases of ESKD in South Korea remained stable from 2018 to April 2022, ranging between 15,338/year to 15,833/year. Even when divided by quarters from 2018 onwards, there was no statistically significant change in the incidence of ESKD. The ITS analysis confirmed that the pandemic had no immediate or long-term impact on the overall KRT incidence. This stability in ESKD incidence may reflect the resilience of the healthcare system in continuing to diagnose and manage ESKD cases despite the challenges posed by the pandemic.

Potential factors that could influence the incidence of ESKD include acute kidney injury (AKI), which frequently occurs in individuals diagnosed with COVID-19, especially among those who are hospitalized, leading to a heightened incidence of AKI overall. Studies have shown an increased risk of developing CKD in COVID-19 patients, with many AKI survivors progressing to CKD within 90 days, and some potentially advancing to ESKD [14]. The occurrence of COVID-19-associated AKI or AKI on CKD during the pandemic might have impacted the incidence of ESKD. A notable decline in incident ESKD cases was observed in the United States early in the pandemic, attributed to increased mortality in patients with advanced CKD and compromised access to KRT preparations [15]. Similarly, the possibility remains that the incidence of ESKD in Korea might have been affected by COVID-19-related premature death in CKD patients.

Contrary to the stability of the ESKD incidence rate, there were notable changes in the distribution of KRT modalities among patients with incident ESKD during this period. Specifically, the percentage of patients undergoing PD decreased from 5.7% in 2018 to 1.3% by 2022. In contrast, the proportion of patients receiving HD increased from 81.6% to 85.0%. This change in the distribution of KRT modalities is speculated to be a continuation of the change in treatment trends for patients with ESKD in Korea, as reported in several previous studies [16], rather than a direct consequence of the COVID-19 pandemic. As seen in the ITS analysis, previously on a decreasing trajectory, the PD incidence rate continued to decline, but have slowed. In addition, the proportion of patients in whom HD was initiated with catheters decreased from 63.6% to 55.4%. This observation indicated that a greater number of patients started HD through established vascular access rather than through emergent catheter insertion, implying that high-quality

medical care was provided even during the coronavirus pandemic.

The proportion of KT recipients remained relatively stable, ranging from 12.7% to 17.3%. However, the preemptive KT rate decreased from 50.8% to 44.6%. This decline is hypothesized to be due to the timing of transplant surgery that may have been affected by difficulties and disruptions in healthcare during the pandemic. Additionally, KT may have been performed with caution because a high dose of immunosuppressant is required in the early stages of transplantation. When considering the long-term benefits of KT over chronic dialysis [17], this highlights the need for a robust and adaptable transplant infrastructure that can navigate the complexities of infectious disease outbreaks while continuing to provide transplant procedures safely.

During the COVID-19 pandemic, significant changes in healthcare access and patient behavior were reflected in the variations in CCI scores observed among ESKD patients from 2018 to 2022. The comorbidity score of ESKD patients gradually decreased from 5.8 to 5.4. Among the 15 conditions examined, myocardial infarction, congestive heart failure, DM, DM complications, and paraplegia all decreased slightly during pandemic and chronic pulmonary disease had the greatest impact on the CCI score, decreasing sharply from 45.2% in 2018 to 31.0% in 2022. The decrease may be partly attributed to the reduced frequency of routine healthcare visits during the pandemic, impacting the management and diagnosis rates of conditions such as DM complications and congestive heart failure. Furthermore, specific public health measures, such as lockdowns reducing physical activity, alongside changes in patient behavior—including increased use of masks and social distancing—likely contributed to the observed decrease in chronic pulmonary disease prevalence [18].

This study investigated the ESKD incidence rates by KRT modality and age. ITS analysis revealed that no immediate change was observed in any KRT modality or age group following the COVID outbreak. Age-specific analysis revealed that higher age groups had higher incidence rates of ESKD, with the elderly population, particularly those aged 75 and older, experiencing notably higher rates. This finding is consistent with the well-established association between aging and the risk of ESKD [19]. The incidence of ESKD in children under 18 decreased before COVID-19, but no significant trend was observed after COVID-19. Chronic kidney disease in children under 18 is mainly associated with congenital

factors such as congenital kidney malformations and congenital urinary tract disorders [20]. During the COVID-19 era, it is plausible that factors such as psychological stress could have exerted a negative effect on fetal health, thereby potentially contributing to the absence of a decline in ESKD incidence among children under 18. Additionally, due to the significantly lower incidence of ESKD in children compared to other age groups, it's impossible to entirely rule out the possibility of error. Contrary to those under 18, older adults aged 65 and older exhibited a tendency of increasing ESKD incidence before the onset of COVID-19. They are more vulnerable to ESKD due to age-related weakening of kidney health, making those with pre-existing conditions such as hypertension and diabetes more susceptible to ESKD [9]. However, there was a tendency for the incidence of ESKD to decrease among the 45-64 age group and the 65-74 age group. The lack of such trends during the COVID-19 era may be attributed to the development of new treatments delaying the progression to ESKD (such as SGLT-2 inhibitors, GLP-1 agonist, RAAS blockers, etc) or changes in healthcare utilization patterns during the pandemic [21]. It is also possible that there was an underestimation of ESKD due to deaths occurring before reaching KRT. As previous data [22], during the COVID-19 pandemic, there were more excess deaths observed in the age groups of '50-64' and '65-79' compared to those aged '80 and older' when compared to the previous years.

We investigated whether the COVID-19 pandemic caused difficulties in hospitalization or led to situations where the necessary medical care was not provided. There were no significant changes in hospitalization-related medical care for PD or KT recipients before and after COVID-19. Only patients undergoing HD showed a tendency for reduced hospitalization and LOS, reflecting potential changes in patient care patterns during the pandemic. While a decrease in hospitalization may, in some instances, be seen as a positive outcome indicative of outpatient management or improved disease management, but their potential impact needs to be examined more carefully. During the COVID-19 pandemic, there was a widespread culture of reluctance to visit and admit hospitals due to concerns about infection, and the provision of medical services was very different from the time when there were no infectious diseases. Despite the fact many patients receiving HD are admitted to nursing hospitals under special circumstance, there continues to be a decrease in both LOS and the number of admissions.

Although informative, this study had some limitations. First, there may have been minor errors in the number of people infected with COVID-19. Patients who could not be traced in claims data owing to data privacy concerns were excluded from the study. Cases that could not be traced in the claims data were as follows. First, if hospitals had treated fewer than three COVID-19 patients during the entire study period, these patients were excluded. Second, patients infected with COVID-19 between January and March 2020 were excluded from the study. However, it is important to note that during January to March 2020, the early stages of the COVID-19 outbreak, the number of COVID-19 cases was extremely low. Although there may have been variations in patient numbers, the patients included in this study adequately represented the overall population of patients who underwent KRT. Second, it was not possible to distinguish between living and deceased donor KT based on claims data alone. However, all preemptive KT cases were probably living donor cases, and there appeared to be no significant change in either total or preemptive KT before and after the COVID pandemic. Third, we could only access the claims data until June 2022. This limited timeframe may have affected the comprehensiveness of our findings. This constrained timeframe restricted our analysis to a specific period, potentially limiting the depth and breadth of insights obtained from a more extended dataset. Future research extending beyond this period is crucial to capture the evolving dynamics and potential long-term consequences of the observed shifts in ESKD and KRT patterns.

This study provides valuable insights into the dynamics of ESKD and KRT during the COVID-19 pandemic in South Korea. These findings highlight the stability of ESKD incidence while revealing shifts in the choice of KRT modalities, with a notable increase in HD utilization. While there have been individualistic differences as COVID-19 has impacted everyone, this study showed that the overall healthcare system remained stable during the pandemic, with no major disruptions to care for patients with ESKD in South Korea. As we navigate the complexities of future infectious disease outbreaks, these insights serve as a foundation for informed strategies to safeguard the well-being of patients with ESKD.

KEY MESSAGE

1. Despite the COVID-19 pandemic, there was no significant increase in the overall incidence of ESKD in South Korea.
2. While ESKD incidence remained stable, there were notable changes in the distribution of KRT modalities, with a decrease in PD utilization and an increase in HD usage, suggesting ongoing treatment trends rather than direct consequences of the pandemic.
3. Patients undergoing HD showed a tendency for reduced hospitalization and LOS, potentially reflecting changes in patient care patterns during the pandemic, highlighting the need for further examination of these trends and their ramifications on patient outcomes.

REFERENCES

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020;382:727-733.
2. ERA-EDTA Council; ERACODA Working Group. Chronic kidney disease is a key risk factor for severe COVID-19: a call to action by the ERA-EDTA. *Nephrol Dial Transplant* 2021;36:87-94.
3. De Meester J, De Bacquer D, Naesens M, et al. Incidence, characteristics, and outcome of COVID-19 in adults on kidney replacement therapy: a regionwide registry study. *J Am Soc Nephrol* 2021;32:385-396.
4. Changsirikulchai S, Sangthawan P, Janma J, Rajborirug S, Ingviya T. COVID-19 incidence and outcomes among patients with kidney replacement therapy. *Kidney Res Clin Pract* 2023;42:649-659.
5. Park HC, Lee YK, Ko E, et al. COVID-19-related clinical outcomes among Korean hemodialysis patients. *Kidney Res Clin Pract* 2022;41:591-600.
6. Chothia MY, Barday Z, Nel J, Davids MR. Impact of COVID-19 on access to chronic kidney replacement therapy in the public sector of Western Cape Province, South Africa. *S Afr Med J* 2021;111:13442.
7. Kyoung DS, Kim HS. Understanding and utilizing claim data from the Korean National Health Insurance Service (NHIS) and Health Insurance Review & Assessment (HIRA) database for research. *J Lipid Atheroscler* 2022;11:103-110.
8. Korean Statistical Information Service. Population Projections for Korea: population trends and projections of the world and Korea [Internet]. Daejeon: Statistics Korea, 2023 [cited 2024 Mar 31]. Available from: https://kosis.kr/statHtml/statHtml.do?orgId=101&tblId=DT_1B040A3.
9. Lee MJ, Ha KH, Kim DJ, Park I. Trends in the incidence, prevalence, and mortality of end-stage kidney disease in South Korea. *Diabetes Metab J* 2020;44:933-937.
10. Obi Y, Kalantar-Zadeh K, Streja E, et al. Seasonal variations in transition, mortality and kidney transplantation among patients with end-stage renal disease in the USA. *Nephrol Dial Transplant* 2017;32(suppl_2):ii99-ii105.
11. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segment-ed regression analysis of interrupted time series studies in medication use research. *J Clin Pharm Ther* 2002;27:299-309.
12. National Health Insurance Service, Health Insurance Review & Assessment Service. 2021 medical aid statistics. Wonju: Health Insurance Review & Assessment Service, 2022.
13. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;43:1130-1139.
14. Hirsch JS, Ng JH, Ross DW, et al. Acute kidney injury in patients hospitalized with COVID-19. *Kidney Int* 2020;98:209-218.
15. Weinhandl ED, Gilbertson DT, Wetmore JB, Johansen KL. COVID-19-associated decline in the size of the end-stage kidney disease population in the United States. *Kidney Int Rep* 2021;6:2698-2701.
16. Hong YA, Ban TH, Kang CY, et al. Trends in epidemiologic characteristics of end-stage renal disease from 2019 Korean Renal Data System (KORDS). *Kidney Res Clin Pract* 2021;40:52-61.
17. Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant* 2011;11:2093-2109.
18. Huang QS, Wood T, Jelley L, et al. Impact of the COVID-19 nonpharmaceutical interventions on influenza and other respiratory viral infections in New Zealand. *Nat Commun* 2021;12:1001.
19. Toyama T, Kitagawa K, Oshima M, et al. Age differences in the relationships between risk factors and loss of kidney function: a general population cohort study. *BMC Nephrol* 2020;21:477.
20. Harambat J, van Stralen KJ, Kim JJ, Tizard EJ. Epidemiolo-

gy of chronic kidney disease in children. *Pediatr Nephrol* 2012;27:363-373.

21. McCullough KP, Morgenstern H, Saran R, Herman WH, Robinson BM. Projecting ESRD incidence and prevalence in the United States through 2030. *J Am Soc Nephrol* 2019;30:127-135.
22. Lee PH, Kim MS. In-depth analysis of changes in mortality since the outbreak of COVID-19 [Internet]. Wonju: Health Insurance Review & Assessment Service, 2023 [cited 2024 Mar 31]. Available from: <https://repository.hira.or.kr/handle/2019.oak/3090>.

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