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Effect of Hypertension on Childhood-onset Systemic Lupus Erythematous in a Tertiary Medical Center in Korea

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Purpose: The purpose of this study was to evaluate the prevalence, clinical characteristics, and long-term clinical effects of hypertension in Korean childhood-onset systemic lupus erythematous (SLE) patients.

Methods: The medical records of SLE patients, diagnosed by 2019 SLE European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria, who visited Samsung Medical Center from January 2009 to May 2019 were reviewed. Disease activity and long-term damage were evaluated using the Modified Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and the Pediatric Systemic Lupus International Collaborating Clinics/ACR Damage Index (Ped-SDI), respectively. The sex-, age- and height-blood pressure standards recommended by the American Academy of Pediatrics 2017 guideline was used to define hypertension.

Results: A total of 32 patients were enrolled in this study. The median follow-up duration was 7.3 years and females were predominant. The median ages at SLE and hypertension diagnoses were 14.2 and 14.3 years, respectively. The biopsy-proven lupus nephritis was detected in 90.6% and 37.5% were class IV. During the follow-up, 12 patients (37.5%) had hypertension. Among them, 2 patients had 3 episodes of posterior reversible encephalopathy syndrome and 5 patients had left ventricular hypertrophy (LVH). Univariate analysis showed baseline hypertension was significantly correlated with a lower estimated glomerular filtration rate, higher body mass index and SLEDAI at baseline. The development of hypertension during the follow-up was significantly correlated with obesity, LVH, and higher Ped-SDI.

Conclusion: Our study revealed that hypertension in pediatric SLE is associated with obesity and renal function at SLE diagnosis and could affect long-term damage.

Key words: Hypertension, Children, Systemic Lupus Erythematous

Introduction

Hypertension is frequent among patients with systemic lupus erythematous (SLE) and studies show it is more prevalent in SLE patients than in people without SLE[1,2]. Especially, resistant hypertension was nearly twice as prevalent in patients with SLE compared to control subjects, with an incidence rate of 10.2 versus 6.1 cases per 1,000 person-years of observation[1]. Recent data

suggest that hypertension is common not only in adult SLE patients, but also in pediatric SLE patients. There are a few published studies from small childhood-onset SLE cohorts that suggest a hypertension point prevalence that ranges from 12% to 74%[3,4].

Despite the high frequency of hypertension in SLE patients, the pathophysiological mechanisms underlying the development of hypertension in this population remain poorly understood. Although renal glomerular damage and renal vascular endothelial dysfunction have been hypothesized to be the main contributors, hypertension is also present in SLE patients without renal involvement[5]. Many possible mechanisms such as renin-angiotensin-aldosterone system activation, dysautonomia, immune complex deposits in tissues, the effect of inflammatory mediators, and anti-inflammatory therapy have been proposed to explain hypertension in SLE patients[5]. In addition to these well-known mechanisms, Sabio JM et al. reported that elevated homocysteine levels could increase the risk of hypertension in SLE patients[6].

A few clinical variables have been reported to be risk factors for hypertension in SLE patients. In patients with SLE, resistant hypertension was reported to be associated with black race, lower renal function, hypercholesterolemia, and increased inflammatory markers[1]. In childhood-onset SLE patients, the presence of lupus nephritis, obesity, and high-extra-renal disease activity at baseline visit were predictors of hypertension[2]. Much is known about the effects of hypertension on the SLE disease course. Several studies have demonstrated that hypertension has been associated with damage accrual, stroke, progression of renal and cardiac disease, and cognitive dysfunction in SLE patients[2,5]. In adult patients with SLE, resistant hypertension was also associated with a significantly higher mortality risk[1].

The purpose of this study was to evaluate the prevalence, clinical characteristics, and long-term clinical effects of hypertension in Korean childhood-onset SLE patients treated in a tertiary medical center in Korea.

Materials and methods

1. Study population

The medical records of pediatric patients under 19 years of age who were diagnosed as having SLE and visited Samsung Medical Center, a tertiary referral center located in Seoul, Korea, between January 2009 and June 2019 were retrospectively reviewed. Their long-term damage was retrospectively assessed by medical records through December 2019. All data were obtained from the electronic medical records in accordance with the ethical principles for medical research involving human subjects established in the Declaration of Helsinki of 1975 as revised in 2000. The Institutional Review Board (IRB) of Samsung Medical Center approved this study (IRB number 2020-06-072). Data on the following demographic characteristics were collected: sex, age at SLE and hypertension diagnoses, family history of autoimmune disease and hypertension, body mass index (BMI), initial presenting symptoms, systolic/diastolic blood pressure at initial diagnosis and last follow-up, and target organ damage including left ventricular hypertrophy (LVH).

2. Definition

Having SLE was defined as patients who were documented as SLE in the medical record and confirmed by 2019 SLE European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria[7]. Lupus nephritis was defined as biopsy-proven nephritis classified by the revised classification of the International Society of Nephrology/Renal Pathology Society (ISN/RPS). Disease activity was scored with the Modified Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K)[8]. The long-term damage according to disease itself or SLE management was assessed by the Pediatric Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (Ped-SDI)[9].

Overweight and obesity was defined by using age and sex standards recommended by the Korea Center for Disease Control and Prevention (overweight 85 percentile ≤ BMI <95 percentile, obesity: BMI ≥ 95 percentile) for BMI measured in patients under 19 years of age[10]. When BMI was measured in patients older than 19 years, overweight and obesity was defined by BMI 23.0–24.9 kg/m2 and ≥25 kg/m^2[11].

Blood pressure at SLE and hypertension diagnosis was average of three consecutive blood pressure measured by clinician and last visit blood pressure was measured once

by clinician. Hypertension was defined according to the American Academy of Pediatrics 2017 guidelines for sex-, age- and height-related blood pressure standards[12]. During the follow-up period, when the patient was over 19 years of age, hypertension was defined as systolic blood pressure above 140 mmHg or diastolic blood pressure above 90 mmHg[13]. Or the patients who have antihypertensive medication, not for proteinuria regulation, was classified as hypertension.

Patients were also evaluated for target organ damage. Two-dimensional echocardiography was performed by pediatric cardiologists to measure cardiac parameters according to the American Society of Echocardiography pediatric guidelines. The LVH was defined as left ventricular mass index (LMVI) (Left ventricular mass (LVM) in grams divided by height in meters to the 2.7th power) ≥the 95th percentile for normal children and adolescents[14].

During the follow-up period, when the patient was older than 19 years of age, the LVM was indexed by body surface area (BSA) and the LVH was defined as LVMI by BSA ≥115 g/m^2 for males and ≥ 95 mg/m^2 for females[15].

3. Statistical analysis

Statistical analysis was conducted using SAS version 9.4. The Student's t-test for numerical normally distributed data and the Mann-Whitney test for numerical non-normally distributed data were used. The Chi-squared and Fisher's exact tests were used to analyze categorical data. Logistic regression was used to evaluate odds ratios (OR) and confidence intervals (CI) for hypertension risk in pediatric SLE patients. A *P* value <0.05 was considered statistically significant.

Results

1. Demographic data

A total of 32 patients were enrolled in this study. The median follow-up duration was 7.3 years and females were predominant. The median age at SLE and hypertension diagnoses were 14.2 and 14.3 years, respectively. Family history of autoimmune disease and hypertension were available in 17 (2/6 in hypertension, 3/11 in non-hypertension) and 4 (1/2 in hypertension, 1/2 in non-hypertension) patients in this study. Initial renal involvement was detected in 12.5% of patients. Finally, biopsy-proven lupus nephritis was detected in 90.6% of patients (n=29) and 37.5% of patients were class IV (n=12). At the diagnosis of SLE, 4 patients were classified as hypertensive, and the median value of SLEDAI-2K score and renal SLEDAI-2K score at SLE diagnosis was 14.0 and 4.0, respectively. The median dose of steroids, converted to prednisolone, at SLE diagnosis was 1.0 mg/kg/day (Table 1).

2. Comparison between SLE patients with hypertension and those without hypertension

A comparison of characteristics between patients with and without baseline hypertension is shown in Table 2. The patients with hypertension had a lower estimated glomerular filtration rate (eGFR), higher BMI, and higher disease activity (SLEDAI-2K) at SLE diagnosis compared to those without hypertension. However, there was no difference in Renal SLEDAI-2K at SLE diagnosis between these patient groups. There was a statistically significant difference in steroid dose. Comparison of patient characteristics with and without hypertension at last visit is shown in Table 3. The patients with hypertension showed more prevalent LVH compared to those without hypertension. There was no significant difference in eGFR, BMI, and disease activity between the two groups. A comparison of characteristics between patients and without hypertension at any period of SLE course is shown in Table 4. There was a significant difference in the prevalence of LVH between the two groups (*P*-value 0.0256).

3. Associated factors for hypertension in pediatric SLE patients

Univariate analysis showed baseline hypertension was significantly correlated with a lower eGFR, obesity, and higher disease activity at the time of SLE diagnosis (Table 5). The development of hypertension during the follow-up period was significantly correlated with obesity, the presence of target organ damage such as LVH, and long-term damage with higher Ped-SDI.

4. Follow-up BP trends

During follow up, the prevalence of hypertension increased and at the last visit, 31.3% of patients were diagnosed

Table 1. Demographic and Clinical Information of Pediatric SLE Patients

Variable	Values
Female/male, N (ratio)	27/5 (5.4)
Age at SLE diagnosis (year), median (range)	14.2 (4.8–18.8)
Initial presentation, N (%)	
Cutaneous	7 (21.9%)
Fever	6 (18.8%)
Arthritis	6 (18.8%)
Hematologic	6 (18.8%)
Renal	4 (12.5%)
Neurologic	2 (6.3%)
Others	1 (3.1%)
Lupus nephritis at baseline, N (%)	17 (53.1%)
Lupus nephritis during follow-up, N (%)	29 (90.6%)
Class I	1 (3.4%)
Class II	1 (3.4%)
Class III	5 (17.2%)
Class IV	12 (41.4%)
Class V	3 (10.3%)
Class V+III	3 (10.3%)
Class VI+V	2 (6.9%)
Others	2 (6.9%)
Follow up duration, median (range)	7.3 (0.2–16.6)
Baseline BMI, median (range)	19.2 (14.7–27.3)
Baseline overweight & obesity, N (%)	5 (18.5 %)
Baseline SBP (mmHg), mean±standard deviation	115.2±18.2
Baseline DBP (mmHg), mean±standard deviation	67.8±14.7
Baseline Blood Pressure Stage, N (%)	
Normotensive	17 (68%)
Elevated blood pressure	4 (16%)
Hypertension stage 1	1 (4%)
Hypertension stage 2	3 (12%)
eGFR at SLE diagnosis (ml/min/1.73m^2), mean±standard deviation	97.5±28.2
Baseline AKI, N (%)	4 (12.9%)
Baseline SLEDAI-2K, median (range)	14.0 (4–41)
Baseline Renal SLEDAI-2K, median (range)	4.0 (0–12)
Baseline Non-renal SLEDAI-2K, median (range)	10 (4–29)
Initial steroid dose, converted to PD (mg/kg/day), median (range)	1.0 (0.3–9.0)

Abbreviations: SLE, systemic lupus erythematous; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; AKI, acute kidney injury; SLEDAI-2K, Modified Systemic Lupus Erythematosus Disease Activity Index; PD, prednisolone.

as having hypertension. Stage 2 hypertension was prevalent (n=9). The median value of Ped-SDI at last follow up was 1.0. Among childhood-onset SLE patients with hypertension, 2 patients had 3 episodes of posterior reversible encephalopathy syndrome. LVH was detected in 5 patients with hypertension.

Table 2. Comparison of Clinical Information in Pediatric SLE Patients with and without Baseline Hypertension

	SLE with hypertension (N=4)*	SLE without hypertension (N=21)*	*P*-value
Female: Male (ratio)	3:1 (3)	17:4 (4.3)	1.000
Age at SLE diagnosis, year	16.2±1.9	13.5±3.6	0.1556
Follow up duration, year	4.9±4.7	7.1±4.8	0.4007
Baseline BMI	23.9±3.2	19.2±2.7	0.0060
Baseline overweight & obesity, N (%)	3 (75)	2 (9.5)	0.0162
Baseline SBP (mmHg)	142.8±27.9	109.9±9.9	0.0976
Baseline DBP (mmHg)	94.6±9.3	62.7±8.7	<0.0001
Baseline eGFR (ml/min/1.73m^2)	55.4±33.2	103.3±18.2	0.0146
AKI at baseline, N (%)	3 (75)	1 (4.8)	0.0067
Lupus nephritis at baseline, N (%)	4 (100)	10 (47.6)	0.0152
Lupus nephritis during follow-up, N (%)	4 (100)	18 (85.7)	1.0000
Initial steroid dose, converted to PD (mg/kg/day)	5.0±4.4	0.9±0.3	0.0426
Baseline SLEDAI-2K	27.0±9.9	13.7±5.5	0.0008
Baseline Renal SLEDAI-2K	10.0±2.3	4.8±5.0	0.0820
Baseline Non-renal SLEDAI-2K	17.0±8.3	9.0±3.5	0.0299
Last visit Ped-SDI	1.3±1.9	1.4±1.6	0.7597
Last LVH†, N (%)	3/3 (100)	2/10 (20)	0.035

*Baseline blood pressure data was available in 25 patients and presented as the mean±standard deviation.
†In 13 patients, data was available.
Abbreviations: SLE, systemic lupus erythematous; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; AKI, acute kidney injury; PD, prednisolone; SLEDAI-2K, Modified Systemic Lupus Erythematosus Disease Activity Index; Ped-SDI, The Pediatric Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; LVH, left ventricular hypertrophy; PRES, posterior reversible encephalopathy syndrome.

Discussion

The results of this study demonstrated that during the follow-up period, 12 patients (37.5%) had hypertension. At baseline, 12.5% of patients were diagnosed as having hypertension, and during the follow-up period, the prevalence of hypertension, especially stage 2 hypertension, increased. These findings suggest that it is very difficult to control blood pressure in SLE patients in spite of the use of antihypertensive medications. In some adult cohorts, the preva-

Table 3. Comparison of Clinical Information in Pediatric SLE patients with and without hypertension at last visit

	SLE with hypertension (N=10)*	SLE without hypertension (N=21)*	*P*-value
Female: Male (ratio)	7:3 (2.3)	20:1 (20)	0.0868
Age at SLE diagnosis, year	14.0±3.0	14.3±2.9	0.8431
Follow up duration, year	5.9±4.4	7.6±4.7	0.3467
Last visit BMI	23.4±4.4	21.0±2.8	0.0793
Last visit overweight and obesity, N (%)	5 (50)	5 (25)	0.2308
Baseline SBP (mmHg)†	124.8±23.3	110.0±12.7	0.0556
Baseline DBP (mmHg)†	74.8±19.3	64.1±10.3	0.1541
Last visit SBP (mmHg)	123.0±11.4	111.7±12.3	0.0076
Last visit DBP (mmHg)	78.0±12.0	67.8±10.5	0.0220
Baseline Blood Pressure Stage, N (%)			
Normotensive	4 (44.4)	12 (80)	0.0782
Elevated blood pressure	2 (22.2)	2 (13.3)	0.0690
Hypertension stage 1	1 (11.1)	0	0.2524
Hypertension stage 2	2 (22.2)	1 (6.7)	0.5328
Baseline eGFR (ml/min/1.73m^2)	83.2±36.0	104.6±21.0	0.8953
AKI at baseline, N (%)	3 (33.3)	1 (4.8)	0.1937
Lupus nephritis at baseline, N (%)	7 (70)	9 (42.9)	0.1695
Lupus nephritis during follow-up, N (%)	10 (100)	18 (85.7)	0.5213
Initial steroid dose, converted to PD (mg/kg/day)	2.0±2.7	1.5±2.1	0.4095
Last steroid dose, converted to PD (mg/kg/day)	0.2±0.1	0.1±0.2	0.1634
Baseline SLEDAI-2K	18.7±10.2	14.1±6.4	0.1695
Baseline Renal SLEDAI-2K	6.7±5.3	4.9±5.2	0.5213
Baseline Non-renal SLEDAI-2K	12.0±7.4	9.1±3.4	0.4095
Last visit Ped-SDI	1.7±1.8	0.7±0.9	0.1634
Last LVH‡, N (%)	4/5 (80)	1/8 (12.5)	0.0319
PRES, N	2	-	

*Data was available in 31 patients and presented as the mean±standard deviation.
†Data was available in 25 patients.
‡In 13 patients, data was available.
Abbreviations: SLE, systemic lupus erythematous; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; AKI, acute kidney injury; PD, prednisolone; SLEDAI-2K, Modified Systemic Lupus Erythematosus Disease Activity Index; Ped-SDI, The Pediatric Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; LVH, left ventricular hypertrophy; PRES, posterior reversible encephalopathy syndrome.

lence of hypertension in SLE is reported to be up to 77%[16]. Aydin et al. reported that 29% and 23% of childhood-onset SLE patients had hypertension and prehypertension at the baseline visit, and there was no significant difference in the prevalence of hypertension over time[2]. In another pediatric

Table 4. Comparison of Clinical Information in Pediatric SLE Patients with and without Hypertension at Any Period of SLE Course

	SLE with hypertension (N=12)	SLE without hypertension (N=20)	*P*-value
Female: Male (ratio)	8:4 (2)	19:1 (19)	0.0531
Age at SLE diagnosis, year	13.5±3.9	14.2±2.9	0.5760
Follow up duration, year	5.2±4.4	7.9±4.7	0.1176
Baseline BMI	21.3±3.9	19.0±2.2	0.0945
Last visit BMI	23.3±4.3	21.0±2.9	0.0890
Baseline overweight & obesity, N (%)	4 (36.4)	1 (6.3)	0.1252
Last visit overweight and obesity, N (%)	5 (45.5)	6 (30)	0.4524
Baseline SBP (mmHg)*	122.8±23.5	109.2±9.8	0.0935
Baseline DBP (mmHg)*	73.2±19.5	63.5±7.8	0.1470
Last visit SBP (mmHg)	121.9±15.0	112.8±11.6	0.0683
Last visit DBP (mmHg)	74.7±15.5	69.1±9.1	0.2850
Baseline Blood Pressure Stage, N (%)			
Normotensive	5 (50)	12 (80)	
Elevated blood pressure	1 (10)	3 (20)	
Hypertension stage 1	1 (10)	-	
Hypertension stage 2	3 (10)	-	
Last visit Blood Pressure stage, N (%)			
Normotensive	2 (20)	14 (66.7)	
Elevated blood pressure	5 (50)	7 (33.3)	
Hypertension stage 1	1 (10)	0	
Hypertension stage 2	2 (20)	0	
Baseline eGFR (ml/min/1.73m^2)	84.7±34.0	106.9±19.2	0.0663
AKI at baseline, N (%)	3 (27.3)	1 (5)	0.1154
Lupus nephritis at baseline, N (%)	8 (66.7)	9 (45)	0.2344
Lupus nephritis during follow-up, N (%)	11 (91.7)	18 (90)	1.000
Initial steroid dose, converted to PD (mg/kg/day)	2.7±3.5	1.0±0.2	9.488
Last steroid dose, converted to PD (mg/kg/day)	0.2±0.1	0.1±0.2	0.2029
Baseline SLEDAI-2K	17.7±9.5	14.1±6.5	0.2443
Baseline Renal SLEDAI-2K	5.8±4.9	5.5±5.4	1.000
Baseline Non-renal SLEDAI-2K	11.9±6.6	8.6±3.6	0.1925
Last visit Ped-SDI	1.91±1.9	0.7±0.9	0.0713
Last LVH, N (%)	5/6 (83.3)	1/8 (12.5)	0.0256
PRES, N	2	-	

Data was presented as the mean±standard deviation.
*Data was available in 25 patients.
†In 14 patients, data was available.
Abbreviations: SLE, systemic lupus erythematous; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; AKI, acute kidney injury; PD, prednisolone; SLEDAI-2K, Modified Systemic Lupus Erythematosus Disease Activity Index; Ped-SDI, The Pediatric Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; LVH, left ventricular hypertrophy; PRES, posterior reversible encephalopathy syndrome.

Table 5. Associated Factors for Hypertension in Pediatric SLE

	Univariate logistic regression	
	Unadjusted OR (95% CI)	*P*-value
Baseline hypertension		
Baseline BMI	1.586 (1.051–2.393)	0.0280
Baseline overweight & obese	28.5 (1.931–420.5)	0.0147
Baseline eGFR	0.918 (0.849–0.992)	0.0302
Baseline AKI	60.0 (2.911– >999.999)	0.0080
Baseline SLEDAI	1.345 (1.014–1.784)	0.0400
Last visit hypertension		
LVH	28 (1.35–580.590)	0.0312
Baseline BMI	1.38 (1.001–1.902)	0.0496
Baseline overweight & obese	12.8 (1.149–142.6)	0.0382
Hypertension at any period of SLE course		
LVH	35.0 (1.743–702.992)	0.0202
Final Ped-SDI	1.954 (1.048–3.645)	0.0352

Abbreviations: SLE, systemic lupus erythematous; OR, odds ratio; CI, confidence interval ; BMI, body mass index; eGFR, estimated glomerular filtration rate; AKI, acute kidney injury; SLEDAI-2K, Modified Systemic Lupus Erythematosus Disease Activity Index; LVH, left ventricular hypertrophy; Ped-SDI, The Pediatric Systemic Lupus International Collaborating Clinics/ American College of Rheumatology Damage Index.

Table 6. Follow-up Blood Pressure Trends

Variable	Values
Last visit SBP (mmHg), mean±standard deviation	116.0±13.4
Last visit DBP (mmHg), mean±standard deviation	71.1±11.9
Last follow up blood pressure stage, N (%) [number of patients with antihypertensive medication]	
Normotensive	16 (51.6) [2]
Elevated blood pressure	12 (38.7) [5]
Hypertension stage 1	1 (3.2) [0]
Hypertension stage 2	2 (6.5) [2]
Last visit BMI, median (range)	21.2 (15.8–31.8)
Last visit overweight and obesity, N (%)	11 (35.5)
Last steroid dose, converted to PD (mg/kg/day), median (range)	0.1 (0.03–0.6)
LVH at any period*, N (%)	6 (42.9)
PRES	2 (6.3)
Last visit Ped-SDI, median (range), N (%)	1.0 (0–5)

*In 14 patients, data was available.
Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; PD, prednisolone; LVH, left ventricular hypertrophy; PRES, posterior reversible encephalopathy syndrome; Ped-SDI, The Pediatric Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

SLE study, hypertension was present in 12.29% of pediatric SLE patients[3]. In another pediatric SLE cohort, 20% met daytime criteria for a diagnosis of hypertension[17]. Our results suggest that there is a high risk of hypertension in childhood-onset SLE patients during follow up although there was no evidence of hypertension at baseline visit.

In our study, the patients with baseline hypertension showed lower eGFR and higher disease activity at SLE diagnosis compared to those without hypertension. However, there was no difference in the prevalence of lupus nephritis and Renal SLEDAI-2K score between patients with and without HTN. Another report showed that hypertension was more common and difficult to control among patients with lupus nephritis than those without[2]. In our study, the prevalence of lupus nephritis was somewhat higher that other country's reports[2,18]. According to US data, 19–37% had lupus nephritis in pediatric patients with SLE[2,18]. This finding could affect our results.

In our study, there was an association between BMI and hypertension. A previous report also showed that there was a significant association between increased BMI and lupus nephritis and hypertension in adult patients[19]. There is a pathophysiologic connection in that both obesity and SLE have been reported to result in inflammation components such as interleukin-1 and c-reactive protein[20]. Based on these findings, higher BMI was considered a predictor of hypertension in SLE patients[21]. Our results suggest that the association between obesity and hypertension could be applied to pediatric SLE patients.

In our study, patients with hypertension showed higher Non-renal SLEDAI-2K at SLE diagnosis. The SLEDAI is a global index that evaluates disease activity over the previous 10 days and includes 24 items on specific symptoms

in a nine organ system[22]. There is a report that increased SLEDAI scores were significantly associated with elevated anti-ds DNA titers and low complement levels[23]. There is another report that disease activity was associated with hypertension in SLE patients, which compared with those with and without hypertension. Individuals with hypertension demonstrated significantly elevated serum levels for C4 and C3 at baseline and serially[24]. These results suggest that high disease activity at diagnosis could be a predictor of hypertension in childhood-onset SLE patients. These findings are also compatible with the hypothesis that the factors known to influence SLE pathogenesis such as chronic inflammation and immune complex deposits contribute to the development of hypertension in childhood-onset SLE regardless of the presence of renal involvement.

There is little data on the long-term effects of hypertension in childhood-onset SLE patients. A previous study showed that almost all SLE patients with cardiovascular disease events presented with hypertension in the 2 years prior to the event[4]. There are a few reports on the association between hypertension and cardiovascular disease in pediatric SLE patients. Campbell JF et al. reported that independent of kidney involvement, there was an increased proportion of pediatric SLE patients with attenuated nocturnal dipping and nocturnal hypertension[17]. The patients who were classified as non-dippers were considered at higher risk of cardiovascular disease[25]. In our study, the SLE patients with hypertension showed higher Ped-SDI at the last visit. The SDI scores reflect irreversible damage regardless of cause. The definition of damage is an irreversible change in an organ or system that has occurred since the onset of SLE and is present for at least 6 months. There is a report that SDI values predict mortality in patients with SLE[22]. In our patients, further research on the development of cardiovascular disease and organ damage over a long-term period is necessary.

There are a few limitations in this study. First, this study was a retrospective, single center design. Second, it is possible that masked hypertension could not be detected because ambulatory blood pressure monitoring was not performed in all patients. Recently, 24-h ambulatory blood pressure monitoring has emerged as a useful tool for determining blood pressure to rule out the white coat effect and masked hypertension[25]. Additionally, the assessment of circadian blood pressure pattern could be useful which has been shown to be associated with cardiovascular risk[26]. Especially, there is a report that nocturnal hypertension was detected in 60% of SLE patients although 20% met daytime criteria for a diagnosis of hypertension in the pediatric SLE cohort[17]. There is a possibility that the prevalence of hypertension could increase if we used 24-h ambulatory blood pressure monitoring.

In conclusion, hypertension in childhood-onset SLE is associated with BMI and renal function at SLE diagnosis. Also, hypertension could affect long-term damage accumulation in childhood-onset SLE patients.

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Conflicts of interest

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

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