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# Relationship between the Number of Deaths due to Renal Failure and Meteorological Parameters in Japan: An Ecological Study

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# Abstract

- Objective: The aim of this study was to clarify the relationship between the number of deaths due to renal failure and meteorological parameters, such as air temperature and humidity, in Japan.
- Methods: The number of deaths due to renal failure and population of each of the 47 prefectures in Japan from 2016 to 2019 were obtained from official websites. Meteorological parameters, such as air temperature and humidity, in the same period were obtained from the Japan Meteorological Agency during same period. The relationship between the population-adjusted number of deaths due to renal failure and metrological parameters were evaluated by an ecological study.
- R e s u l t s: The number of deaths due to renal failure was significantly correlated with some air temperature parameters and mean humidity. Multiple regression analysis showed that mean humidity (women) was important factor for the number of deaths due to renal failure.
- Conclusion: These results suggest that metrological parameters, especially mean humidity, are closely associated with the number of deaths due to renal failure.

Key Words : renal failure, ecological study, air temperature, humidity

# 1. Introduction

In Japan, the number of patients on chronic hemodialysis has been increasing. According to the Japanese Society for Dialysis Therapy, in 2018, over 300,000 patients were on chronic hemodialysis<sup>1)</sup>, and 26,000 patients died due to renal failure<sup>2)</sup>. Therefore, a strategy for improving chronic renal failure treatment is required in Japan. Although many factors are associated with the number of deaths due to renal failure, including diabetes, cardiovascular disease, hypertension<sup>3, 4)</sup>, body weight and body mass index<sup>5)</sup>, nutrients<sup>6, 7)</sup>, sepsis<sup>8, 9)</sup>, and dialysis<sup>10)</sup>, metrological parameters were also reported to be associated with introduction of chronic hemodialysis<sup>11, 12)</sup>. A study investigating mortality in patients with end-stage renal disease using the database of the Japanese Society for Dialysis Therapy Renal

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Data Registry found that mortality was associated with seasonal variation<sup>12)</sup>. We reported that the number of deaths due to renal failure was the highest in January, and it was closely associated with air temperature parameters in Gifu prefecture, Japan by ecological study<sup>13)</sup>.

In the present study, we evaluated the relationship between the number of deaths due to renal failure and metrological parameters, such as air temperature and humidity, in Japan by an ecological study.

# 2. Methods

#### Deaths due to renal failure

The number of deaths due to renal failure stratified by sex from 2016 to 2019 was obtained from the Official Statistics of Japan portal site<sup>14)</sup>. Deaths due to renal failure were divided by a simple classification of causes of death based on the International Classification of Diseases and Related Health Problems-10 (ICD-10) 2013 edition. Population data during same period was obtained from the Statistics Bureau of Japan<sup>15)</sup>. A population-adjusted number of deaths due to renal failure (/100,000 people/year) was calculated for each of the 47 prefectures of Japan.

# Metrological parameters

Metrological parameters, such as mean air temperature (°C), mean of the highest air temperature (°C), mean of the lowest air temperature (°C), the highest air temperature (°C), the lowest air temperature (°C), mean humidity (%), and the lowest humidity (%), were obtained from Japan Metrological Agency's official website<sup>16)</sup>.

#### Ethical approval

All variables used in this study were obtained by official websites.

#### Statistical analysis

All data are expressed as mean  $\pm$  standard deviation (SD). The relationship between the number of deaths due to renal failure and metrological parameters was evaluated by simple correlation analysis. Data for the four years from 2016 to 2019 were analyzed to ensure the certainty of the association of the relationship between the number of deaths due to renal failure and metrological parameters. In addition, to evaluate the factors that contributed to the number of deaths due to renal failure, we used multiple regression analysis, where p < 0.05 was significant. The analyses were performed by JMP version 13 (SAS Institute Inc., Cary, NC, USA).

### 3. Results

The number of deaths due to renal failure (/100,000 people/year) for each of the 47 prefectures of Japan are summarized in **Figure 1**. The number of deaths due to renal failure varied from region to region.



Figure 1. The number of deaths due to renal failure (/100,000 people/year) in Japan (Total).

The clinical profiles of the number of deaths by renal failure and air temperature parameters from 2016 to 2019 are summarized in **Table 1**. The number of deaths due to renal failure (/100,000 people/year) was 22.6  $\pm$  5.4, 23.1  $\pm$  4.9, 24.0  $\pm$  5.3 and 24.5  $\pm$  5.3, respectively. Mean air temperature was from 2016 to 2019 was 16.2  $\pm$  2.4°C, 15.4  $\pm$  2.3°C, 16.0  $\pm$  2.3°C and 16.2  $\pm$  2.3°C, respectively.

Next, we evaluated the relationship between the number of deaths due to renal failure and meteorological parameters by simple correlation analysis (**Table 2**). For all subjects, the number of deaths due to renal failure from 2016 to 2018 was positively correlated with mean humidity. In men, the number of deaths due to renal failure in 2016 and 2018 was negatively correlated with the lowest air temperature. Mean air temperature, mean of the highest air temperature and mean of the lowest air temperature ware negatively correlated with the number of deaths due to renal failure in 2018. In women, the number of deaths due to renal failure was positively correlated with mean humidity in all years.

Finally, we used multiple regression analysis to evaluate the factors affecting the number of deaths due to renal failure (**Table 3**). We used the number of deaths due to renal failure as the dependent variable, and mean air temperature, the lowest air temperature, and mean humidity as independent variables. Mean humidity was a significant factor for the number of deaths due to renal failure in total subjects from 2016 to 2018, and in women in all years. In 2016, the lowest air temperature was a significant factor for the number of deaths due to renal failure in both sexes.

# Table 1. Profile of Japan.

	$Mean \pm SD$			Minimum	Maximum
2016					
Number of deaths by renal failure (/one hundred thousand people/year) (Total)	22.6	±	5.4	12.6	35.0
Number of deaths by renal failure (/one hundred thousand people/year) (Men)	22.9	±	5.3	13.1	36.8
Number of deaths by renal failure (/one hundred thousand people/year) (Women)	22.4	±	5.8	12.1	33.8
Mean air temperature (°C)	16.2	±	2.4	9.3	24.1
Mean of the highest air temperature (°C)	20.7	±	2.3	13.1	26.8
Mean of the lowest air temperature (°C)	12.4	±	2.6	5.9	21.9
The highest air temperature (°C)	36.7	±	1.3	31.9	38.5
The lowest air temperature (°C)	-4.6	±	2.6	-10.9	6.1
Mean humidity (%)	70.6	±	4.2	63.0	78.0
The lowest humidity (%)	12.7	±	4.0	5.0	30.0
2017					
Number of deaths by renal failure (/one hundred thousand people/year) (Total)	23.1	±	4.9	13.7	33.1
Number of deaths by renal failure (/one hundred thousand people/year) (Men)	23.5	±	4.9	14.5	33.7
Number of deaths by renal failure (/one hundred thousand people/year) (Women)	22.8	±	5.5	12.7	35.9
Mean air temperature (°C)	15.4	±	2.3	9.1	23.6
Mean of the highest air temperature (°C)	19.9	±	2.2	13.1	26.3
Mean of the lowest air temperature (°C)	11.5	±	2.6	5.5	21.5
The highest air temperature (°C)	36.5	±	1.0	33.0	38.0
The lowest air temperature (°C)	-3.5	±	3.6	-13.0	10.7
Mean humidity (%)	69.3	±	4.8	58.0	78.0
The lowest humidity (%)	13.0	±	3.8	6.0	25.0
2018					
Number of deaths by renal failure (/one hundred thousand people/year) (Total)	24.0	±	5.3	14.0	35.6
Number of deaths by renal failure (/one hundred thousand people/year) (Men)	24.8	±	5.5	13.5	39.1
Number of deaths by renal failure (/one hundred thousand people/year) (Women)	23.3	±	5.8	13.2	35.0
Mean air temperature (°C)	16.0	±	2.3	9.5	23.5
Mean of the highest air temperature (°C)	20.6	±	2.2	13.3	26.2
Mean of the lowest air temperature (°C)	12.1	±	2.5	6.0	21.3
The highest air temperature (°C)	37.7	±	1.6	33.1	41.1
The lowest air temperature (°C)	-4.9	±	3.5	-12.7	9.3
Mean humidity (%)	70.3	±	4.6	60.0	78.0
The lowest humidity (%)	13.1	±	3.9	5.0	30.0
2019					
Number of deaths by renal failure (/one hundred thousand people/year) (Total)	24.5	±	5.3	15.2	35.9
Number of deaths by renal failure (/one hundred thousand people/year) (Men)	25.2	±	5.5	16.8	40.2
Number of deaths by renal failure (/one hundred thousand people/year) (Women)	23.8	±	5.6	13.3	35.8
Mean air temperature (°C)	16.2	±	2.3	9.8	23.9
Mean of the highest air temperature (°C)	20.7	±	2.1	14.0	26.5
Mean of the lowest air temperature (°C)	12.3	±	2.6	6.2	21.7
The highest air temperature (°C)	36.8	±	1.2	33.9	39.2
The lowest air temperature (°C)	-2.2	±	3.6	-13.1	12.0
Mean humidity (%)	70.3	±	4.2	61.0	78.0
The lowest humidity (%)	12.2	±	3.6	4.0	23.0

SD: standard deviation

	To	Total		en	Women		
	r	р	r	р	r	р	
2016							
Mean air temperature (°C)	-0.150	0.309	-0.256	0.079	-0.050	0.738	
Mean of the highest air temperature (°C)	-0.152	0.302	-0.232	0.113	-0.075	0.611	
Mean of the lowest air temperature (°C)	-0.155	0.291	-0.272	0.061	-0.046	0.759	
The highest air temperature (°C)	-0.126	0.394	-0.136	0.357	-0.112	0.450	
The lowest air temperature (°C)	-0.369	0.010	-0.452	0.001	-0.273	0.060	
Mean humidity (%)	0.344	0.017	0.231	0.115	0.421	0.003	
The lowest humidity (%)	-0.060	0.684	-0.167	0.258	0.040	0.790	
2017							
Mean air temperature (°C)	-0.020	0.893	-0.124	0.403	0.064	0.666	
Mean of the highest air temperature (°C)	-0.044	0.765	-0.145	0.325	0.039	0.793	
Mean of the lowest air temperature (°C)	-0.031	0.834	-0.134	0.363	0.054	0.714	
The highest air temperature (°C)	0.213	0.146	0.173	0.239	0.224	0.127	
The lowest air temperature (°C)	-0.078	0.600	-0.163	0.268	-0.002	0.991	
Mean humidity (%)	0.347	0.016	0.240	0.101	0.407	0.004	
The lowest humidity (%)	0.122	0.409	0.076	0.610	0.152	0.302	
2018							
Mean air temperature (°C)	-0.208	0.155	-0.340	0.018	-0.069	0.644	
Mean of the highest air temperature (°C)	-0.216	0.141	-0.321	0.026	-0.100	0.502	
Mean of the lowest air temperature (°C)	-0.211	0.150	-0.352	0.014	-0.062	0.677	
The highest air temperature (°C)	-0.230	0.116	-0.161	0.275	-0.266	0.067	
The lowest air temperature (°C)	-0.259	0.075	-0.405	0.004	-0.099	0.503	
Mean humidity (%)	0.305	0.035	0.244	0.095	0.324	0.025	
The lowest humidity (%)	-0.071	0.633	-0.099	0.503	-0.032	0.827	
2019							
Mean air temperature (°C)	-0.169	0.250	-0.258	0.077	-0.078	0.599	
Mean of the highest air temperature (°C)	-0.167	0.257	-0.254	0.082	-0.078	0.601	
Mean of the lowest air temperature (°C)	-0.178	0.227	-0.262	0.072	-0.089	0.546	
The highest air temperature (°C)	-0.099	0.504	-0.077	0.605	-0.106	0.474	
The lowest air temperature (°C)	-0.200	0.172	-0.282	0.052	-0.111	0.455	
Mean humidity (%)	0.266	0.067	0.124	0.405	0.374	0.009	
The lowest humidity (%)	0.084	0.571	0.031	0.832	0.120	0.415	

Table 2. Simple correlation analysis between the number of deaths due to renal failure and air temperature parameters.

Bold values:  $p \le 0.05$  by a simple correlation analysis

	Total			М	Men			Women			
	standardized $\beta$	р	VIF	standardized $\beta$	р	VIF	standardized $\beta$	р	VIF		
2016											
Mean air temperature (°C)	0.224	0.247	2.186	0.139	0.473	2.186	0.280	0.146	2.186		
The lowest air temperature (°C)	-0.518	0.010	2.190	-0.544	0.007	2.190	-0.460	0.019	2.190		
Mean humidity (%)	0.315	0.020	1.009	0.202	0.130	1.009	0.393	0.004	1.009		
	$R^2=0.27$	R <sup>2</sup> =0.27 <i>p</i> = <b>0.003</b>			R <sup>2</sup> =0.26 <i>p</i> = <b>0.004</b>			R <sup>2</sup> =0.28 <i>p</i> = <b>0.002</b>			
2017											
Mean air temperature (°C)	0.542	0.130	6.515	0.297	0.423	6.515	0.681	0.048	6.515		
The lowest air temperature (°C)	-0.498	0.156	6.279	-0.389	0.288	6.279	-0.533	0.112	6.279		
Mean humidity (%)	0.397	0.009	1.097	0.245	0.111	1.097	0.487	0.001	1.097		
	R <sup>2</sup> =0.17	R <sup>2</sup> =0.17 <i>p</i> = <b>0.045</b>			R <sup>2</sup> =0.09 <i>p</i> =0.264			R <sup>2</sup> =0.24 <i>p</i> = <b>0.006</b>			
2018											
Mean air temperature (°C)	0.406	0.303	7.914	0.389	0.301	7.914	0.358	0.373	7.914		
The lowest air temperature (°C)	-0.582	0.138	7.718	-0.729	0.056	7.718	-0.367	0.354	7.718		
Mean humidity (%)	0.293	0.047	1.077	0.200	0.156	1.077	0.342	0.024	1.077		
	R <sup>2</sup> =0.16 <i>p</i> =0.057			R <sup>2</sup> =0.21 <i>p</i> = <b>0.014</b>			R <sup>2</sup> =0.12 <i>p</i> =0.121				
2019											
Mean air temperature (°C)	0.246	0.521	7.220	0.084	0.827	7.220	0.356	0.339	7.220		
The lowest air temperature (°C)	-0.430	0.263	7.195	-0.361	0.352	7.195	-0.443	0.234	7.195		
Mean humidity (%)	0.284	0.054	1.032	0.131	0.373	1.032	0.398	0.007	1.032		
	R <sup>2</sup> =0.12 <i>p</i> =0.127			R <sup>2</sup> =0.10	R <sup>2</sup> =0.10 <i>p</i> =0.212			R <sup>2</sup> =0.17 <i>p</i> = <b>0.040</b>			

Table 3. Multiple regression analysis between the number of deaths due to renal failure and air temperature parameters.

VIF : variance inflation factor

### 4. Discussion

In this study, we evaluated the relationship between the number of deaths due to renal failure and metrological parameters, such as air temperature and humidity, in Japan by an ecological study. We found that mean humidity was a determinant factor for the number of deaths due to renal failure in women.

There have been some reports on the relationship between renal failure and air temperature parameters <sup>17-19)</sup>. In the USA, monthly transition to end-stage renal disease (ESRD) was the highest in January<sup>17)</sup>. In Japan, Iwagami et al. reported that acute kidney injury often occurred in winter and was more likely to progress to severe illness<sup>18)</sup>. Iseki et al. showed that there was a strong correlation between the number of ESRD patients and ambient temperature in Okinawa prefecture<sup>19)</sup>. We reported the number of deaths due to renal failure was significantly negatively correlated with air temperature parameters in Gifu prefecture <sup>13)</sup>. Ogata et al. reported that lower average annual temperature was associated with a lower dialysis survival rate<sup>20)</sup>. Additionally, there have been several reports on the factors that influence the relationship between the number of deaths from renal failure and meteorological parameters. de Castro et al. showed that blood pressure was higher in winter in patients on chronic hemodialysis<sup>21)</sup>. During a four-year study investigating the relationship between climate and blood pressure in patients with end-stage renal disease treated with hemodialysis, blood pressure was inversely correlated with monthly maximum air temperature, and positively correlated with minimum humidity<sup>22)</sup>. In addition, seasonal changes in nutritional status have been reported<sup>23, 24)</sup>. These factors affect the relationship between the number of deaths due to renal failure and meteorological parameters.

In particular, Masugata et al. reported that the estimated glomerular filtration rate (eGFR) was lower in summer than in spring in Japanese hypertensive patients managed in outpatient clinics<sup>25)</sup>. In addition, heat stress and dehydration cause hyperosmolarity in the blood leading to exacerbation of renal failure<sup>26)</sup>. Therefore, renal failure may worsen under high humidity in summer. From the above, this study suggests a relationship between the death due to renal failure and seasonal fluctuations in mean humidity.

In this study, mean humidity was an important factor of death due to renal failure after adjusting for mean air temperature and the lowest air temperature in women in all years. The lowest air temperature parameter was significantly correlated with the number of deaths due to renal failure in total, men and women in 2016. Ogata et al. reported a significant relationship between average humidity and the transition to chronic hemodialysis in men<sup>27)</sup>. In addition, renal failure is less resistant to infections. Therefore, complications of infectious disease can rapidly worsen renal failure and affect the prognosis. High average humidity significantly increases the incidence of peritonitis caused by bacteria in patients undergoing peritoneal dialysis (PD), and the prognosis of peritonitis is particularly poor in summer<sup>28)</sup>. Taken together, humidity might be an important factor for the number of deaths due to renal failure. Indeed, there was a significant relationship between the number of deaths due to renal failure and mean humidity in women by multiple regression analysis in this study. Women have sexual cycle fluctuations, and their thermoregulatory and acclimatization abilities due to blood flow and sweat gland secretion are different from those of men<sup>29)</sup>. We speculate that these factors influence the relationship between humidity and renal failure death in women. Further study is required to clarify why the number of deaths due to renal failure was associated with humidity only in women in this study.

There are potential limitations to this study. First, this was an ecological study. Therefore, the link between the number of deaths due to renal failure and meteorological parameters found in our study may not apply to individual cases. Second, we could not obtain individual data of deaths due to renal failure. Especially, renal failure is often associated with diabetes, hypertension, coronary artery disease and heart failure  $^{3, 4)}$  . In addition, cardiovascular complications are the leading cause of death in patients with kidney disease<sup>30)</sup>. In this study, the relationships with these factors could not be investigated. Third, we could not clarify the mechanism between the number of deaths due to renal failure, and mean humidity and air temperature parameters. Fourth, we used only one observation point for meteorological parameters in each prefecture. Therefore, the location of the renal failure death and the observation point of the meteorological parameters may be different. Fifth, the number of deaths due to renal failure included both acute and chronic renal failure. Nevertheless, this study may suggest that it is important for patients with renal failure to pay attention to environmental factors, such as average humidity, in addition to receiving conventional lifestyle guidance on nutrition and exercise.

### 5. Conclusion

We evaluated the relationship between meteorological parameters and the number of deaths due to renal failure by ecological study. Metrological parameters, especially mean humidity, were closely associated with the number of deaths due to renal failure in Japan. Further studies using individual date are urgently required in the future.

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# 生態学的研究による腎不全死亡者数と気象パラメータとの関連

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#### 要旨

- 目的:日本における腎不全による死亡者数と気温や湿度等の気象パラメータとの関係を明らかにした.
- 方法:2016年から2019年までの47都道府県における腎不全による死亡者数と人口は政府統計公式 webサイトから取得した.同時期の気温や湿度等の気象パラメータは,気象庁公式webサ イトから取得した.腎不全による人口調整死亡数と気象パラメータとの関係は,生態学的研 究によって検討した.
- 結果:腎不全による死亡者数は、いくつかの気温パラメータ及び平均湿度と有意に相関していた. 重回帰分析の結果は、女性において、平均湿度が腎不全による死亡者数の重要な要因である ことを示した.
- 結論:気象パラメータ,特に平均湿度が腎不全による死亡者数と関連していた.

Key Words: 腎不全, 生態学的研究, 大気温, 湿度