Associations of Long-term PM$_{10}$ Exposure with Mortality in Dialysis Patients: A Population Based Cohort Study

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ABSTRACT

Exposure to PM$_{2.5}$ has been observed to be associated with an increased risk of mortality in dialysis patients, while sporadic studies have hinted at the adverse effects of coarse particulate matter (PM$_{10}$) on kidney health. However, the impact of PM$_{10}$ on survival in end-stage renal disease patients remains unclear. To address this gap, we conducted a retrospective cohort study, linking the Taiwan Air Quality-Monitoring Database (TAQMD) with the National Health Insurance Research Database (NHIRD) based on patients' zip codes. We included 34,088 adult dialysis patients living in areas with ambient measurements of PM$_{10}$, NO$_2$, CO, and SO$_2$ between 1 January, 2000 and 31 December, 2013. We used a multivariate Cox proportional hazards model to estimate mortality risk and observed that each interquartile range (IQR) increase in the mean PM$_{10}$ concentration during follow-up period was associated with a 13.2% higher risk of mortality (adjusted hazard ratio [aHR] = 1.132, 95% confidence interval [CI] = 1.097–1.169). Even in two-pollutant scenarios, the association between long-term exposure to PM$_{10}$ and mortality remained significant. Spline analysis demonstrated a non-linear concentration-response relationship between PM$_{10}$ and mortality, with an increase in aHR when the average PM$_{10}$ exposure exceeded a threshold of 43 $\mu$g m$^{-3}$. Stratification analysis revealed that male patients had a significantly higher increase in mortality risk per IQR increase in PM$_{10}$ compared to female patients (aHR 1.185 vs. 1.074; $p$-interaction < 0.001).

Our study demonstrated a significant association between long-term ambient PM$_{10}$ exposure and mortality risk among dialysis patients, especially in males. A non-linear concentration-response relationship between PM$_{10}$ and mortality was noted, with mortality risk increasing when the mean PM$_{10}$ surpassed a specific threshold. The PM$_{10}$-mortality association persisted after considering co-exposures to other air pollutants. These findings strongly indicate a positive association between long-term ambient PM$_{10}$ exposure and mortality among dialysis patients.

Keywords: Coarse particulate matter, TAQMD, NHIRD, Two-pollutant scenarios, Spline analysis

1 INTRODUCTION

Chronic kidney disease (CKD) affects over 10% of the world's population and is a growing global concern, significantly contributing to worldwide mortality (Kovesdy, 2022). The geographic disparities in global disease burden attributed to CKD cannot be solely explained by traditional factors like diabetes mellitus and hypertension (Xie et al., 2018). Environmental pollution, including...
air pollution, has emerged as a key driver of variations in the CKD’s impact worldwide (Xu et al., 2018).

Recent research has linked prolonged exposure to ambient fine particulate matter (PM$_{2.5}$) with an increased risk of adverse renal outcomes, including the development and progression of CKD, the incidence of end-stage renal disease (ESRD) (Bowe et al., 2018; Chan et al., 2018; Lin et al., 2020; Wu et al., 2020; Li et al., 2021; Ghazi et al., 2022), and higher mortality in dialysis patients (Feng et al., 2021; Chen et al., 2023). Additionally, emerging studies suggest that PM$_{10}$ may also have adverse effects on kidney health. For instance, Yang et al. (2017) identified a connection between exposure to PM$_{10}$ and PM$_{coarse}$ and a decline in renal function in Taiwanese adults (Yang et al., 2017). Bowe et al. (2017) observed a significant link between concentrations of PM$_{10}$, NO$_2$, and CO and the risk of both developing kidney disease and its progression to ESRD (Bowe et al., 2017).

Taiwan faces a significant CKD burden, affecting around 12% of the population (Wen et al., 2008). It also has the highest global incidence and prevalence of ESRD patients requiring dialysis (USRDS, 2022). The progression from CKD to ESRD increases the complexity and severity of the disease burden, resulting in elevated mortality rates (Van Walraven et al., 2014), diminished health-related quality of life (Chen et al., 2016), and considerable medical costs due to the necessity of dialysis (Zhang et al., 2020). In addition to these challenges, Taiwan contends with high levels of air pollution, ranking fourth out of 39 OECD countries, adding another layer of concern (OECD, 2023). Despite sporadic researches demonstrating that prolonged exposure to PM$_{2.5}$ is linked to adverse effects on mortality among adult dialysis patients (Feng et al., 2021; Chen et al., 2023), the specific impact of long-term PM$_{10}$ exposure on the mortality of dialysis patients remains unclear. Up to the present, only one previous study has examined the relationship between long-term PM$_{10}$ exposure and mortality in dialysis patients exclusively from hospital-attached dialysis units in Korea, limiting its representativeness (Jung et al., 2020). Our study aims to explore the association between long-term exposure to PM$_{10}$ and mortality among dialysis patients in Taiwan. To the best of our knowledge, this study is the first ever to investigate PM$_{10}$-mortality association in dialysis patients using nationwide population-based data.

Our hypothesis suggests that adult dialysis patients exposed to high levels of long-term ambient PM$_{10}$ have an increased risk of mortality. To explore this, we’ve connected the TAQMD with the NHIRD for our cohort study. Our goal is not only to investigate the association between PM$_{10}$ exposure and mortality but also to uncover the impact of different gaseous air pollutants on the PM$_{10}$-mortality relationship in adult dialysis patients.

## 2 METHOD

### 2.1 Data Source

This retrospective population-based cohort study utilized the NHIRD and TAQMD as its foundational datasets. Taiwan’s National Health Insurance provides coverage for over 99.6% of the country’s citizens, ensuring universal healthcare access. Physicians in this system are mandated to upload claims data to the National Health Insurance Ministry. This claims data, anonymized and released as the NHIRD, serves as a robust and representative biomedical research database (Lin et al., 2018). Patients initiating maintenance dialysis are required to register for a dialysis catastrophic illness card within this system, granting them exemption from dialysis-related medical expenses. Within the NHIRD context, we integrated the registry data of dialysis patients from the Catastrophic Illness Patients dataset with both inpatient and outpatient claims related to dialysis treatment. This linkage utilized encrypted personal information numbers to accurately identify patients initiating maintenance dialysis. Additionally, Taiwan’s Environmental Protection Administration (EPA) releases hourly measurements of various air pollutants from 77 air-quality monitoring stations spanning the country. These pollutants include particulate matter, NO$_2$, CO, and SO$_2$, and are crucial in calculating the Air-Quality Index. Collectively, these datasets constitute the TAQMD (EPA, 2023).

### 2.2 Study Population

The study focused on adults (≥ 18 years old) undergoing maintenance dialysis in regions with...
PM₁₀ monitoring, who survived beyond 183 days after initiating dialysis between 1 January, 2000 and 31 December, 2013. We utilized a cohort established in our prior research on PM₂.₅ and dialysis patient mortality (Chen et al., 2023). Patient selection involved linking NHIRD with TAQMD, matching patients’ dialysis institution zip codes with air-quality monitoring station coordinates. Because NHIRD covered no information regarding the residential area of a person, we defined the residential areas as the locations of the hospital or clinic where patients received dialysis (Jung et al., 2020; Feng et al., 2021; Xi et al., 2022; Chen et al., 2023), specifically at one month after registering for a dialysis catastrophic illness card (Chen et al., 2023). Based on the fact that dialysis needs to be performed regularly (typically three times a week) and dialysis centers in Taiwan are easily accessible (Chen et al., 2023). We identified 129,381 patients as catastrophic illness cases with over 183 days of dialysis. Exclusions were applied for missing age records, individuals under 18, unknown sex, residence in areas without air-quality monitoring, and lack of ambient particulate matter measurements in their residential zones. The final nationwide cohort comprised 34,088 individuals (Chen et al., 2023).

2.3 Exposure Measurement and Study Outcome

For all dialysis patients included in this investigation, we determined the average daily concentrations of ambient PM₁₀ and various gaseous air pollutants (NO₂, CO, SO₂) through the following process: Initially, we gathered hourly measurements from the TAQMD based on the 3-digit zip codes corresponding to the patients’ residential locations. Subsequently, we calculated the average 24-hour concentrations of these air pollutants for all days throughout the follow-up period. Finally, we established the mean daily concentrations of both PM₁₀ and gaseous air pollutants over the follow-up period. The primary outcome of interest in this study was all-cause mortality. Each patient, upon initiating maintenance dialysis for a period exceeding 183 days, was monitored until either their death or 31 December, 2013. The presence of a death record in the Catastrophic Illness registry or a patient’s withdrawal from the NHI program served as the criteria for defining death. In Taiwan, the primary reason for withdrawal from the NHI program is death, especially for individuals with catastrophic illness whose high medical expenditures were nearly fully covered by NHI (Wu et al., 2012). Less common reasons include permanent emigration, being missing for more than 6 months, or being incarcerated for more than 6 months (Chung et al., 2022; Ho et al., 2022).

2.4 Baseline Characteristics and Confounding Factors

Several fundamental traits of the study participants at the index date were examined as potential confounding factors for the primary outcome and were incorporated into our analysis. Individual-level factors were extracted from the NHIRD, encompassing demographic aspects (age, sex) and health-related factors such as hypertension, diabetes mellitus, coronary artery disease, heart failure, stroke, chronic obstructive pulmonary disease, asthma, malignancy, and major depression. Regarding zip code-level factors, we took into account monthly insurance salary and the urbanization level of the residential area. Urbanization levels were classified into three tiers based on the original classification raised by Liu et al. (2006), considering factors such as percentage of elderly residents, percentage of agricultural population, medical resource availability, and education level (Liu et al., 2006).

2.5 Statistical Analysis

Concerning baseline characteristics, we utilized analysis of variance to examine differences in means for continuous variables (e.g., age) among dialysis patients with varying long-term ambient PM₁₀ exposures. To evaluate disparities in the distribution proportions of categorical variables (e.g., sex, the presence of comorbidities, and levels of monthly salary), we utilized Pearson’s chi-square test. Patients were sorted into quartiles based on PM₁₀ exposure from low to high. To investigate the association between mortality in dialysis patients and long-term PM₁₀ exposure, we utilized multivariate Cox proportional hazard models. The impact of each IQR-µg m⁻³ increase in PM₁₀ on the mortality risk in dialysis patients was calculated. Four models were formulated to adjust for confounding baseline characteristics: a) an unadjusted model, b) Model I adjusting for
age and sex, c) Model II adjusting for all individual-level attributes (e.g., age at dialysis initiation, sex, specific comorbidities), and d) Model III additionally adjusting for zip-code level factors (monthly insurance salary, urbanization level of residence). To illustrate the concentration-response relationship between PM$_{10}$ and mortality in dialysis patients, restricted cubic spline analysis was employed. Additionally, we explored the influence of gaseous air pollutants on the PM$_{10}$-mortality relationship through two-pollutant scenarios based on PM$_{10}$. Potential modifications of the PM$_{10}$ effect on mortality through significant baseline characteristics such as age, gender, diabetes, hypertension, and monthly salary were also investigated by stratification analyses. All statistical analyses were conducted using IBM SPSS Statistics 22, and a significance level of $p < 0.05$ was applied to all tests in the study.

2.6 Ethics
This study was granted approval by the Research Ethics Review Committee of New Taipei City Hospital, and the certificate of approval was issued under protocol No. 108001-N.

3 RESULTS

3.1 Study Population Characteristics
This study included a total of 34,088 adult dialysis patients residing in areas with recorded ambient PM$_{10}$ measurements. The average follow-up duration was 6.91 years, with a median follow-up of 6.22 years. The cohort’s average age at enrollment was 58.26 years, with 51% being female. Long-term average ambient PM$_{10}$ exposure levels varied from 14.97 to 118.74 µg m$^{-3}$, with a mean of 53.99 µg m$^{-3}$ and a median of 50.90 µg m$^{-3}$. Categorizing the study population based on ascending order of PM$_{10}$ exposure concentration, Quartile I (Q1) comprised 8,648 individuals exposed to a mean PM$_{10}$ ranging from 14.97 to 43.94 µg m$^{-3}$. Quartile II (Q2) included 8,625 individuals exposed to a mean PM$_{10}$ ranging from 43.94 to 50.90 µg m$^{-3}$. Quartile III (Q3) consisted of 8,671 individuals exposed to a mean PM$_{10}$ ranging from 50.90 to 65.60 µg m$^{-3}$, while Quartile IV (Q4) encompassed 8,144 individuals exposed to a mean PM$_{10}$ ranging from 65.60 to 118.74 µg m$^{-3}$ (Table 1).

Significant disparities were observed in both personal-level characteristics and post-code level characteristics across quartiles of patients with diverse ambient PM$_{10}$ exposure. Upon closer examination, participants in the lowest quartile (Q1) of PM$_{10}$ exposure exhibited several distinct characteristics. They tended to be older and had a higher prevalence of diabetes, hypertension, coronary artery disease, stroke, heart failure, chronic obstructive pulmonary disease, asthma, and major depression. Additionally, they demonstrated a higher percentage of lower monthly incomes. Concerning their residential areas, Q1 participants resided in areas with more favorable urbanization levels compared to other groups, with a total of 89.9% residing in areas classified within the highest two urbanization levels (Table 1). Furthermore, our study revealed that among adult dialysis patients with long-term PM$_{10}$ exposure, those who were older, male, with the comorbidities examined in this study, and lower monthly income were at a higher risk of mortality (Supplementary Table S1).

3.2 Association between Air Pollutants and Mortality
We examined the correlation between average PM$_{10}$ exposure and mortality risk among all participants in the cohort during the follow-up period. Our analysis revealed that each IQR increase in mean PM$_{10}$ concentration (i.e., 21.66 µg m$^{-3}$) was associated with a 3.0–13.2% rise in the risk of mortality across different models, incorporating stepwise adjustments with individual-level and zip-code level baseline characteristics (unadjusted model, model I, model II, and model III; Table 2). In the restricted cubic spline analysis, accounting for all confounding factors (model III), we identified a non-linear relationship between long-term mean PM$_{10}$ concentration and hazard ratios (HRs) of mortality among dialysis patients, with a statistically significant nonlinearity ($p < 0.001$). Our findings revealed an initial gradual decrease in mortality risk up to approximately 43 µg m$^{-3}$ of PM$_{10}$ exposure, followed by a gradual increase up to around 63 µg m$^{-3}$. Beyond this level, there was a more pronounced rise in mortality risk, continuing up to the 118.74 µg m$^{-3}$.
level of PM$_{10}$ exposure (Fig. 1). Additionally, we calculated HRs for PM$_{10}$-associated mortality in two-pollutant scenarios, considering gaseous air pollutants (NO$_2$, CO, SO$_2$). The findings consistently indicated a notable correlation between PM$_{10}$ and mortality, even when accounting for exposure factors.

**Table 1. Baseline characteristics of dialysis patients across different groups of mean PM$_{10}$ exposure by quartile.**

<table>
<thead>
<tr>
<th>Mean PM$_{10}$ ($\mu$g m$^{-3}$) exposure during follow-up &amp; Case No. (N)</th>
<th>Quartile I (N = 8648)</th>
<th>Quartile II (N = 8625)</th>
<th>Quartile III (N = 8671)</th>
<th>Quartile IV (N = 8144)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at enrollment (mean ± SD, years)</td>
<td>59.24 ± 14.74</td>
<td>57.61 ± 14.73</td>
<td>58.29 ± 14.64</td>
<td>57.88 ± 13.88</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Follow-up duration (mean ± SD, years)</td>
<td>6.27 ± 3.71</td>
<td>7.34 ± 3.71</td>
<td>6.91 ± 3.65</td>
<td>7.11 ± 3.57</td>
<td>0.135</td>
</tr>
<tr>
<td>Sex, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>4340 (50.2)</td>
<td>4395 (51.0)</td>
<td>4409 (50.8)</td>
<td>4234 (52)</td>
<td>0.135</td>
</tr>
<tr>
<td>male</td>
<td>4308 (49.8)</td>
<td>4230 (49.0)</td>
<td>4262 (49.2)</td>
<td>3910 (48)</td>
<td>0.135</td>
</tr>
<tr>
<td>Comorbidities, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5027 (58.1)</td>
<td>4533 (52.6)</td>
<td>4694 (54.1)</td>
<td>4392 (53.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7359 (85.1)</td>
<td>7142 (82.8)</td>
<td>7128 (82.2)</td>
<td>6777 (83.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CAD</td>
<td>4176 (48.3)</td>
<td>3843 (44.6)</td>
<td>4048 (46.7)</td>
<td>3496 (42.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>2549 (29.5)</td>
<td>2335 (27.1)</td>
<td>2506 (28.9)</td>
<td>2197 (27.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Heart failure</td>
<td>3155 (36.5)</td>
<td>2823 (32.7)</td>
<td>2861 (33.0)</td>
<td>2256 (27.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>COPD</td>
<td>2414 (27.9)</td>
<td>2195 (25.4)</td>
<td>2359 (27.2)</td>
<td>2367 (29.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Asthma</td>
<td>1702 (19.7)</td>
<td>1480 (17.2)</td>
<td>1534 (17.7)</td>
<td>1269 (15.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Major depression</td>
<td>210 (2.4)</td>
<td>161 (1.9)</td>
<td>165 (1.9)</td>
<td>189 (2.3)</td>
<td>0.019</td>
</tr>
<tr>
<td>Malignancy</td>
<td>1108 (12.8)</td>
<td>1033 (12.0)</td>
<td>1085 (12.5)</td>
<td>978 (12.0)</td>
<td>0.272</td>
</tr>
<tr>
<td>Zip-code level factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Monthly salary, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 43,900</td>
<td>503 (5.8)</td>
<td>490 (5.7)</td>
<td>386 (4.5)</td>
<td>390 (4.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>31,800–43,900</td>
<td>311 (3.6)</td>
<td>323 (3.7)</td>
<td>270 (3.1)</td>
<td>269 (3.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>19,200–31,800</td>
<td>1299 (22.3)</td>
<td>2097 (24.3)</td>
<td>2628 (30.3)</td>
<td>3040 (37.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>&lt; 19,200</td>
<td>5905 (68.3)</td>
<td>5715 (66.3)</td>
<td>5387 (62.1)</td>
<td>4445 (54.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Urbanization level of residence area, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>high</td>
<td>2699 (31.2)</td>
<td>3800 (44.1)</td>
<td>1809 (20.9)</td>
<td>297 (3.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>moderate</td>
<td>5078 (58.7)</td>
<td>3492 (40.5)</td>
<td>4765 (55.0)</td>
<td>4853 (59.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>low</td>
<td>871 (10.1)</td>
<td>1333 (15.4)</td>
<td>2097 (24.1)</td>
<td>2994 (36.8)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

SD = standard deviation; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease.

**Table 2. Relationship between PM$_{10}$ and all-cause mortality in adult dialysis patients (single-pollutant scenario).**

<table>
<thead>
<tr>
<th>Unadjusted</th>
<th>HR (95% CI)</th>
<th>P for slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model I$^a$</td>
<td>1.304 (1.004–1.606)</td>
<td>0.027</td>
</tr>
<tr>
<td>Model II$^b$</td>
<td>1.089 (1.057–1.121)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Model III$^c$</td>
<td>1.120 (1.088–1.154)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

HR: hazard ratio for mortality by every IQR (21.66 $\mu$g m$^{-3}$) increase of ambient PM$_{10}$. P for slope indicated the p effect of per IQR increase of ambient PM$_{10}$.

$^a$ Model I: adjusted for age, sex.

$^b$ Model II: adjusted for age, sex, comorbidities (diabetes, hypertension, coronary artery disease, stroke, heart failure, chronic obstructive pulmonary disease, asthma, major depression, malignancy).

$^c$ Model III: adjusted for age, sex, comorbidities, monthly insurance salary, urbanization level of residential area.
levels of other air pollutants. Specifically, among dialysis patients, an increase of one IQR in PM$_{10}$ concentration led to a 7.1%–13.1% increase in mortality across different two-pollutant scenarios (Fig. 2). Moreover, in the two-pollutant scenario, we observed that NO$_2$ increases mortality more than PM$_{10}$. For every IQR increase in the mean concentration, it leads to a 14.8% increase in mortality risk, compared to a 7.1% increase caused by the latter (Fig. 2).

### 3.3 Stratification Analysis
We conducted a stratification analysis to investigate potential modifications in the effect of PM$_{10}$ on mortality risk based on age, gender, diabetes mellitus, hypertension, and monthly income. Our findings showed that an IQR increase in PM$_{10}$ exposure resulted in a significant increase in HRs for mortality in both patients aged 65 and over and their younger counterparts. In contrast to the younger cohort, the older group displayed a slightly higher increase in HR (HR 1.15 vs. HR 1.12), although this difference did not attain statistical significance ($p$ for interaction = 0.79). Regarding sex, an IQR increase in PM$_{10}$ exposure led to a significant increase in mortality risk for both male and female patients. Notably, the modification effect was significantly stronger in males (HR 1.19 vs. HR 1.07; $p$ for interaction < 0.001). Diabetes mellitus and hypertension are the two most prevalent primary diseases among ESRD patients. We observed that an IQR increase in PM$_{10}$ exposure led to a significant increase in HRs for mortality in both dialysis patients with and without diabetes (HR 1.10 vs. HR 1.19). Nevertheless, the extent of HR increase did not exhibit a significant difference between dialysis patients with diabetes and those without ($p$ for interaction = 0.29), despite the fact that the latter group faced a higher increase in mortality risk. Similarly, an IQR increase in PM$_{10}$ exposure resulted in a significant increase in HRs for mortality in both dialysis patients with and without hypertension (HR 1.13 vs. HR 1.18). However, akin to diabetes, the degree of HR increase did not display a significant difference between dialysis patients with hypertension and those without ($p$ for interaction = 0.44), even though the non-hypertension group exhibited a greater rise in mortality risk. In terms of the modification effect of monthly income, we found that patients with lower monthly incomes (< 19,200 NTD) exhibited a higher mortality risk increase per IQR increase in PM$_{10}$ exposure compared to their counterparts. However, the difference in the magnitude of HR increase did not reach statistical significance ($p$ for interaction = 0.53) (Fig. 3).
Fig. 2. Associations between PM$_{10}$ and mortality risk among adult dialysis patients in two-pollutant scenarios.

Fig. 3. Stratified analyses of the association between PM$_{10}$ and mortality among dialysis patients. * All of the stratified analyses have been adjusted for the covariates in model III (i.e., age, sex, comorbidities, monthly salary, and urbanization level of living area), with the exception of the stratified variables themselves.
4 DISCUSSION

4.1 Relationship between Ambient PM$_{10}$ Concentration and Mortality Risk

This retrospective cohort study used two nationwide electronic databases to investigate the impact of air pollutants exposure on mortality among 34,088 adult patients who initiated dialysis between 2000 and 2013. It provides a comprehensive examination of the relationship between PM$_{10}$ and mortality risk within the Asian dialysis population, while also assessing the combined effects of PM$_{10}$ and various gaseous air pollutants (NO$_2$, CO, SO$_2$) on mortality risk.

Our study uncovered that each IQR increase in long-term ambient PM$_{10}$ exposure is linked to a 13.2% higher mortality risk in adult dialysis patients. Furthermore, this association persists even when incorporating gaseous air pollutants (NO$_2$, CO, SO$_2$) into the analysis in two pollutant scenarios. These findings align with results from previous studies (Lin et al., 2015; Jung et al., 2020; Kim et al., 2021). Jung et al. (2020) demonstrated a significant relationship between mortality risk in the dialysis population and long-term exposure to PM$_{10}$, NO$_2$, and SO$_2$, particularly among elderly patients in metropolitan areas. However, the study’s representativeness might be limited due to its focus on hospital-associated dialysis centers. Kim et al. (2021) observed a noteworthy correlation between prolonged exposure to PM$_{10}$ and all-cause mortality in kidney transplant recipients. The findings indicated a 9% escalation in mortality risk for each 1 µg m$^{-3}$ increase in PM$_{10}$ concentration. Moreover, we observed that NO$_2$ increases mortality more than PM$_{10}$ does in dialysis patients. This finding is in line with some previous studies (Lin et al., 2015; Jung et al., 2020). Jung’s study found that every IQR increase of NO$_2$ concentration increases mortality risk more than PM$_{10}$ in most subgroup analyses among hemodialysis patients (Jung et al., 2020). Lin’s study noted that high environmental NO$_2$ significantly increases two-year mortality, while PM$_{10}$ has no significant impact on mortality in patients undergoing peritoneal dialysis. Specifically, 5 out of 10 patients who died from infection were attributed to pneumonia, with all 5 patients with pneumonia exposed to high environmental NO$_2$ (Lin et al., 2015). The stronger impact on pneumonia development caused by NO$_2$ exposure than that caused by PM$_{10}$ observed in Wang’s study might explain the differing impact on mortality observed between NO$_2$ and PM$_{10}$ in our study (Wang et al., 2023). Our research innovation stems from the representative nature of our study cohort, which utilized nationwide population-based data. This enhances the generalizability of our results in East Asia compared to the aforementioned study by Jung et al. (2020), which exclusively utilized patient data from hospital-associated dialysis centers. As far as we are aware, our study is the first ever nationwide population-based cohort investigation aiming to explore the impact of prolonged PM$_{10}$ exposure on mortality risk among dialysis patients. Its potential for considerable contributions to public health, particularly in East Asia, is noteworthy. Various studies have proposed biological mechanisms for how inhaled particulate matter affects human health. Inhaled PM or the inflammatory mediators it induces in the lung can enter the systemic circulation, causing systemic inflammation, metabolic activation, oxidative stress, vascular endothelial injury, and genotoxicity, ultimately leading to kidney injuries (Alfaro-Moreno et al., 2002; Feng et al., 2016; Cho et al., 2018; Afzar et al., 2019; Zhang et al., 2021).

Moreover, utilizing restricted cubic spline analysis, our study precisely delineated a non-linear association between PM$_{10}$ levels and the hazard ratio of mortality among adult dialysis patients. Furthermore, adverse impacts on mortality were evident only when the average long-term PM$_{10}$ exposure exceeded a specific threshold of 43 µg m$^{-3}$. This finding aligns with a previous Taiwanese study that demonstrated a similar concentration-response relationship between long-term PM$_{2.5}$ exposure and mortality risk among dialysis patients, where an increase in mortality was observed when PM$_{2.5}$ concentration exceeded 26 µg m$^{-3}$ (Chen et al., 2023). Similarly, Feng’s study identified a non-linear association between PM$_{2.5}$ and mortality risk in the elderly dialysis population in the United States, with an elevation in mortality risk occurring when PM$_{2.5}$ concentration surpassed 12 µg m$^{-3}$ (Feng et al., 2021). One potential explanation for the non-linear relationship between PM and mortality risk is that the initial inflammatory effect triggered by low levels of PM might be relatively minor compared to the already heightened inflammation experienced by patients with ESRD (Chen et al., 2023). However, as PM$_{10}$ exposure reaches a certain threshold (i.e., 43 µg m$^{-3}$), it could significantly exacerbate the inflammatory response, becoming substantial enough to
negatively affect the survival of adult dialysis patients. Furthermore, this negative effect on survival sharply intensifies with even higher PM$_{10}$ exposure levels (i.e., $>63$ $\mu g$ m$^{-3}$). Additionally, we propose that at lower PM$_{10}$ levels (i.e., $<43$ $\mu g$ m$^{-3}$), undisclosed patient characteristics leading to residual confounding effects may play a more significant role in influencing mortality risk among dialysis patients than the direct impact of PM$_{10}$ itself.

4.2 Baseline Characteristics’ Effects on PM$_{10}$-Mortality Relationship

Our observations revealed that the risk of mortality among adult dialysis patients exposed to prolonged ambient PM$_{10}$ significantly increased with age, in males, in individuals with the specific comorbidities under focus, and with lower monthly income.

In our subgroup analysis, we observed that patients aged 65 and older had a higher increase in mortality risk per IQR increase in PM$_{10}$ compared to their younger counterpart, although this difference did not reach statistical significance. This finding is consistent with previous evidence indicating that dialysis patients in older age groups tend to be more susceptible to ambient particulate matter exposure compared to younger age groups (Jung et al., 2020; Feng et al., 2021; Xi et al., 2022; Chen et al., 2023). Our study also revealed that an IQR increase in PM$_{10}$ concentration heightened the mortality risk in both male and female dialysis patients. Notably, male patients experienced a significantly higher increase in mortality risk. This finding aligns with prior studies indicating a greater vulnerability of male patients to particulate matter exposure in terms of mortality risk compared to female patients (Kuźma et al., 2020; Xia et al., 2021; Chen et al., 2023). The higher mortality risk for men may be attributed to particulate matter’s interaction with male-specific factors, such as lifestyle, occupation, or male hormones (Chen et al., 2023). Additionally, we categorized dialysis patients based on the presence of the most prevalent primary diseases: diabetes and hypertension. We observed that an IQR increase in PM$_{10}$ concentration resulted in a larger increase in mortality risk among dialysis patients without diabetes compared to those with diabetes, although this difference was not statistically significant. This finding aligns with previous studies indicating that non-diabetic patients tend to have higher HR estimates for the relationship between particulate matter exposure and mortality (Pinault et al., 2018; Xi et al., 2022; Chen et al., 2023). Given that diabetes is associated with an elevated inflammatory state (Xie and Du, 2011; Tsalamandris et al., 2019), the impact of particulate matter-induced pro-inflammatory effects on mortality risk among diabetic dialysis patients may be relatively modest compared to those without pre-existing diabetes (Chen et al., 2023). Furthermore, we observed that an IQR increase in PM$_{10}$ concentration led to a greater increase in mortality risk among dialysis patients without hypertension compared to those with hypertension, although this difference did not reach statistical significance. It’s worth noting that hypertension itself is a risk factor for all-cause mortality, particularly through cardiovascular events (Aune et al., 2021; Martín-Fernández et al., 2023). Therefore, the impact of particulate matter-induced mortality among hypertensive dialysis patients may also be relatively modest compared to those without pre-existing hypertension. Finally, our study showed that the magnitude of the increase in mortality risk did not significantly differ between the higher ($\geq19,200$ NTD) and lower ($<19,200$ NTD) monthly income subgroups, even though the latter subgroup tended to be more susceptible to every IQR increase in PM$_{10}$. Our findings differed from previous studies that suggested a significantly higher magnitude of the increase in mortality risk for each unit of elevation in air pollution in populations with lower socioeconomic status (Forastiere et al., 2007; Blanco-Becerra et al., 2014; Boing et al., 2022). This difference indicates that while income is an important factor in measuring socioeconomic status, relying solely on income when conducting research may introduce a certain degree of bias.

4.3 Strengths and Limitations

Our study boasts several notable strengths. Firstly, it is a cohort study utilizing nationwide population-based big data to investigate the association between long-term PM$_{10}$ exposure and mortality. This approach not only allowed us to consider significant personal baseline characteristics that could potentially influence the mortality of dialysis patients but also empowered us to conduct subgroup analyses within this cohort. Therefore, it has enhanced the reliability and generalizability of the research results. Secondly, our study examined the PM$_{10}$-mortality association not only in a single-pollution scenario but also in pairs of two-pollutant scenarios built on a PM$_{10}$ foundation.
These approaches helped us identify and address potential confounding effects on the PM\textsubscript{10}-mortality association among dialysis patients resulting from other gaseous air pollutants, further enhancing the strength of our study’s findings. Thirdly, our study is pioneering in examining the impact of PM\textsubscript{10} exposure on mortality risk among dialysis patients through the application of restricted cubic analysis. This approach unveiled a nonlinear association between PM\textsubscript{10} exposure and mortality, with a positive PM\textsubscript{10}-mortality association emerging when mean PM\textsubscript{10} levels approached a threshold of 43 µg m\textsuperscript{-3}. The concentration-response relationship demonstrated here strengthens the link between PM\textsubscript{10} and mortality among dialysis patients.

However, our study has several limitations. Firstly, the interpolation of ambient air pollutant concentrations (PM\textsubscript{10}, NO\textsubscript{2}, CO, SO\textsubscript{2}) from fixed-site monitoring stations to the 3-digit zip codes of study participants’ residential areas may introduce misclassification of PM\textsubscript{10} exposure, particularly when these 3-digit zip codes cover large administrative regions. Variations in PM\textsubscript{10} exposure within zip codes could arise from various complex factors, including the presence of green spaces around residences (Meo et al., 2021), levels of outdoor activities (Jung et al., 2019), the dispersion characteristics of PM\textsubscript{10} emitted by road transport near participants’ homes (Pospisil et al., 2020), traffic patterns around patients’ residences that influence particle number size distribution (Chen et al., 2024), and the distance between patients’ residence and the coordinated monitoring station. In addition, fixed monitoring stations do not provide information about specific PM components or sources relevant to health effects, which might also lead to potential exposure misclassification. However, Jung’s study has shown a significant and consistent correlation between PM\textsubscript{10} exposure and mortality risk among ESRD patients, irrespective of the distance between patients’ residences and air-quality monitoring stations within a 10 km radius (Jung et al., 2020). Moreover, it is worth noting that non-differential misclassification of exposure usually leads to bias towards the null, resulting in conclusions of irrelevance between exposure and outcome (Jepsen et al., 2004). Against this backdrop, our study still demonstrates a positive association between long-term PM\textsubscript{10} exposure and mortality in dialysis patients, indicating the robustness of the results. Secondly, our measurement of ambient PM\textsubscript{10} concentrations from regional monitors does not account for indoor PM\textsubscript{10} effects. However, it has been suggested that indoor PM pollution originating from outdoor sources significantly contributes to increased mortality associated with outdoor PM exposure (Ji and Zhao, 2015). Thirdly, the consideration of time-varying PM\textsubscript{10} concentrations and other time-dependent factors was precluded by our limited access, which only encompassed zip codes and baseline characteristics of patients at the index time. This limitation could have led to information bias in our research. Fourthly, the NHIRD lacks physical information, personal health behaviors, and biochemistry data related to dialysis adequacy. These omissions also have the potential to induce bias in the assessment of the association between PM\textsubscript{10} exposure and mortality risk among dialysis patients. Lastly, because our study aimed to explore the impact of ‘long-term PM\textsubscript{10} exposure’ on the mortality of dialysis patients, our results might not extrapolate to the vulnerable dialysis patients who passed away in less than 183 days after initiating maintenance dialysis.

5 CONCLUSION

Our study revealed a significant association between long-term ambient PM\textsubscript{10} exposure and mortality risk among adult dialysis patients. This association remained robust even when considering two-pollutant scenarios centered on PM\textsubscript{10}. A non-linear concentration-response relationship between PM\textsubscript{10} and mortality was noted, with mortality risk increasing when mean PM\textsubscript{10} exceeded a certain threshold (43 µg m\textsuperscript{-3}). These findings strongly suggest a positive association between ambient PM\textsubscript{10} levels and mortality among dialysis patients. Additionally, male dialysis patients faced a greater rise in mortality risk with each PM\textsubscript{10} increase compared to their counterparts. The results of this study could be invaluable for policymakers seeking to mitigate the public health impact caused by air pollution, especially in vulnerable populations.

ACKNOWLEDGEMENTS

We would like to thank Taiwan’s Environmental Protect Administration for providing public
data (TAQMD). We also appreciate the important contributions of Mr. Tein-Ling Tsai and Mr. Xing-Fang Lin to data mining and data management, as well as Mr. Yen-Chang Chen for his assistance with English revision.

ADDITIONAL INFORMATION AND DECLARATIONS

Funding

This research did not receive any specific grants from public, commercial, or not-for-profit finding agencies.

Declaration of Competing Interest

We declare that all authors have no competing interests.

Supplementary Material

Supplementary material for this article can be found in the online version at https://doi.org/10.4209/aaqr.240028

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