Association of Short-term Particulate Matter Exposure with Suicide Death Among Major Depressive Disorder Patients: A Time-Stratified Case-Crossover Analysis

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Research Article

Keywords: particulate matter (PM), suicide, major depressive disorder (MDD) , National Health Insurance Service (NHIS)

Posted Date: March 22nd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-290077/v1

Abstract

Objective: There is growing evidence that suggests a potential association between particulate matter (PM) and suicide. However, it is unclear that PM exposure and suicide death among major depressive disorder (MDD) patients, a high-risk group for suicide.

Methods: We investigated the risk of suicide among 1,046,169 newly-diagnosed MDD patients from 2004 to 2015 within the Korean National Health Insurance Service (NHIS) database. We identified 3,372 suicide cases from January 1, 2015, to December 31, 2017, within the death statistics database of the Korean National Statistical Office. PMs with diameter less than 2.5 μm (PM2.5), less than 10 μm (PM10), and 2.5 μm to 10 μm (PM2.5-10) were considered, which were provided from the National Ambient Air Monitoring System in South Korea. Time-stratified case-crossover analysis was performed to investigate the association of particulate matter exposure to suicide events.

Results: The risk of suicide was significantly high upon the high level of exposure to PM2.5-10, PM10 on lag 1 (*p* for trend = 0.044, 0.035, respectively). A similar association was observed in the multi-day lag model (lag 0-3). Increasing exposure to PM 2.5 was not associated with increased suicide risk.

Conclusions: Short-term exposure to a high level of PM2.5-10 and PM10 was associated with an elevated risk for suicide among MDD patients, while PM2.5 did not. There is a clear dose-response relationship between short-term coarse particle exposures with suicide death among Major Depressive Disorder patients. This result will be used as an essential basis for consideration when establishing an air pollution alarm system and implementing a suicide prevention program for reducing adverse health outcomes by PM.

Introduction

There has been a significant increase in suicide cases in recent decades, posing a severe public health problem worldwide[1,2]. Globally, it is the second leading cause of death among young adults[3] and approximately 800,000 people suicide every year[4]. Various social and environmental factors affect suicide, including culture, gender, age, socioeconomic status, as well as meteorological factors[3,5,6]. The risk of suicide is even higher with underlying disease[7–9], especially with a psychiatric disorder[10]. Previous study has noted that patients with depression or other mood disorders have a 20-fold increased suicide risk compared to the general population[8]. Meanwhile, depression is becoming increasingly burdensome, and the number of incident cases of depression worldwide increased from 172 million in 1990 to 258 million in 2017, representing an increase of 49.9%[11]. Considering this trend, identifying and managing risk factors affecting suicide in major depressive disorder (MDD) patients is crucial.

Previous studies have shown that long-term exposure to particulate matter (PM) might increase the risk of depression through chronic inflammation and brain structure changes[12,13]. Additional studies were done to evaluated the effect of short-term exposure to PM and noted that it aggravates several

psychiatric symptoms, including suicide attempts, increases emergency center visits, and hospitalization[14,15]. Based on these findings, recent studies have investigated the association of short-term exposure to PM with suicide and reported an elevated risk for suicide in the general population[15–18].

However, this association of PM short-term exposure and suicide has not been explored in the depressive population. Since MDD patients are at high risk for suicide and vulnerable to short-term mood swings that PM might aggravate, a further investigation among MDD patients is merited. Therefore, we aimed to assess the effect of short-term exposure to PM on the risk of suicide in newly diagnosed MDD patients in Korea, using the National Health Insurance Service (NHIS) database.

Methods

Study population

The study population was derived from the Korean NHIS database. The NHIS is a single-payer of the Korean healthcare system and provides universal health insurance for 97% of Korean citizens [19]. The NHIS collects all forms of claimed healthcare service data, which includes outpatient visits, hospital admissions, emergency department usages, and pharmaceutic drug prescriptions. The NHIS provides collected data for research purposes, and multiple epidemiologic studies using this data have demonstrated its validity [20].

We enrolled 1,046,169 newly-diagnosed major depressive disorder (MDD) patients from the NHIS database who was diagnosed between January 1, 2004, to December 31, 2015. The diagnosis of MDD was defined as the use of anti-depressant medication with diagnosis codes of MDD (F32, F33) from the International Classification of Diseases, Tenth Revision (ICD-10) and those who diagnosed bipolar disease (ICD-10 code F31) were excluded. We followed the study participants from their initial diagnosis date of MDD until December 31, 2017.

Among 1,046,169 newly-diagnosed MDD patients, we identified 3,372 suicide cases after January 1, 2015. Suicide events before January 1, 2015 were excluded in the main analysis due to the lack of PM2.5 data before 2015. The suicide events were defined by death due to intentional self-harm (ICD-10 codes X60-X84). 51 suicide cases were excluded from the analysis due to missing value for PM2.5 data and average daily temperature. Total 3,321 suicide cases were included in the main analysis.

Particulate matter exposure

The NHIS database also provides demographic information of the participants, which include the residential district code. Using the code, we have linked the residential district to the daily ambient level of PM10 and PM2.5 which were provided from the National Ambient Air Monitoring System in South Korea. The concentration of the coarse particle (PM2.5 -10) was calculated by subtraction of the PM2.5 value from that of PM10.

Statistical analysis

We used a time-stratified case-crossover analysis study design to investigate the association of particulate matter exposure with suicide events. The case-crossover study is a validated study design to assess the short-term effect of the exposure. Each patient serves as his or her own control, thereby time-invariant individual variables such as age, sex, and individual comorbidities, are automatically controlled. Among several case-crossover designs, time-stratified case-crossover design yielded better results with least bias on previous systemic reviews [21,22]. We used single-day lag models to investigate the effect of PM exposure on suicide from lag0 (the day of the suicide event) to lag3 (3 days prior to the suicide event). Also, we used a multi-day lag model (lag0-3) to assess the effect of short-term cumulative PM exposure on suicidality. The control days were matched by other days with the same day of the week, from the same calendar month. The PM value of each case day (lag0 to lag3, and lag0-3) and control days were divided into approximate quartile. The conditional logistic regression was used to estimate the adjusted odds ratios (aORs) and 95% confidence intervals (CIs) of each quartile compared to the 1st quartile of the PM10, PM2.5, and coarse particle (PM2.5-10) exposure, which represented the least exposure to the PM. Stratified analysis according to subgroups of age, sex, household income, and duration of MDD were conducted to examine the effect modification. Additional stratified analysis according to the individual's physical activity and alcohol consumption were conducted on 1,606 suicide cases which occurred among MDD patients who underwent health examinations within 2 years before the suicide event. All statistical tests were two-sided manner with a p-value of less than 0.05. Data collection and statistical analyses were performed using SAS Enterprise Guide 7.1 (SAS Institute Inc., Cary, NC).

Ethical consideration

This study was conducted in accordance with the Declaration of Helsinki, and the study protocol approved by the Institutional Review Board (IRB) at the National Center for Mental Health, Seoul, Korea (IRB number: 116271-1027-57).The requirement for informed consent was waived by IRB at National Center for Mental Health since the patient information was de-identified and anonymized according to South Korean personal data protection laws.

Results

The descriptive characteristics of the study population is depicted in Table 1. Among 3,321 suicide cases we have enrolled, 814, 825, 847 and 835 cases were allocated for the first, second, third, and fourth quartile of lag0 PM10 exposure respectively. The mean PM10 values of the suicide day on each quartile was 21.8, 35.3, 48.0, and 77.3 □/m3, respectively. Participants exposed to higher concentration of PM10 on the day of suicide (lag0) were more likely to be exposed to high PM2.5 concentration, but less concentration of coarse particle (PM2.5-10). The participants who were on the 4th quartile were more likely to had suicide event within 5 years of MDD diagnosis (*p* value = 0.040). However, the distribution of age, gender, household income, alcohol consumption and physical activity were not significantly different between study groups.

Table 1
Descriptive characteristics of study population.

	PM10 1st Quartile	PM10 2nd Quartile	PM10 3rd Quartile	PM10 4th Quartile	*p* value
N	814	825	847	835	
PM10 Range	4.0-29.5	29.5–41.0	41.0-55.4	55.4-494.7	
Lag0 PM10, □/m^3, mean (SD)	21.8 (5.7)	35.3 (3.3)	48.0 (4.1)	77.3 (33.9)	< 0.001
Lag0 PM2.5, □/m^3, mean (SD)	11.6 (4.1)	20.0 (4.4)	27.5 (6.1)	41.4 (13.4)	< 0.001
Lag0 PM2.5-10, □/m^3, mean (SD)	17.1 (9.1)	14.6 (10.7)	12.0 (10.0)	10.5 (8.1)	< 0.001
Age, years, mean (SD)	43.0 (6.1)	43.6 (6.1)	43.2 (5.9)	43.7 (6.0	0.107
Age, years, N (%)					0.202
20–39	258 (31.7)	226 (27.4)	255 (30.1)	234 (28.0)	
≥ 40	556 (68.3)	599 (72.6)	592 (69.9)	601 (72.0)	
Sex, N (%)					0.463
Men	438 (53.8)	459 (55.6)	482 (56.9)	447 (53.5)	
Women	376 (46.2)	366 (44.4)	365 (43.1)	388 (46.5)	
Household income, N (%)					0.736
1st (highest)	168 (20.6)	159 (19.3)	161 (19.0)	165 (19.8)	
2nd	160 (19.7)	175 (21.2)	181 (21.4)	193 (23.1)	
3rd	195 (24.0)	189 (22.9)	192 (22.7)	203 (24.3)	
4th (lowest)	291 (35.8)	302 (36.6)	313 (37.0)	274 (32.8)	
Disease duration, N (%)					0.040
< 5 years	421 (51.7)	463 (56.1)	496 (58.6)	472 (56.5)	
≥ 5 years	393 (48.3)	362 (43.9)	351 (41.4)	363 (43.5)	
Participants who underwent health examinations	395	399	405	407	
Alcohol intake, N (%)					0.172
No	155 (39.2)	160 (40.7)	162 (40.0)	188 (46.2)	

Acronym: N, number of participants; PM, particulate matter;

	PM10 1st Quartile	PM10 2nd Quartile	PM10 3rd Quartile	PM10 4th Quartile	*p* value
Yes	240 (60.8)	233 (59.3)	243 (60.0)	219 (53.8)	
Physical activity, N (%)					0.243
No	182 (46.1)	207 (52.7)	196 (48.4)	209 (51.4)	
Yes	213 (53.9)	186 (47.3)	209 (51.6)	198 (48.7)	
Acronym: N, number of participants; PM, particulate matter;					

Table 2 shows the association of PM10 exposure and completed suicide events among MDD patients. Compared to those who were exposed to the lowest concentration of PM10 on lag1 (a day before the suicide event), those who were exposed to highest concentration of PM10 on lag1 had higher odds of completed suicide (aOR 1.14, 95% CI 1.01–1.30). Furthermore, the risk of suicide increased upon the higher exposure to PM10 on lag1 (*p* for trend = 0.035). The similar association was observed on the multi-day lag model (lag0-3). Compared to MDD patients who were exposed to the least concentration of average PM10 on lag0-3, those who were exposed to the highest PM10 concentration had increased odds for suicide (aOR 1.18, 95% CI 1.03–1.36). Dose-responsive relationship of PM10 concentration on lag0-3 and suicide was also observed (*p* for trend 0.018).

Table 2
Association of PM10 exposure and suicide events among major depressive disorder patients.

		1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	P for trend
Lag0	Range	4.0-29.5	29.5–41.0	41.0-55.4	55.4-494.7	
	N	814	825	847	835	
	aOR (95% CI)	1.00 (reference)	1.03 (0.91–1.15)	1.06 (0.94–1.20)	1.05 (0.92–1.19)	0.442
Lag1	Range	2.0-29.6	29.6–41.6	41.7–56.2	56.2–309.0	
	N	813	810	832	866	
	aOR (95% CI)	1.00 (reference)	1.02 (0.91–1.14)	1.06 (0.94–1.20)	1.14 (1.01–1.30)	0.035
Lag2	Range	2.0-29.8	29.8–41.6	41.6–56.5	56.5-566.5	
	N	845	798	821	857	
	aOR (95% CI)	1.00 (reference)	0.93 (0.83–1.04)	0.97 (0.86–1.09)	1.06 (0.93–1.20)	0.314
Lag3	Range	3.7–30.0	30.0-41.5	41.5–56.3	56.3-584.2	
	N	806	804	879	832	
	aOR (95% CI)	1.00 (reference)	1.01 (0.90–1.13)	1.14 (1.01–1.28)	1.09 (0.95–1.24)	0.084
Lag0-3	Range	6.5–32.7	32.7–43.3	43.3–54.7	54.7-246.6	
	N	802	820	841	858	
	aOR (95% CI)	1.00 (reference)	1.05 (0.93–1.18)	1.11 (0.97–1.27)	1.18 (1.03–1.36)	0.018

Odds ratio estimated by conditional logistic regression adjusted for mean daily temperature.

Acronym: PM, particulate matter; N, number of participants; aOR, adjusted odds ratios; CI, confidence interval;

The association of PM2.5 exposure and suicide events on MDD patients is demonstrated in Table 3. While there was a trend toward mild increased odds for suicide on patients who were exposed to higher level of PM2.5 on lag1 and lag0-3, the association was not statistically significant (aOR 1.12, 95% CI 0.99–1.27; aOR 1.10, 95% CI 0.97–1.26). Also, the dose-responsive association of PM2.5 exposure and suicide were not statistically significant (*p* for trend 0.156, and 0.192, respectively).

Table 3
Association of PM2.5 exposure and suicide events among major depressive disorder patients.

		1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	P for trend
Lag0	Range	0.0-15.3	15.3–22.8	22.8–31.9	31.9–118.0	
	N	819	832	821	849	
	aOR (95% CI)	1.00 (reference)	1.01 (0.90–1.13)	1.00 (0.89–1.13)	1.05 (0.93–1.20)	0.495
Lag1	Range	1.0-15.5	15.5–23.0	23.0-32.3	32.4–120.0	
	N	712	839	805	865	
	aOR (95% CI)	1.00 (reference)	1.05 (0.94–1.18)	1.01 (0.89–1.13)	1.12 (0.99–1.27)	0.156
Lag2	Range	0.0-15.6	15.6–23.2	23.2–32.3	32.3–108.0	
	N	864	820	768	868	
	aOR (95% CI)	1.00 (reference)	0.93 (0.83–1.04)	0.86 (0.76–0.96)	1.02 (0.90–1.15)	0.936
Lag3	Range	0.0-15.6	15.6–23.0	23.0-32.5	32.5–113.0	
	N	795	820	870	836	
	aOR (95% CI)	1.00 (reference)	1.04 (0.93–1.17)	1.13 (1.00-1.27)	1.09 (0.96–1.23)	0.106
Lag0-3	Range	1.9–17.8	17.8–24.1	24.1–30.9	30.9-101.7	
	N	825	823	805	868	
	aOR (95% CI)	1.00 (reference)	1.00 (0.89–1.12)	0.97 (0.86–1.10)	1.10 (0.97–1.26)	0.192
Odds ratio estimated by conditional logistic regression adjusted for mean daily temperature.						
Acronym: PM, particulate matter; N, number of participants; aOR, adjusted odds ratios; CI, confidence interval;						

The association of coarse particle exposure and suicide events is depicted in Table 4. There were statistically significant dose-responsive associations of completed suicide with coarse particle exposure on lag1 and lag0-3 (*p* for trend 0.044, and 0.004, respectively). MDD patients who were exposed to highest concentration of coarse particle on lag0-3 (4th quartile) had higher odds for suicide (aOR 1.23, 95% CI 1.05–1.44), compared to those who were exposed to the lowest concentration of coarse particle (1st Quartile).

Table 4
Association of PM2.5-10 exposure and suicide events among major depressive disorder patients.

		1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	P for trend
Lag0	Range	0.0-12.1	12.1–16.8	16.8–23.8	23.8-425.9	
	N	810	810	860	841	
	aOR (95% CI)	1.00 (reference)	1.02 (0.91–1.14)	1.11 (0.98–1.26)	1.10 (0.95–1.26)	0.106
Lag1	Range	0.0-12.2	12.2–17.0	17.0–24.0	24.0-264.1	
	N	815	799	854	853	
	aOR (95% CI)	1.00 (reference)	0.99 (0.89–1.12)	1.10 (0.97–1.25)	1.13 (0.98–1.29)	0.044
Lag2	Range	0.0-12.1	12.1–17.0	17.0–24.0	24.0-505.6	
	N	824	812	836	849	
	aOR (95% CI)	1.00 (reference)	0.99 (0.88–1.11)	1.03 (0.91–1.17)	1.09 (0.95–1.25)	0.180
Lag3	Range	0.0-12.3	12.3–17.1	17.1–24.0	24.0-518.9	
	N	812	813	886	810	
	aOR (95% CI)	1.00 (reference)	1.01 (0.90–1.13)	1.14 (1.01–1.29)	1.03 (0.89–1.18)	0.354
Lag0-3	Range	0.0-13.1	13.1–17.6	17.6–23.8	23.8-208.3	
	N	783	825	876	837	
	aOR (95% CI)	1.00 (reference)	1.12 (0.99–1.27)	1.26 (1.10–1.44)	1.23 (1.05–1.44)	0.004
Odds ratio estimated by conditional logistic regression adjusted for mean daily temperature.						
Acronym: PM, particulate matter; N, number of participants; aOR, adjusted odds ratios; CI, confidence interval;						

Table 5 shows the results of the stratified analysis on the association of PM10 exposure and the suicidal events. The risk elevating effect of PM10 was prominent among MDD patients aged 40 years or older. Although the statistical significance tended to be attenuated most likely due to the reduce number of cases upon stratification, exposure to high concentration of PM10 on lag1 and lag0-3 had tendency to increase the risk for suicide among MDD patients in multiple subgroups.

Table 5
Association of PM10 exposure and suicide events among major depressive disorder patients according to subgroups.

		1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	P for trend
Age						
20–39						
Lag1	aOR (95% CI)	1.00 (reference)	1.02 (0.83–1.26)	0.90 (0.72–1.12)	0.94 (0.74–1.20)	0.438
Lag0-3	aOR (95% CI)	1.00 (reference)	1.04 (0.84–1.29)	1.07 (0.84–1.37)	1.02 (0.78–1.33)	0.865
≥ 40						
Lag1	aOR (95% CI)	1.00 (reference)	1.01 (0.88–1.16)	1.14 (0.99–1.32)	1.24 (1.06–1.45)	0.002
Lag0-3	aOR (95% CI)	1.00 (reference)	1.06 (0.92–1.22)	1.13 (0.97–1.32)	1.24 (1.06–1.48)	0.007
Sex						
Men						
Lag1	aOR (95% CI)	1.00 (reference)	1.01 (0.86–1.18)	1.03 (0.88–1.22)	1.13 (0.95–1.35)	0.158
Lag0-3	aOR (95% CI)	1.00 (reference)	0.99 (0.84–1.16)	1.06 (0.89–1.26)	1.12 (0.93–1.36)	0.179
Women						
Lag1	aOR (95% CI)	1.00 (reference)	1.03 (0.87–1.22)	1.10 (0.92–1.31)	1.16 (0.95–1.41)	0.112
Lag0-3	aOR (95% CI)	1.00 (reference)	1.13 (0.95–1.35)	1.18 (0.97–1.43)	1.26 (1.02–1.56)	0.039
Income						
High						
Lag1	aOR (95% CI)	1.00 (reference)	0.95 (0.79–1.13)	1.06 (0.88–1.28)	1.22 (1.00-1.50)	0.033
Lag0-3	aOR (95% CI)	1.00 (reference)	1.05 (0.87–1.26)	1.19 (0.97–1.46)	1.26 (1.01–1.58)	0.026

Odds ratio estimated by conditional logistic regression adjusted for mean daily temperature.

Acronym: PM, particulate matter; N, number of participants; aOR, adjusted odds ratios; CI, confidence interval;

		1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	P for trend
Low						
Lag1	aOR (95% CI)	1.00 (reference)	1.07 (0.92–1.24)	1.07 (0.910–1.25)	1.10 (0.93–1.30)	0.326
Lag0-3	aOR (95% CI)	1.00 (reference)	1.06 (0.90–1.23)	1.06 (0.89–1.26)	1.13 (0.94–1.36)	0.210
Disease duration						
< 5 years						
Lag1	aOR (95% CI)	1.00 (reference)	1.04 (0.89–1.22)	1.07 (0.91–1.26)	1.15 (0.97–1.37)	0.104
Lag0-3	aOR (95% CI)	1.00 (reference)	1.10 (0.94–1.30)	1.22 (1.02–1.45)	1.19 (0.98–1.44)	0.066
≥ 5years						
Lag1	aOR (95% CI)	1.00 (reference)	0.99 (0.83–1.17)	1.06 (0.88–1.26)	1.13 (0.93–1.38)	0.174
Lag0-3	aOR (95% CI)	1.00 (reference)	1.00 (0.83–1.19)	1.00 (0.82–1.21)	1.19 (0.96–1.48)	0.129
Alcohol						
No						
Lag1	aOR (95% CI)	1.00 (reference)	1.14 (0.87–1.48)	1.05 (0.79–1.39)	1.32 (0.98–1.77)	0.111
Lag0-3	aOR (95% CI)	1.00 (reference)	0.95 (0.72–1.24)	0.97 (0.72–1.30)	1.10 (0.80–1.51)	0.532
Yes						
Lag1	aOR (95% CI)	1.00 (reference)	1.03 (0.83–1.27)	1.08 (0.86–1.36)	1.20 (0.94–1.52)	0.139
Lag0-3	aOR (95% CI)	1.00 (reference)	1.11 (0.89–1.39)	1.43 (1.12–1.82)	1.34 (1.03–1.75)	0.011
Exercise						

Odds ratio estimated by conditional logistic regression adjusted for mean daily temperature.

Acronym: PM, particulate matter; N, number of participants; aOR, adjusted odds ratios; CI, confidence interval;

		1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	P for trend
No						
Lag1	aOR (95% CI)	1.00 (reference)	1.08 (0.85–1.38)	1.08 (0.84–1.38)	1.29 (0.99–1.67)	0.080
Lag0-3	aOR (95% CI)	1.00 (reference)	1.05 (0.82–1.34)	1.18 (0.90–1.54)	1.27 (0.95–1.69)	0.085
Yes						
Lag1	aOR (95% CI)	1.00 (reference)	1.05 (0.84–1.33)	1.05 (0.82–1.35)	1.20 (0.92–1.57)	0.203
Lag0-3	aOR (95% CI)	1.00 (reference)	1.04 (0.82–1.32)	1.26 (0.97–1.63)	1.21 (0.91–1.61)	0.106
Odds ratio estimated by conditional logistic regression adjusted for mean daily temperature.						
Acronym: PM, particulate matter; N, number of participants; aOR, adjusted odds ratios; CI, confidence interval;						

Finally, Table 6 depicted the association of coarse particle (PM2.5-10) and the risk of suicide according to subgroups. Similarly, the risk elevating associations were observed among various subgroups, although the statistical significance tended to be attenuated which was attributed to the decrease number of cases due to dividing the study populations into subgroups.

Table 6
Association of PM2.5-10 exposure and suicide events among major depressive disorder patients according to subgroups.

		1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	P for trend
Age						
20–39						
Lag1	aOR (95% CI)	1.00 (reference)	0.89 (0.72–1.10)	1.06 (0.84–1.33)	0.90 (0.70–1.16)	0.700
Lag0-3	aOR (95% CI)	1.00 (reference)	1.01 (0.80–1.26)	1.18 (0.91–1.53)	1.08 (0.81–1.44)	0.444
≥ 40						
Lag1	aOR (95% CI)	1.00 (reference)	1.05 (0.91–1.20)	1.22 (0.97–1.30)	1.24 (1.05–1.45)	0.008
Lag0-3	aOR (95% CI)	1.00 (reference)	1.17 (1.01–1.36)	1.29 (1.10–1.52)	1.30 (1.08–1.57)	0.004
Sex						
Men						
Lag1	aOR (95% CI)	1.00 (reference)	1.01 (0.86–1.18)	1.15 (0.97–1.35)	1.12 (0.93–1.34)	0.129
Lag0-3	aOR (95% CI)	1.00 (reference)	0.99 (0.84–1.17)	1.20 (1.00-1.44)	1.05 (0.85–1.30)	0.288
Women						
Lag1	aOR (95% CI)	1.00 (reference)	0.98 (0.83–1.16)	1.05 (0.87–1.26)	1.14 (0.93–1.39)	0.184
Lag0-3	aOR (95% CI)	1.00 (reference)	1.30 (1.08–1.55)	1.33 (1.08–1.64)	1.47 (1.17–1.85)	0.002
Income						
High						
Lag1	aOR (95% CI)	1.00 (reference)	1.09 (0.91–1.30)	1.29 (1.07–1.57)	1.24 (1.01–1.54)	0.017
Lag0-3	aOR (95% CI)	1.00 (reference)	1.22 (1.01–1.47)	1.41 (1.14–1.75)	1.40 (1.10–1.78)	0.004

Odds ratio estimated by conditional logistic regression adjusted for mean daily temperature.

Acronym: PM, particulate matter; N, number of participants; aOR, adjusted odds ratios; CI, confidence interval;

		1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	P for trend
Low						
Lag1	aOR (95% CI)	1.00 (reference)	0.93 (0.80–1.09)	0.98 (0.84–1.16)	1.05 (0.88–1.25)	0.522
Lag0-3	aOR (95% CI)	1.00 (reference)	1.05 (0.89–1.23)	1.16 (0.97–1.39)	1.12 (0.92–1.38)	0.174
Disease duration						
< 5 years						
Lag1	aOR (95% CI)	1.00 (reference)	1.02 (0.87–1.19)	1.11 (0.94–1.30)	1.04 (0.86–1.24)	0.523
Lag0-3	aOR (95% CI)	1.00 (reference)	1.19 (1.01–1.41)	1.29 (1.07–1.55)	1.18 (0.96–1.46)	0.096
≥ 5years						
Lag1	aOR (95% CI)	1.00 (reference)	0.96 (0.81–1.14)	1.09 (0.91–1.32)	1.26 (1.03–1.54)	0.020
Lag0-3	aOR (95% CI)	1.00 (reference)	1.04 (0.87–1.25)	1.22 (0.99–1.49)	1.30 (1.03–1.63)	0.014
Alcohol						
No						
Lag1	aOR (95% CI)	1.00 (reference)	1.15 (0.88–1.49)	1.05 (0.79–1.39)	1.29 (0.95–1.76)	0.190
Lag0-3	aOR (95% CI)	1.00 (reference)	1.09 (0.83–1.43)	1.03 (0.76–1.39)	1.15 (0.81–1.63)	0.540
Yes						
Lag1	aOR (95% CI)	1.00 (reference)	0.95 (0.76–1.18)	1.25 (0.99–1.58)	1.24 (0.95–1.60)	0.032
Lag0-3	aOR (95% CI)	1.00 (reference)	1.16 (0.92–1.45)	1.43 (1.11–1.84)	1.49 (1.11-2.00)	0.003
Exercise						

Odds ratio estimated by conditional logistic regression adjusted for mean daily temperature.

Acronym: PM, particulate matter; N, number of participants; aOR, adjusted odds ratios; CI, confidence interval;

		1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	P for trend
No						
Lag1	aOR (95% CI)	1.00 (reference)	1.12 (0.89–1.42)	1.19 (0.92–1.53)	1.21 (0.91–1.60)	0.169
Lag0-3	aOR (95% CI)	1.00 (reference)	1.13 (0.89–1.45)	1.20 (0.91–1.59)	1.19 (0.86–1.65)	0.261
Yes						
Lag1	aOR (95% CI)	1.00 (reference)	0.94 (0.74–1.19)	1.13 (0.88–1.45)	1.31 (0.99–1.73)	0.032
Lag0-3	aOR (95% CI)	1.00 (reference)	1.13 (0.88–1.45)	1.29 (0.98–1.70)	1.51 (1.10–2.06)	0.008
Odds ratio estimated by conditional logistic regression adjusted for mean daily temperature.						
Acronym: PM, particulate matter; N, number of participants; aOR, adjusted odds ratios; CI, confidence interval;						

Discussion

In this study of 3,372 suicide cases from 1,046,169 newly diagnosed MDD patients in South Korea, we found that short-term exposure to a high PM level was associated with an increase in suicide risk. The higher the concentration of PM2.5 -10 and PM 10 (lag 0–3, lag1) was, the higher the risk for completed suicide MDD patients had (p for trend < 0.05), confirming a dose-responsive relationship between PM level and risk of completed suicide. To our knowledge, this is the first and largest epidemiological study to assess suicide risk among MDD patients to PM exposure. Interestingly, we found a significant association between suicide risk and PM 10, as well as coarse particles. However, there was no association between suicide risk and PM 2.5.

A recent study on 134,811 suicide cases in 10 cities in northeast Asia significantly increased suicidal risk upon the increased level of PM10 and PM 2.5–10 at lag 0–1 but not with PM2.5 [23]. Similar findings were noted in multiple previous studies among the general population, although the results were slightly different from each other [16–18,23]. A study on 4,341 suicide cases in 2004 in South Korea reported a significantly increased suicidal risk upon the increased level of both PM 10 at lag 0–2 and PM 2.5 at lag 1 [17], while another study on 1,546 suicide cases from 2001 to 2010 in Utah USA reported an increased suicide risk associated with PM 2.5 levels at lag 2 but not with PM10 [16]. Our study shows similar results with these studies, supporting increased suicidal risk upon the increased level of the coarse particle, and further expands the concept to depression patients who are at high risk for suicide. Also, there was a dose-responsive elevated risk for suicide upon PM exposure in our study, showing an 18% and 23% increase risk for suicide among participants who were exposed to the highest level of PM10 and PM2.5-10 respectively, compared to the least exposed group. Previous studies on general population used

different measure of exposure such as an increase in interquartile range [16,17,23]. These studies reported 2 ~ 9% increased risk for suicide per interquartile range increase of PM level. Directly comparison of the strength of association is difficult with previous studies, however the result from our study was similar to the previous studies in general population.

PM increases suicide by affecting mood and impulsivity through various mechanisms, and the effect is thought to be more important as it is associated with the etiology of depression. The major effects of PM are explained through low-grade systemic inflammation originating in peripheral tissues such as the lung and skin. Systemic-induced cytokines circulate the body and possibly causing neuroinflammation, neuronal damage, and neurotransmitter change[12]. Since smaller particles enter the systemic circulation and invade the brain parenchyma more easily, PM2.5 and ultrafine PM (diameter < 0.1 μm) are usually considered as the main cause of inflammatory damage from the PM [12]. However, our study showed that the PM10 and coarse particles are significantly associated with suicide risk in MDD patients, while PM2.5 is not. Therefore, we thought certain parts of coarse particles would cause greater neuroinflammation compared to fine particles and increase the risk of suicide.

For example, a previous study noted that coarse particles induced more TNF-α response than fine particles in mouse monocyte and macrophage cell within 24h hours [24] and similarly there was another study reported that coarse particles induced ten times more cytokine responses than fine particles in human alveolar macrophages [25]. Also, a study on rats reported that only coarse particle-induced inflammation and expressed cancer-related genes in brains [26]. This means that coarse particles might play an important role in neuroinflammation, especially shortly after the exposure. The coarse particles deposit easily in the respiratory system [27] or olfactory system [28], induce systemic inflammation via endotoxins, soluble compounds, and metals in PM's surface. Also, coarse particles contain organic components such as dander, spores, or pollen which can also lead to inflammation, sometimes immediate and excessive inflammatory reactions such as allergic reactions [27]. Since chemical components enter through the olfactory mucosa and bulb affect the brain rapidly and directly, this concept also supports the idea that coarse particles might be a major cause of short-term neuroinflammatory. This exacerbation of neuroinflammation may aggravate the depressive symptoms and stimulate the hyperactivated hypothalamic-pituitary-adrenal axis, which might cause mood instability and future suicide risk.

Moreover, PM can affect mood swings and inadequate control of impulsivity in another ways. Previous studies reported that PM can cause circadian rhythm disturbance by reducing sunlight or solar radiation and also affects mood swings [29,30]. This association can be explained by decreased serotonin activity. Serotonin is a crucial neurotransmitter in stabilizing mood and regulating aggression, and impulsivity [31,32], and is produced according to sunlight exposure [33,34]. Since PM decreases sunlight exposure, it might reduce serotonin level and possibly cause aggressiveness or uncontrolled impulsivity which is directly linked to completed suicide. Particularly serotonin's rapid turnover is especially crucial in the pathophysiology of MDD [35], so the impact due to serotonin reduction would be critical for MDD patients.

In stratified analysis, the association between PM exposure and the risk of suicide was particularly significant among high-income, women, over 40 years of age, and people who drink. It was similar to the previously reported nature of suicide in Korea [3]. This result means that PM accelerated suicide by acting as an additional burden in high-risk group, and suggesting that PM can be regarded as one of several risk factors upon the stress-diathesis model of suicide.

Our study has several limitations. First, suicide cases might have been underreported because it can be recorded as accidental or undetermined. Second, the participants' residence area might be different from the actual place where the participants spend most of the time, such as the workplace or school. The level of exposure to PM might not be accurately calculated in such cases. Further studies with a more accurate measure of an individual's exposure to PM will be needed. Third, other underlying diseases that could be affected the risk for suicide were not considered. However, we used a time-stratified case-crossover design, in which each participant serves as their control. Fourth, the severity of the disease among MDD participants was not reflected. Drug compliance and symptoms of depression at the time of suicide were not accounted for. Therefore, further studies considering the severity of psychiatric symptoms and treatment regimen will be merited. Finally, the suicide date in our study was based on death registry data, so it is possible directly reflect the suicide attempted date. For example, if a participant has attempted suicide but died in the hospital a couple of days later, the recorded suicide date would be later than the exposure day. However, the multi-day lag model takes account for this possibility and suggests that short-term exposure to high level of PM in MDD patients increases the risk for suicide.

Despite these limitations, this study was the first large-scale study to investigate PM's effects on suicide among MDD patients. Coarse PM's mechanism causes depression, and mood swings were explained in detail, and in conjunction with the etiology of depression, we tried to elucidate the effects of Coarse PM exposure on suicide in depressed patients.

Conclusion

Short-term exposure to coarse particles aggravates acute neuroinflammation and increases the risk of suicide by causing mood swings in existing depressed patients. This result will be used as an essential basis for consideration when establishing an air pollution alarm system and implementing suicide prevention programs. Further researches on PM's neurophysiological responses are needed to understand the potential mechanism of PM's impact on suicide.

Declarations

Conflicts of Interest

The authors declare no conflicts of interest.

Funding

This research was supported by the National Health Insurance Service of Korea.

Role of the Sponsors

The National Health Insurance Service of Korea had no role in the design and conduct of the study, the collection, management, analysis, and interpretation of the data, or the preparation, review, or approval of the manuscript, and decision to submit for publication.

Author Contributions

SM Park had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Analysis and interpretation of data: All authors

Drafting of the manuscript: IY Hwang, D Choi, JA Kim

Critical revision of the manuscript: All authors

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