

## **Letter to editor**

### **I am a general dentist: Why is screening of obstructive sleep apnea in chronic kidney disease patients my concern?**

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Dear Editor,

Obstructive sleep apnea (OSA) is characterized by upper airway collapse while sleeping at night. There is an increasing body of evidence that links OSA with chronic kidney disease (CKD)<sup>1,2</sup>. Though this combination is seen commonly in this patient group, documented current global evidence ends with a note stating under-diagnosis of OSA.<sup>1</sup> Family physicians (FP) are the front-liners to identify the disease and serving their best. In such circumstances, why is screening of OSA in CKD patients', a general dentist's (GD) concern? Readers could raise the question that dental considerations for sleep apnea would be sufficient to elucidate this scenario? Given yes would mislead the title and not

to get confused with the sleep apnea considerations in dental offices. The core discussion is about why a GD should screen OSA and most importantly why is it compulsory in CKD patients, rather than the diagnostic methods?

The first reason is that GDs equally have opportunities like FPs to diagnose OSA during their routine practice. Interestingly, dental findings suggest that dentists could be better diagnosticians for OSA than the specialized physicians considering the two main visible signs of this disorder: enlarged tonsils and tongue, which are easily noticeable during dental care.<sup>2</sup> In addition, recent reports express that neck circumference >40cm, large tongue, Mallampati score of Class 3,4 and deep palatal vault as independent predictors in high-risk OSA patients.<sup>3</sup> Therefore, CKD and OSA despite sharing the common risk factors such as obesity, hypertension, smoking, and alcohol, the mentioned intra-oral and extra-oral signs can aid the dentists in diagnosing OSA before CKD is reported. This indeed increases the confidence of a GD.

Secondly the current knowledge in the medical field suggests a potential bidirectional association between CKD and OSA.<sup>4,5</sup> The mechanism suggests that CKD patients often carry excess fluid that can lead to upper airway narrowing. The fluid overload often leads to interstitial pulmonary edema causing central apnea, which could be responsible for the OSA. The similar pathophysiology of both the diseases increases the possibility of them to be possible risk factors for each other.<sup>4</sup> Therefore, OSA may be consequent to and aggravate CKD progression. OSA

appears as a potential trigger and mandatory that GDs understand the seriousness of comorbidities.

Thirdly, 80% of the moderate and severe cases remain undiagnosed according to American Sleep Association.<sup>2</sup> A recent exhaustive meta-analysis undertaken by Voulgaris A and team showed that prevalence of moderate and severe OSA in CKD patients was 34% and 37% respectively.<sup>5</sup> Indeed true that GD potentially sees their patients more frequently than physicians, especially those who regularly visit for a routine check-up. Given such an opportunity in dental practice should be utilized to identify the undiagnosed OSA in CKD patients. The good news is that the identification and treatment of OSA may lead to an intervention considerably delaying the progression of kidney disease.<sup>5,6</sup>

The health of the CKD population is facing a new threat (risk factor) every day and OSA is one such. It is emphatic to GDs to welcome new perspectives wherein compulsory screening for OSA as a part of comprehensive medical and dental history, focusing on the existence of the bidirectional association between CKD and OSA would help the patients to receive the most effective care. In the patient's best interests, prioritize them as high-risk candidates based on the associated risk factor and mutually refer to sleep physicians. It's in good belief that increasing basic science and clinical medicine courses in dental schools would help the dentists to become oral physicians and provide an opportunity to participate in major reform of the health-care system.

Conflict of Interest: None Declared

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## **Review**

### **Association of air pollution and hospital admissions due to exacerbation of chronic obstructive pulmonary disease in Asia: A scoping review**

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## **Abstract**

**Background:** Air pollution is highly associated with health-related problems. Particulate matters (PM) such as PM10, PM2.5, nitrogen dioxide, sulfur dioxide, carbon monoxide and ozone levels are associated with exacerbation in chronic obstructive pulmonary disease patients. This review aims to identify the relationship between air pollution and the rate of hospitalisation due to exacerbation of chronic obstructive pulmonary disease in Asia.

**Methods:** A scoping review was performed using the method of Arksey and O'Malley.—Systematic searching of articles was conducted from PubMed and ScienceDirect. Articles were only included if they reported on the association between exacerbation of chronic obstructive pulmonary disease and hospitalisations among adults aged 18 years and above in Asian countries.

**Results:** 65 articles were retrieved from two search engines. Eight articles met the inclusion criteria for review. Most of the studies have shown linear correlation between PM2.5 and acute

exacerbation of chronic obstructive pulmonary disease hospitalisations. Three studies have shown that there is a significant association between PM10 and acute exacerbation of chronic obstructive pulmonary disease, while four studies have proved that there is positive correlation between PM2.5, nitrogen dioxide, sulfur dioxide, carbon monoxide and acute exacerbation of chronic obstructive pulmonary disease hospitalisations. Four studies had also concluded that female patients and older patients are more susceptible to acute exacerbation of chronic obstructive pulmonary disease hospitalisations.

**Conclusion:** Particulate matters such as PM2.5, PM10, nitrogen dioxide, sulfur dioxide, carbon monoxide, ozone, as well as female gender and old age is highly associated with hospital admissions due to acute exacerbation of chronic obstructive pulmonary disease cases in Asia.

**Keywords:** Air pollution, Asia, COPD, exacerbation, and hospitalisation

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## **Introduction**

Air pollution is a phenomenon that has happened for a long time across the world and it brings a lot of problems to us especially health related problems.<sup>1</sup> Air pollution refers to the release of pollutants into the air that are detrimental to human health and the

planet as a whole.<sup>2</sup> The condition of air pollution has become more and more severe compared to decades ago, and we as human beings who are affected by this problem, need to pay more attention to this problem.<sup>3</sup>

There are various types of pollutants that have been released into the atmosphere and cause air pollution, for example nitrogen dioxide, sulfur dioxide, carbon monoxide and so on.<sup>3,4</sup> Human activities are the main source of these pollutants such as emission from factories, wastes emitted from vehicle, construction and agriculture activities.<sup>3-5</sup> Some pollutants are also contributed from indoor air pollution such as secondary smoke from smoking cigarettes, emission from air conditioning, smoke from cooking and burning of coal. Besides all those pollutants mentioned above, PM10 and PM2.5 forms of pollutants are the most harmful pollutants to human beings. PM10 and PM2.5 are particular matter with diameter less than 10 and 2.5 micrometer.<sup>6</sup> For PM2.5 pollutants, it is mainly emitted from combustion of gasoline, oil, diesel fuel and wood while for PM10 pollutants are come from dust in construction sites, landfills and agriculture.<sup>7</sup>

The most common health issue related to air pollution are respiratory related diseases such as asthma, chronic obstructive pulmonary disease (COPD) and respiratory disease.<sup>8</sup> This is because these particular matters are able to pass through our pulmonary protective system and reach to the very deep side of lungs.<sup>9</sup> With the increase in severity of air pollution, cases of respiratory infection such as influenza and bacterial pneumonia are increasing.<sup>10</sup> As people with pulmonary disease have a higher

risk than normal healthy people to get affected by air pollution,<sup>11</sup> a scoping review was done to understand how the air pollution is associated with hospitalisation due to exacerbation in COPD patients.<sup>12</sup>

## **Methods**

A scoping review was conducted on the association of air pollution and hospital admissions due to exacerbation of COPD patients in Asia. A 6-step methodological framework that was developed by Arksey and O'Malley was defined for the review<sup>13</sup>. However, in our scoping review, only steps 1 to 5 of the framework were defined. The structure of the framework was outlined in the following manner:

- 1) Identification of the research question.
- 2) Identification of relevant studies.
- 3) Selection of studies for review.
- 4) Charting the data.
- 5) Collating and summarizing the results

### **Step 1: Identification of the research question**

The research question is “What is the association of air pollution and hospital admissions due to exacerbation of chronic obstructive pulmonary disease in Asia?”

### **Step 2: Identification of relevant studies.**



A search strategy was conducted according to the Preferred Reporting Items for Systematic and Meta-Analyses (PRISMA) Statement Protocol as figure 1. The electronic database, Pubmed and ScienceDirect were utilised mainly to identify, define, and recognize the available potential pieces of literature present that were associated with air pollution and hospital admissions due to the exacerbation of COPD patients throughout Asia. Through this, a Boolean strategy was implemented for further effective searching by using combined keywords to locate the relevant studies based on the stated review. The combined keywords used were “air pollution AND hospitalisation AND exacerbation AND COPD AND Asia” for both Pubmed and Science Direct. Through this search, a total of 65 articles were obtained, 29 of which were from the Pubmed database, and the remaining 36 from Science Direct. Table 1 shows the words used on the PubMed search strategy on hospitalisations due to AECOPD from air pollution.

### **Step 3: Selection of studies for review.**

The selection of 8 relevant articles out of 65, pertaining to air pollutants associated with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), was based on the following inclusion and exclusion criteria.

**Inclusion criteria:** Studies that were related to hospitalization due to the exacerbation of COPD cases from air pollution in Asia involving adults aged 18 years and above in Asia.

**Exclusion criteria:** Studies that were not done in English, articles with irrelevant or inadequate information, were excluded.

#### **Step 4: Mapping the data**

Among the 8 selected qualitative studies, details and data obtained were mapped out and tabulated. This tabulation comprised of authors, years of publication, the aim of the study, country or region of study, characteristic of studies, design or methodology and key findings of each relevant articles. The summary of air pollutants associated with AECOPD among eight qualitative studies can be observed in (Table 2).

#### **Step 5: Collating and summarizing the results**

The acquired evidence was collated, summarized, and reviewed thoroughly throughout the entire process.

#### **Results**

A total of 65 articles were retrieved from two databases which are PubMed and ScienceDirect, however, there are 2 duplicated articles. Thus, 63 articles were left for title and abstract screening. After the primary screening, 15 articles were chosen for full text screening. A total of 7 articles were excluded with due to language barrier and inadequate information. Lastly, 8 qualitative studies met our inclusion criteria, key concepts, and theme of our research question. These studies were conducted in China or Korea. The different study cities from China that are being investigated include Jinan, Shijiazhuang, Shanghai, Yancheng and Beijing. The steps and summary of the studies were shown clearly with the PRISMA diagram in figure 1 and table 2, respectively.

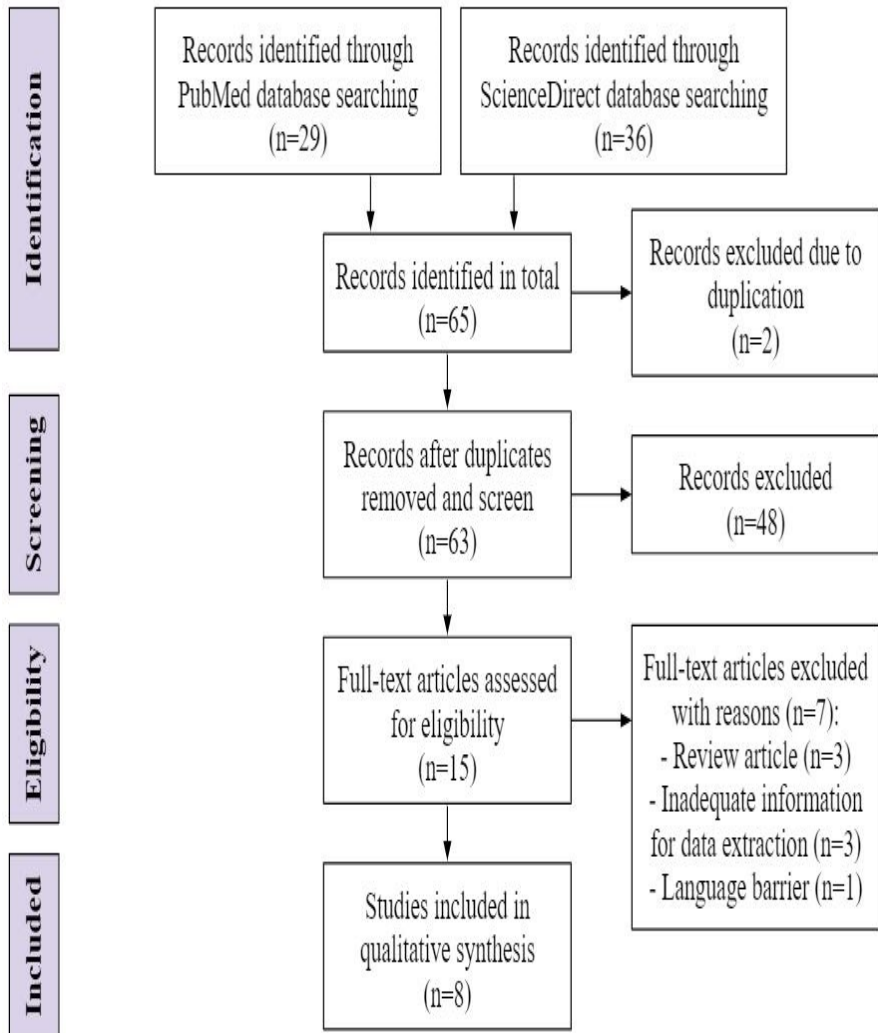


Figure 1 - PRISMA diagram in the selection of articles for scoping review

Table 1 – Summary of words used on PubMed as a search strategy

Concept	Keyword	MeSH
Air pollution	Air pollute*	Air pollution [MeSH Terms]
Hospitalisation	Hospital*	Hospitalization [MeSH Terms]
Exacerbation	Exacerbate*	-
Chronic obstructive pulmonary disease		pulmonary disease, chronic obstructive [MeSH Terms]
Asia	Asia*	Asia [MeSH Terms]

### **PM2.5 and PM10 associated with AECOPD hospitalisations**

Six out of the eight qualitative studies have reported a linear correlation between PM2.5 and AECOPD hospitalisations.<sup>14–19</sup> In the six studies, all of the studies have concluded that the rate of AECOPD hospitalisations increased when the concentration of PM2.5 increased in the short-term period. Three out of the six studies have shown that there is a significant association between PM10 and AECOPD.<sup>15,16,20</sup>

## **NO<sub>2</sub>, CO, SO<sub>2</sub> and O<sub>3</sub> associated with AECOPD hospitalisations**

Five studies have investigated the relationship between NO<sub>2</sub>, CO, SO<sub>2</sub> and O<sub>3</sub> with AECOPD hospitalisations.<sup>15,19</sup> Four out of these five studies reported that there is a strong positive correlation between PM<sub>2.5</sub>, NO<sub>2</sub>, CO, SO<sub>2</sub> and AECOPD hospitalisations, but showed a negative correlation with O<sub>3</sub> level.<sup>16-19</sup> According to Liang et al., PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub> and CO demonstrated a positive correlation to each other but showed a moderate positive correlation with SO<sub>2</sub>.<sup>15</sup> Besides that, it was also mentioned that AECOPD hospitalisations can be increased when exposure to O<sub>3</sub>, during the warm season and decreases AECOPD hospitalisations by increasing with O<sub>3</sub> exposure during the cold season.<sup>15</sup>

## **Gender and age associated with AECOPD hospitalisations**

There are five studies which discussed association of gender and age with AECOPD hospitalisations.<sup>15-18,21</sup> Chen et al. has reported that male patients are more sensitive to air pollutants and have a higher risk of AECOPD hospitalisations.<sup>21</sup> On the other hand, another four studies had concluded that female patients and older patients are more susceptible to AECOPD hospitalisations.<sup>15-18</sup> Out of these four studies, Xu et al. reported that females aged 60 years and above are at high risk of AECOPD hospitalisations.<sup>18</sup> Liang et al. reported on females aged 65 years and above while Sun et al. has recorded that females aged more than 75 years are most susceptible to AECOPD hospitalisations.<sup>15,17</sup> Qu et al. also mentioned that retired female patients are at high risk in AECOPD hospitalisations.<sup>16</sup>

Table 2 - Summary of air pollutants associated with AECOPD among eight qualitative studies						
No	Authors/ year of publication/ origin	Aim of the study	Country/ region of the study	Study characteristics	Design/ methodology	Key findings
1	Chen et al. 2018 China <sup>21</sup>	To study the short-term effects of air pollution on the hospitalisation rates of the individual with AECOPD, stroke, myocardial infarction (MI) in Jinan, China	Jinan, China	Population from Jinan Qilu Hospital, Provincial Hospital of Shandong Province and Central Hospital of Shandong Province.  Inclusion: (1) $\geq 18$ years old (2) resided and worked in the study area (Jinan City) during the study period	Observational study for 3 years	(1) Male patients aged $\geq 65$ years were more sensitive to air pollutants and were at higher risk of hospitalisation for AECOPD. (2) PM <sub>2.5</sub> and daily exposure to SO <sub>2</sub> and NO <sub>2</sub> can lead to cardiovascular disease and affect the admission risk of stroke patients. (3) SO <sub>2</sub> has an adverse impact on the admission of individuals with MI.
2	Qu et al. 2019 China <sup>16</sup>	To analyse the relative cumulative risk factors from air pollution associated with AECOPD under exposure to high pollution levels and calculate the attributable percentage of AECOPD in Shijiazhuang, China	Shijiazhuang, China	Population from Health Insurance Center of Shijiazhuang City, Hebei Province and electronic medical records of all primary and secondary discharges diagnose as AECOPD patient from tertiary and secondary hospitals. Inclusion: (1) primary diagnosis of	Time-series study for 4 years	(1) A linear positive relationship between AECOPD and PM <sub>2.5</sub> , PM <sub>10</sub> , NO <sub>2</sub> , CO and SO <sub>2</sub> . (2) A negative linear correlation between AECOPD and O <sub>3</sub> . (3) Every increase of 10 $\mu\text{g}/\text{m}^3$ in PM <sub>2.5</sub> , PM <sub>10</sub> , SO <sub>2</sub> and NO <sub>2</sub> level were associated with 1.1%.

				<p>AECOPD and defined according to the ninth version of International Classification of Diseases (ICD-9) (2) resided at urban area of Shijiazhuang (3) patient with AECOPD from tertiary and secondary hospitals (4) <math>\geq 35</math> years old</p>		<p>0.4%, 0.3% and 1.6% increases in COPD hospitalisation, respectively. Every increase of <math>0.1 \text{ mg/m}^3</math> of CO levels, it increases 0.5% of hospitalisation. (4) Short-term exposure to high concentrations of PM significantly increased the daily rates of AECOPD hospitalisation. (5) PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, CO caused the significant burden of AECOPD hospitalisation in Shijiazhuang, China. (6) The risk of female and retired patients is higher.</p>
3	Wang et al. 2015 China <sup>20</sup>	To investigate the Geographical Information System (GIS) based on the spatial relationship between ambient air pollution and AECOPD hospitalisation	Jinan, China	<p>Population from five large-scale hospitals in Jinan.</p> <p>Inclusion: (1) AECOPD hospitalisation and identified by ICD-10 (2) resided and worked in Jinan City during the</p>	Generalised linear model (GLM) for 1 year	<p>(1) PM<sub>10</sub> has the greatest spatial correlation with AECOPD hospitalisation in the workplace. (2) SO<sub>2</sub> has the greatest spatial correlation with AECOPD hospitalisation</p>

		on in Jinan, China		study period (3) >18 years old		n in the residence. (3) Every 10 µg/m <sup>3</sup> increase of PM10 at the workplace, it increases 7% of AECOPD hospitalisations.
4	Zhang et al. 2018 China <sup>19</sup>	To study the association between various air pollutants and hospitalisations of various specific respiratory disease and medical expenditure for these diseases in Shanghai, China	Shanghai, China	Population from XinHua hospital in Shanghai.  Inclusion: (1) resided and living in Shanghai (2) primary diagnosis with five independent respiratory diseases which is pediatric respiratory disease (PRD), upper respiratory infection (URI), lower respiratory infection (LRI), asthma and COPD	Time-series study for 3 years	(1) It showed a significant relationship between PM2.5, CO, SO <sub>2</sub> and NO <sub>2</sub> level with PRD and URI visits along with 128-352 CNY and 332-467 CNY per IQR increments in air pollutants, respectively. (2) A significant association between PM2.5 and O <sub>3</sub> with COPD visits by 432 and 774 CNY respective per IQR increments. (3) Non-significant association between all pollutants with asthma and LRI.
5	Jo et al. 2018 Korea <sup>14</sup>	To investigate the effect of PM2,5 and its chemical constituents on AECOPD	Chuncheon, Korea	Population in Chuncheon, Gangwon-do from Korean National Health	Time-series study for 6 years	(1) Hospital admissions were not affected by an increase in PM2.5 concentration.



		hospital visits in Chuncheon, Korea.		Insurance Service (KNHIS).  Inclusion: (1) according to ICD-10 code (2) all-age		(2) As PM2.5 concentration increases, the outpatient visit and total hospital visits increase. (3) Chemical constituents of Mg, Al, Si, Ti, As, Br and elemental carbon were having a high risk of AECOPD hospitalisation in males only.
6	Xu et al. 2016 China <sup>18</sup>	To explore the association between PM2.5 pollution and hospital emergency room visits (ERV) for total and cause-specific respiratory diseases in urban areas in Beijing, China.	Beijing, China	Population from ten general hospitals located in urban areas in Beijing.  Inclusion: (1) according to ICD-10 code (2) diagnosis with total respiratory diseases which included upper respiratory tract infection (URTI), lower respiratory tract infection (LRTI), AECOPD and asthma	Time-series study for 1 year	(1) Every 10 µg/m <sup>3</sup> increase in PM2.5, it increases ERV of 0.19% for URTI, 0.34 % for LRTI and 1.46% for AECOPD. (2) No significant association between PM2.5 and asthma. (3) PM2.5 was strongly correlated with SO <sub>2</sub> , CO and NO <sub>2</sub> but negatively correlated with O <sub>3</sub> . (4) PM2.5 more affects females and people ≥ 60 years old.
7	Sun et al. 2018 China <sup>17</sup>	To study the association between PM2.5 and AECOPD in	Yancheng, China	Population from Yancheng First People's	Time-series study for 3 years	(1) A positive and significant relationship between

		Yancheng, China.		<p>Hospital and Third People's Hospital.</p> <p>Inclusion:  (1) according to ICD-10 code  (2) diagnose with AECOPD</p>	<p>short-term exposure to PM2.5 and AECOPD hospitalisation.</p> <p>(2) A 10 <math>\mu\text{g}/\text{m}^3</math> increase in PM2.5 was associated with 1.05 % increase in AECOPD.</p> <p>(3) Among the population, females and people aged &gt; 75 years old are at higher risk. The cold season also represents a higher risk in AECOPD hospitalisation.</p> <p>(4) Relationship between PM2.5 and AECOPD was robust after controlling O<sub>3</sub> level but decreased after controlling NO<sub>2</sub>, SO<sub>2</sub> and CO levels.</p>
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8	Liang et al. 2019 China <sup>15</sup>	To investigate the associations between the number of cases of AECOPD advanced by air pollution each year in Beijing, China.	Beijing, China	Population from the hospital discharge database operated by the Beijing Public Health Information Centre.  Inclusion: (1) according to ICD-10 code (2) primary discharge diagnosis of AECOPD (3) ≥18 years old	Time-series study for 5 years	(1) Total of 161613 of AECOPD hospitalisation cases, with most males patients and people aged ≥ 65 years old. (2) Reduction risk (RR) of AECOPD hospitalisation per IQR increase in pollutant was 1.029. (3) Increase with O <sub>3</sub> exposure, it significantly increases AECOPD hospitalisation during the warm season and decreases hospitalisation during the cold season. (4) PM <sub>2.5</sub> , PM <sub>10</sub> , NO <sub>2</sub> and CO showed a positive correlation to each other but showed a moderate positive correlation with SO <sub>2</sub> . (5) Women and aged 65 years or older were most susceptible.
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## Discussion

All the studies have reported significant association between the atmospheric PM and AECOPD. Majority of the studies (6 out of 8) have concluded that PM<sub>2.5</sub> has caused a higher prevalence of

AECOPD hospitalisation<sup>14-19</sup> while three studies found out a significant association between PM10 and AECOPD hospitalisation.<sup>15,16,20</sup> PM10 are usually trapped in the upper airway after being inhaled. However, PM2.5 may be able to approach the bronchioles and alveolar spaces.<sup>22</sup> Furthermore, water-soluble pollutants can enter the systemic circulation through the alveolar capillaries.<sup>22</sup> Subsequently, this activates the inflammation on the epithelial cells.<sup>23</sup> Besides, the particulate matters may also increase oxidative stress.<sup>23</sup> Thus, this may aggravate underlying pulmonary disease such as COPD. Toxicological studies have proposed that acute impairment of the lung cellular defence is also one of the causative factors that contribute to the exacerbation of COPD.<sup>24</sup> The hospitalisation rate was also found to be increased when the PM2.5 increased by every 10  $\mu\text{g}/\text{m}^3$ .<sup>18</sup>

Increment of gaseous pollutants such as NO<sub>2</sub>, CO, SO<sub>2</sub> and O<sub>3</sub> in the atmospheric air were found to have a strong association with AECOPD hospitalisation. Qu et al reported that the relative risk of NO<sub>2</sub> - associated AECOPD hospitalisation is the greatest.<sup>16</sup> However, Wang et al and Xu et al have recorded that SO<sub>2</sub> has a greater association with AECOPD hospitalisation.<sup>18,20</sup> This may be caused by exhaustion of air pollutants from heavy industries in the area associate with the combustion of fossil fuels including sulfur.<sup>25</sup> According to a statistic from World Health Organisation (WHO), there are approximately 1.6 million death due to exposure of solid fuels per year.<sup>26</sup> Of these, approximately 6930000 cases are associated with COPD.<sup>26</sup> The exposure to SO<sub>2</sub>

was found to be associated with respiratory symptoms such as wheezing and shortness of breath.<sup>25</sup> This in turn increases the risk of exacerbation of previously occurred respiratory disease such as COPD.<sup>27</sup> In contrast, the implementation of Air Pollution Prevention and Control Action Plan (APPCAP) in Beijing has greatly reduced the SO<sub>2</sub> concentration.<sup>15</sup> Furthermore, it is found that increased amount of NO<sub>2</sub> and SO<sub>2</sub> causes the inflammation of the epithelial cell as they act as an irritant due to their property as high reactive oxidant.<sup>28</sup>

Most of the studies did not find any correlation between O<sub>3</sub> exposure and hospital admission due to AECOPD.<sup>16-19</sup> However, there were approximately 254,000 deaths from COPD which were attributable to O<sub>3</sub> in 2015.<sup>19</sup> A causal link was found between increased COPD mortality and long-term exposure to ozone.<sup>19</sup> There is a large body of evidence that links the ozone exposure mortality to the adverse effects on the human respiratory system. This includes significant changes in structure and function of lungs in humans and increased morbidity and mortality from COPD, especially during warmer seasons.<sup>29</sup> In the study by Liang et al, they have noted that there is a positive association during warm seasons.<sup>15</sup> Nevertheless, the seasonal effect of O<sub>3</sub> on AECOPD is unclear. It can be due to the behavioural pattern of the people during different seasons. For instance, people tend to open the window or attend outdoor activities more frequently when the weather is hot. This indirectly increases their exposure to the polluted air. In another way, most people may stay indoor during cold seasons. Therefore, the exposure to O<sub>3</sub>

decreases significantly and the rate of AECOPD hospitalisation declines. However, it may be different in people in Yancheng, China where the condition is the opposite and exacerbation is higher during cold seasons according to Sun et al.<sup>17</sup>

Liang et al observed that there is a 3% increase in acute exacerbations of COPD per 1 mg/m<sup>3</sup> increase in CO.<sup>15</sup> However, two studies from Shang Hai<sup>30</sup> and Hong Kong<sup>31</sup> reported that low concentration of CO is negatively associated with the exacerbation of COPD. Both authors suggested that this may relate to the anti-microbial activity and anti-inflammatory properties of low concentration CO. Nonetheless, there are only a few studies available from Asia that are investigating the relationship of CO and AECOPD. Therefore, more studies are needed to confirm the association of AECOPD and CO in ambient air pollution. In studies in Europe and North America, it is found out that there were stronger association between hospitalisation due to AECOPD and CO pollution in ambient air. A possible explanation is that may be due to the difference of the concentration of ambient CO.<sup>32</sup>

In the study by Chen et al., the authors have analysed that elderly aged 65 years and above has a higher risk of hospitalisation due to AECOPD. They were also found to be more sensitive to air pollutants when compared to females aged below 65 years old. The prevalence of AECOPD in male is higher than females in China. This is due to a higher smoking rate of males in China. Approximately 74% of male that is older than 35 years old in China smoke.<sup>33</sup> Age is also one of the factors for hospital

admission due to AECOPD. As age increases, one is more vulnerable to the exposure of PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and CO. For instance, Qu et al noted that retired individuals were more likely to experience AECOPD. This may be due to weak immune systems, decline of respiratory system function or other comorbidities. As a result, weakened immune function, poor lung function, higher prevalence of COPD and increased sensitivity to air pollutants can be an underlying reason of AECOPD in elderly aged 65 years and above.<sup>34</sup>

Sun et al have found out that there is a large association between female patients and PM<sub>2.5</sub> in ambient air. Besides, Qu et al. and Xu et al. have also noticed that females are more susceptible to the effects of PM<sub>2.5</sub> compared to male.<sup>16,18</sup> It is suggested that it may be due to the physiological difference between male and female. For instance, the size of the airway where male have larger airway compared to female.<sup>35</sup> Jo et al. have also explained that the difference in gene expression of male and female should also be considered.<sup>14</sup>

## **Conclusion**

In the nutshell, the increased amount of PM in the atmosphere increases hospital admissions due to AECOPD. Other gaseous pollutants such as NO<sub>2</sub>, CO, SO<sub>2</sub> and O<sub>3</sub> in the atmosphere also contribute to AECOPD but not as much as PM. Factors such as the old age and female gender are also associated with increased AECOPD hospitalisations from air pollution.

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