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Factors Related to Club Cell Protein 16 (CC16) and Quality of Life in Northern Thailand

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Abstract

Exposure to poor air quality can cause adverse health effects, especially club cell protein 16 (CC16) as potential marker for a lung injury, and a reduced quality of life (QoL). This study aimed to evaluate factors related to CC16 and QoL among people living near the air quality monitoring stations in Northern Thailand. A cross-sectional study was conducted. A total of 240 individuals were recruited. Data was collected using structured 36-item short-form survey (SF-36) questionnaires. Air quality was measured using air quality monitoring stations by the Pollution Control Department (PCD), Thailand. Diseases and related health problems were defined using the International Classification of Diseases ICD-10) by the Information and Communication Technology Center, Thailand. Venous blood was collected and analyzed for serum CC16 by medical laboratory technicians. The daily PM_{10} and $PM_{2.5}$ concentrations were significantly positively associated with I00-I99 and J00-J99.8. The mean ± SD of serum CC16 levels in participants under 60 years old was 5.33 ± 4.24 ng/ml, which was significantly lower than 10.01 ± 6.91 ng/ml in participants 60 years and older (p value < 0.001). The serum CC16 level was significantly associated with physical health (PH), mental health (MH), and overall QoL. Multiple linear regression analysis showed that an increase in serum CC16 level was associated with a decrease in overall QoL after adjusting for confounding variables. Concerned agencies should provide policymakers and health promotion interventions for reducing pollution exposure and self-protective behaviors to prevent airway inflammatory responses, chronic respiratory diseases, and poor QoL.

Keywords: Club cell protein16 (CC16); Air pollution; PM_{10}; $PM_{2.5}$; Quality of life (QoL)

1. Introduction

Club cell (formerly Clara cell) protein16 (CC16) is a 16 kDa homodimeric protein secreted by non-ciliated epithelial cells of the respiratory bronchioles. CC16 is one of the anti-oxidative and anti-inflammatory proteins involved in epithelium integrity and airway inflammation (Cooper *et al.,* 2019; Thimmulappa *et al.,* 2020; Thongtip *et al.,* 2020). Previous studies found that the significant reduction of CC16 along the terminal and respiratory bronchioles has been associated with chronic lung damage caused by tobacco smoke, air pollution from industry and the transport sector, including emissions from biomass burning, forest fires, and transboundary haze (Cooper *et al.,* 2019; Almuntashiri *et al.,* 2020; Thimmulappa *et al.,* 2020; Thongtip *et al.,* 2020).

These pollutants, especially air pollutants such as particulate matter less than 2.5 microns ($PM_{2.5}$), carbon monoxide (CO), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3) (Xia *et al.,* 2018; Guo *et al.,* 2019; Manisalidis *et al.,* 2020; US EPA, 2022), can be inhaled deep into the lower respiratory system and lung and enter the blood system (Kim *et al.,* 2018; WHO, 2021; Sakunkoo *et al.,*2022). Small particulate matter can lead to injury, inflammation, and reduced lung function in the terminal bronchioles of the lungs (Leikauf *et al.,* 2020; Sakunkoo *et al.,* 2022). Moreover, these pollutants contribute to the development and progression of chronic obstructive pulmonary disease (COPD), asthma, lung cancer, heart disease, and lung disease (Leikauf *et al.,* 2020; Manisalidis *et al.,* 2020). Thus, previous research has found that these air pollutants can cause airway inflammation, health-related diseases, and a lower QoL (Landrigan *et al.,* 2017; Han *et al.,* 2020; Leikauf *et al.,* 2020; Sakunkoo *et al.,* 2022). Importantly, previous studies found that these air pollutants have been associated with CC16 and QoL in the population living near the air quality monitoring stations (Broeckaert *et al.,* 2000; Darçın *et al.,* 2014; Cooper *et al.,* 2019; Thimmulappa *et al.,* 2020; Thongtip *et al.,* 2020; Hautekiet *et al.,* 2022).

Moreover, previous studies found that high levels of these pollutants occurred in the dry or summer season as a result of the meteorological conditions, increased burning during the dry or summer season, and other factors (Arunrat *et al.,* 2018; Kliengchuay *et al.,* 2018; Outapa P, *et al.,* 2019; Aslam *et al.,* 2020; Mueller *et al.,* 2020). The increased concentrations of air pollutants such as PM_{10}, $PM_{2.5}$, CO, NO_2, and O_3 were associated with health problems in Northern Thailand (Mueller *et al.,* 2020; Thongtip *et al.,* 2022). In a preliminary study, the monthly concentrations of $PM_{2.5}$ at air quality monitoring stations in Phayao Province, Northern Thailand in March, February, April, and January of 2020 were 93.8 ± 47.8 µg/m³, 59.7 ± 19.3 µg/m³, 57.3 ± 29.1 µg/m³, 55.4 ± 1.0 µg/m³, respectively as shown in figure 2.

Prolonged exposure to pollutants can lead to lung epithelial injury and cell death, which lead to a reduction in serum CC16 levels (Castro-Rodriguez *et al.,* 2018; Lam *et al.,* 2018; Rong *et al.,* 2020; Thongtip *et al.,* 2020; Zhang *et al.,* 2022). Importantly, CC16 can be used as a predictor of respiratory health and a novel biomarker for early detection (Pandey *et al.,* 2012; Cooper *et al.,* 2019; Almuntashiri *et al.,* 2020; Thimmulappa *et al.,* 2020; Thongtip *et al.,* 2020). Furthermore, previous research has found that respiratory disorders and poor air quality increase the risk of severe morbidity and mortality while decreasing physical and mental health-related quality of life (HRQOL) (Darçın *et al.,* 2014; Han Darçın *et al.,* 2020; Manisalidis *et al.,* 2020; Hautekiet *et al.,* 2022). This study is aimed at assessing the factors associated with CC16 and QoL among people living near air quality monitoring stations in Phayao Province, Northern Thailand.

2. Materials and Methods

2.1 Study design and population

This study conducted a cross-sectional study in Ban Tom Sub-District, Phayao Province, Thailand during February and March 2022. The proportion of quality of life was 79.2% (Thongtip *et al.,* 2019). The sample size was determined using the population proportion formula.

$$n = \frac{Np(1-p)z^2_{1-\frac{\alpha}{2}}}{d^2(N-1)+p(1-p)z^2_{1-\frac{\alpha}{2}}}$$

where the size of the population (N) is 2,300, p = 0.792, Delta (d) is 0.05, Alpha is 0.05, Z (0.975) is 1.960, and sample size (n) is 228.1. This study added at least 5% to the estimated sample size to allow for losses. Therefore, the sample size (n) of this study was 240 participants.

2.2 Data collection

The data was collected by trained researchers using a questionnaire. The questionnaire is comprised of two main sections: characteristics of the sample population and QoL. SF-36 was used to measure QoL in this study. The SF-36 contains 36 items that measure physical health (PH) and mental health (MH) constructs in eight domains. PH is divided into five categories: physical functioning, role limitations due to PH, bodily pain, general health, and energy/fatigue, while MH is divided into three categories: social functioning, role limitations due to emotional problems, and emotional well-being.

2.3 PM_{10} and $PM_{2.5}$ measurements

The air quality monitoring stations in the study area were in Phayao Province (Latitude 19°12'01.5"N Longitude 99°53'35.1"E, Phayao Provincial Sports Stadium (70T), Ban Tom Sub-District, Phayao Province, Northern Thailand (figure 1). The daily mean air pollution of PM_{10}, $PM_{2.5}$, CO, NO_2, and O_3 at air quality monitoring stations in Phayao Province between July 2019 and December 2020 was measured and recorded by PCD, Ministry of Natural Resources and Environment, Thailand.

Figure 1. Location map of study area

2.4 The daily number of health related diseases

The daily number of health-related diseases in Phayao Province between July 2019 and December 2020 was defined using the ICD - 10 by the Information and Communication Technology Center, Ministry of Health, Thailand as follows: diseases of the circulatory system (I00 - I99), diseases of the respiratory system (J00 - J99.8), diseases of the skin and subcutaneous tissue (L00 - L99), diseases of the eye (H10 - H19.8), rash and other nonspecific skin eruptions (R21), and neoplasms (C00 - D48).

2.5 CC16 measurement

Medical laboratory technicians collected 3 mL of venous blood in EDTA and analyzed it for serum CC16 levels. The blood samples were centrifuged immediately at 1000 x g at 4 ºC for 10 minutes and the serum was stored at -80 ºC. The concentrations of CC16 in the serum were determined by commercially available human CC16 enzyme-linked immunosorbent assays (ELISA) test kits (Bio Vendor®, Czech Republic) according to the manufacturer's recommendation. The analytical linearity was 1.57 - 50.0 ng/mL, with r^2 values of 0.95 - 0.97. The reliability of reported results was demonstrated by the values of internal controls within +/-2SD. The specificity of antibodies used in this ELISA is specific for human CC16 with no detectable cross-reactivities to cytokines, hemoglobin (1.0 mg/ml), bilirubin (170 µmol/l) and triglycerides (5.0 mmol/l) that may be present in human serum.

2.6 Statistical analysis

Descriptive statistics were performed to describe the findings, including frequency and percentages, mean and standard deviations (SD). The Mann-Whitney U test, Spearman's rank correlation coefficient, and Kruskal-Wallis test were compared between demographic data and QoL. Multiple linear regression analysis was also used to estimate associations between PH, MH, overall QoL, and serum CC16 levels.

2.7 Ethical Considerations

The study was approved by the Research Ethics Committee of University of Phayao, Thailand (No. 1.2/004/64).

2.8 Preliminary study of PM_{10} and $PM_{2.5}$ concentrations

The results of the study between July 2019 and December 2020 indicated that the monthly concentrations of PM_{10} at air quality monitoring stations in Phayao Province, Northern Thailand in March, February, April, and January of 2020 were 120.4 ± 52.5 µg/m3, 82.4 ± 21.8 µg/m³, 79.5 ± 36.0 µg/m³, 73.9 ± 24.6 µg/m³, respectively. The monthly concentrations of PM_{10} were higher than the WHO guideline (45 µg/m³), but lower than US National Ambient Air Quality (US NAAQS) standard (150 µg/m³) and the monthly concentrations of PM_{10} in February, April, and January of 2020 lower than Thailand NAAQS standard (120 µg/m³) (PCD, 2004; WHO, 2021; WHO, 2022). Moreover, the monthly concentrations of $PM_{2.5}$ in March, February, April, and January of 2020 were 93.8 ± 47.8 µg/m³, 59.7 ± 19.3 µg/m³, 57.3 ± 29.1 µg/m³, 55.4 ± 1.0 µg/m³, respectively. The monthly concentrations of $PM_{2.5}$ were higher than US NAAQS standard (35 µg/m³), Thailand NAAQS standard (37.5 µg/m³) and the WHO guideline (15 µg/m³) (WHO, 2021; PCD, 2022; WHO, 2022) (Figure 2).

2.9 Preliminary study of PM_{10} and $PM_{2.5}$ concentrations and the daily number of health-related diseases

The results of the study between July 2019 and December 2020 indicated that daily PM_{10} and $PM_{2.5}$ concentrations were significantly positively associated with I00 - I99 and J00 - J99.8, while daily PM_{10} and $PM_{2.5}$ concentrations were significantly negatively associated with L00 - L99 and R21. The daily CO was significantly positively associated with I00 - I99 and J00 - J99.8. The daily NO_2 was significantly positively associated with I00 - I99 and J00 - J99.8, while the daily NO_2 was significantly negatively associated with L00 - L99. The daily O_3 was significantly negatively associated with L00 - L99, H10-H19.8, R21, and C00 - D48 (Table 1).

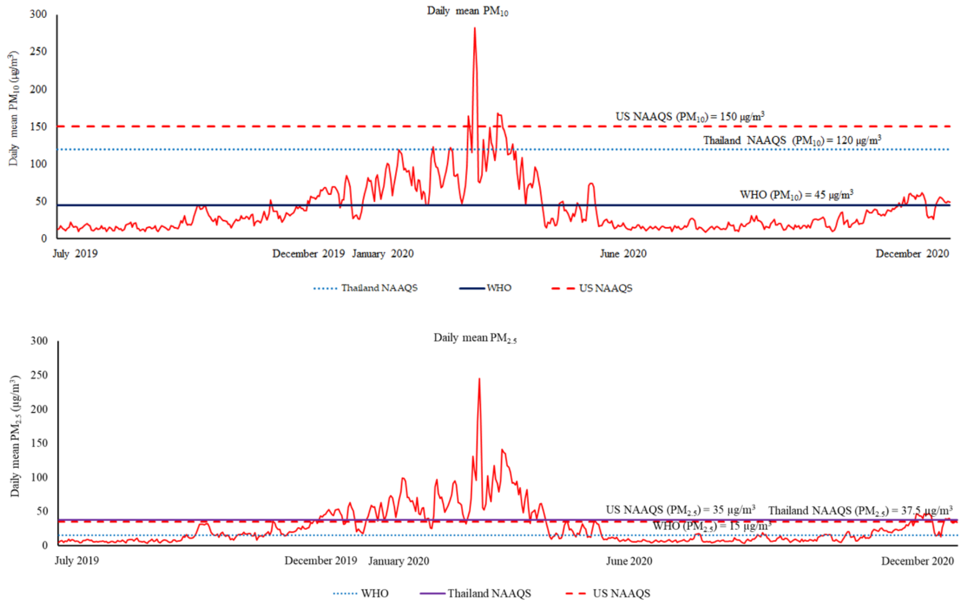

Figure 2. The daily mean of PM_{10} and $PM_{2.5}$ concentrations during 2019-2020

Table 1. Association between daily air pollution and the daily number of health-related diseases

Variables	The daily number of health-related diseases					
	I00-I99	J00-J99.8	L00-L99	H10-H19.8	R21	C00-D48
PM_{10}	0.141**	0.273***	- 0.256***	- 0.040	- 0.183***	- 0.066
$PM_{2.5}$	0.134**	0.276***	- 0.272***	- 0.055	- 0.201***	- 0.075
CO	0.088*	0.271***	-0.045	0.005	-0.019	- 0.069
NO_2	0.200***	0.296***	- 0.129**	0.010	-0.067	- 0.047
O_3	0.028	0.072	- 0.270***	- 0.112**	- 0.193***	- 0.160***

Spearman's correlation coefficient. **p* value <0.05, ***p* value <0.01, ****p* value <0.001

3. Results and Discussion

3.1 Results

The sample was comprised of 240 participants, with a mean age of 58.8 ± 12.8 years, and 53.8 were aged 60 years of age or older. The mean income was THB 3302.0 per month (SD = 5436.6). The mean living period in the community was 51.1 years (SD = 18.1). The majority of participants were female (75.0%), married (65.4%), had a level of education in primary school (71.3%), no smoking (95.4%), no alcohol use (82.9%), had no respiratory symptoms (56.3%), and had no co-morbidities (46.31%) (Table 2).

The results of this study showed that sex, age, education, and occupation were significantly different in serum CC16 levels, while income and time of living in the community were significantly associated with serum CC16 levels (Table 3).

The result of this study showed that the mean of PH, physical functioning, role limitations due to PH, general health, MH, social functioning, and role limitations due to emotional problems were lower than QoL Thai volunteer, while the mean of bodily pain, energy/fatigue, and emotional well-being were higher than QoL ThaiS' volunteer (Table 4).

According to the findings, time of living in the community was associated with MH and overall QoL, while alcohol use was associated with PH and overall QoL. Age and education were significantly different in PH, MH, and overall QoL, while serum CC16 levels were associated with PH, MH, and overall QoL (Table 5).

Table 2. Characteristics of sample populations (n = 240)

Variables	n (%)
Sex[a]	
Male	60 (25.0)
Female	180 (75.0)
Age (years)[a], mean±SD	58.8 ± 12.8
< 60	111 (46.3)
≥ 60	129 (53.8)
Income (baht/month)[b], mean ± SD	3302.0 ± 5436.6
Marital status[c]	
Single	33 (13.8)
Married	157 (65.4)
Divorce	50 (20.8)
Education[a]	
≤ Primary school	171 (71.3)
> Primary school	69 (28.7)
Occupation[c]	
Daily hired workers	36 (15.0)
Agriculture	98 (40.8)
Own business	30 (12.5)
Others	76 (31.7)
Time of living in the community (years)[b], mean ± SD	51.1 ± 18.1
Smoking[a]	
No	229 (95.4)
Yes	11 (4.6)
Alcohol use[a]	
No	199 (82.9)
Yes	41 (17.1)
Respiratory symptoms (number)[c]	
None	135 (56.3)
1-2	44 (18.3)
≥ 3	61 (25.4)
Co-morbidities (number)[c]	
None	111 (46.3)
1	81 (33.8)
≥ 2	48 (20.0)

Table 3. Factors associated with serum CC16 level (n = 240)

Variables	Serum CC16 level, Mean ± SD	*p* value
Sex[a]		
Male	9.38 ± 6.39	0.011*
Female	7.34 ± 6.16	
Age (years)[a], mean±SD		
< 60	5.34 ± 4.24	< 0.001**
≥ 60	10.01 ± 6.91	
Income (baht/month)[b], mean ± SD	-	< 0.001**
Marital status[c]		
Single	6.42 ± 6.28	0.149
Married	7.82 ± 6.18	
Divorce	8.88 ± 6.46	
Education[a]		
≤ Primary school	8.61 ± 6.78	0.011*
> Primary school	5.97 ± 4.24	
Occupation[c]		
Daily hired workers	6.64 ± 5.40	< 0.001**
Agriculture	7.01 ± 5.57	
Own business	5.43 ± 4.90	
Others	10.46 ± 7.17	
Time of living in the community (years)[b], mean ± SD	-	< 0.001**
Smoking[a]		
No	8.00 ± 6.356	0.094
Yes	4.70 ± 2.99	
Alcohol use[a]		
No	7.93 ± 6.48	0.932
Yes	7.44 ± 5.19	
Respiratory symptoms (number)[c]		
None	7.34 ± 5.99	0.444
1-2	8.75 ± 7.04	
≥ 3	8.34 ± 6.28	
Co-morbidities (number)[c]		
None	7.46 ± 5.51	0.439
1	7.50 ± 6.33	
≥ 2	9.36 ± 7.58	

[a]Mann-Whitney U test, [b]Spearman's rank correlation coefficient, [c]Kruskal-Wallis test. *p value <0.05, **p value <0.001

Table 4. Mean ± SD of QoL score

Items	QoL score	QoL Thai volunteer[a]
PH	67.2 ± 16.9	75.1 ± 20.6
Physical functioning	68.5 ± 24.2	77.3 ± 17.4
Role limitations due to PH	55.4 ± 44.4	82.2 ± 28.6
Bodily pain	77.4 ± 20.8	75.6 ± 18.4
General health	64.8 ± 18.3	65.1 ± 18.1
Energy/fatigue	69.6 ± 17.2	62.2 ± 13.3
MH	69.0 ± 17.0	76.7 ± 19.1
Social functioning	77.2 ± 19.4	78.2 ± 18.2
Role limitations due to emotional problems	50.4 ± 46.6	80.4 ± 31.9
Emotional well-being	79.3 ± 18.0	66.1 ± 12.9

[a]Lim *et al.*, 2008

Table 5. Factors associated with PH, MH, and overall QoL

Variables (n = 240)	PH, *p* value	MH, *p* value	Overall QoL, *p* value
Sex[a]			
Male	0.112	0.948	0.267
Female			
Age (years)[a]	0.023*	0.004**	0.005**
< 60			
≥ 60			
Income (baht/month)[b], mean ± SD	0.224	0.339	0.186
Marital status[c]			
Single	0.480	0.331	0.269
Married			
Divorce			
Education[a]			
≤ Primary school	< 0.001***	0.005**	< 0.001**
> Secondary school			
Occupation[c]			
Daily hired workers	0.986	0.901	0.939
Agriculture			
Own business			
Others			
Time of living in the community (years)[b], mean ± SD	0.097	0.007**	0.020**
Smoking[a]			
No	0.938	0.113	0.696
Yes			
Alcohol use[a]			
No	0.001**	0.204	0.004**
Yes			
Respiratory symptoms (number)[c]	0.193	0.082	0.129
None			
1-2			
≥ 3			
Co-morbidities (number)[c]			
None	0.558	0.358	0.424
1			
≥ 2			
Serum CC16 level[b], mean ± SD	0.012*	0.030*	0.004**

[a]Mann-Whitney U test, [b]Spearman's rank correlation coefficient, [c]Kruskal-Wallis test. *p value < 0.05, **p value < 0.01, ***p value < 0.001

The mean ± SD of serum CC16 levels in participants aged < 60 years was 5.34 ± 4.24 ng/ml, which was significantly lower than that in participants aged ≥ 60 years, 10.01 ± 6.91 ng/ml (p value < 0.001) (Figure 3).

Multiple linear regression analysis showed that an increase in serum CC16 level was associated with a decrease in overall QoL after adjusting for sex, income, marital status, education, occupation, time of living in the community, smoking, and alcohol use (Table 6).

3.2 Discussion

Air pollution, especially PM_{10} and $PM_{2.5}$, can have adverse health effects and can lead to cardiovascular and respiratory diseases and reduced HRQOL (Darçın *et al.,* 2014; Hwang *et al.,* 2020; Leikauf *et al.,* 2020; Manisalidis *et al.,* 2020; Mueller *et al.,* 2020; Hautekiet *et al.,* 2022). A preliminary study found that the monthly concentrations of PM_{10} in March, February, April, and January of 2020 were higher than the WHO guideline (45 µg/m³),

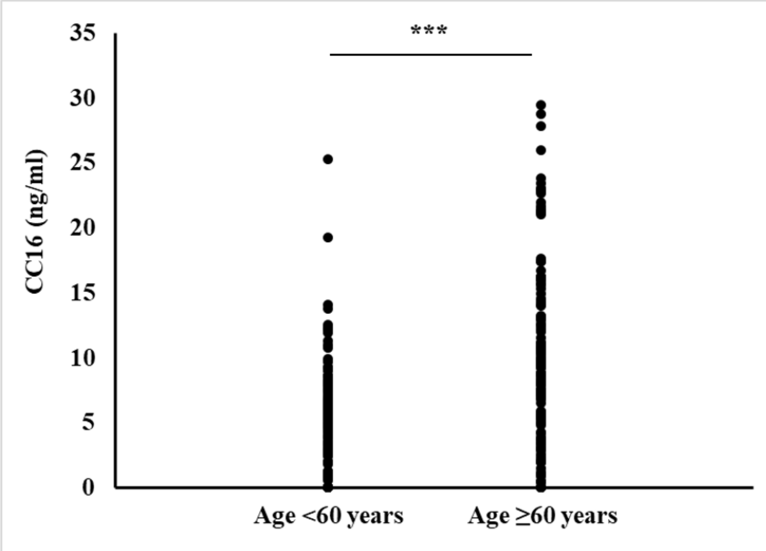

Figure 3. Serum CC16 levels

Table 6. Associations of serum CC16 level and overall QoL

	B	SE	p-value
Serum CC16 level	-0.385	0.177	0.031*

Adjust with sex, income, marital status, education, occupation, time of living in the community, smoking, and alcohol use. *p value < 0.05

but lower than US NAAQS standard (150 µg/m^3). Moreover, the monthly concentrations of PM_{10} in March of 2020 were higher than Thailand NAAQS standard (120 µg/m^3) (PCD, 2004; WHO, 2021; WHO, 2022). Furthermore, the monthly concentrations of $PM_{2.5}$ in March, February, April, and January of 2020 were higher than US NAAQS standard (35 µg/m^3), Thailand NAAQS standard (37.5 µg/m^3) and the WHO guideline (15 µg/m^3) (WHO, 2021; PCD, 2022; WHO, 2022). Previous studies found that the climate of Thailand is determined by three seasons: summer (mid-February to mid-May); rainy (mid-May to mid-October); and winter (mid-October to mid-February) (Sangkham *et al.,* 2021). This is similar to the findings of the previous studies that found high levels of these pollutants in the dry or summer season, which were a result of the meteorological conditions, increased burning during the dry or summer season, and other factors such as emissions from commercial areas, industries, and vehicles (Arunrat *et al.,* 2018; Kliengchuay *et al.,* 2018; Outapa *et al.,* 2019; Aslam *et al.,* 2020; Mueller et al., 2020).

According to a preliminary study of PM_{10} and $PM_{2.5}$ concentrations and the daily number of health-related diseases, the Pearson coefficient indicates that the daily PM_{10} and $PM_{2.5}$ concentrations were significantly positively associated with I00 - I99 and J00 - J99.8 while the daily PM_{10} and $PM_{2.5}$ concentrations were significantly negatively associated with L00 - L99 and R21. The daily CO was significantly positively associated with I00 - I99 and J00 - J99.8. The daily NO_2 was significantly positively associated with I00 - I99 and J00 - J99.8, while the daily NO_2 was significantly negatively associated with L00 - L99. The daily O3 was significantly negatively associated with L00 - L99, H10 - H19.8, R21, and C00 - D48.

Previous research has linked air pollution to an increased risk of respiratory symptoms, respiratory diseases, and other diseases and health problems in the short and long term (Cho *et al.,* 2014; Esposito *et al.,* 2014; Thongtip *et al.,* 2019; WHO, 2021). Moreover, previous studies found that exposure to air pollution is associated with an increased risk of stress, cardiovascular or respiratory disease, and poor QoL, which can lead to increased morbidity and mortality (Cho *et al.,* 2014; Shin *et al.,* 2018; WHO, 2021). Air pollution was significantly associated with an increased risk of emergency department visits (Cho *et al.,* 2014).

This study found that PH, physical functioning, role limitations due to PH, general health, MH, social functioning, and role limitations due to emotional problems were lower than QoL Thai volunteers, while bodily pain, energy/fatigue, and emotional well-being were higher than QoL Thai volunteers. Previous studies found that perceived environmental pollution could lead to an increase in PH and MH (Han *et al.,* 2020). However, other risk factors may lead to increasing or decreasing QoL (Cho *et al.,* 2014; Shin *et al.,* 2018; Thongtip *et al.,* 2019; AAbed Al Ahad *et al.,* 2022). This study found that time of living in the community was associated with MH and overall QoLwhile alcohol use was associated with PH and overall QoL. Age and education were significantly different in PH, MH, and overall QoL. Previous studies found that socioeconomic factors, various types of pollution, and lifestyle variables were associated with QoL (Roswall *et al.,* 2015; Thongtip *et al.,* 2019; Han *et al.,* 2020; AAbed Al Ahad *et al.,* 2022).

This study found that sex, age, education, and occupation were significantly different in serum CC16 levels, while income and time of living in the community were significantly associated with serum CC16 levels. Previous studies found that socioeconomic factors such as sex, age, and decreased education were significantly associated with serum CC16 levels (Guerra *et al.,* 2013; Guerra *et al.,* 2015; Wang *et al.,* 2018; Zhai *et al.,* 2018). Furthermore, previous research has linked serum CC16 levels to decreased lung function and a lower QoL (Negrin *et al.,* 2017; Wang *et al.,* 2018; Rong *et al.,* 2020; Thongtip *et al.,* 2020). Evidence shows that CC16 has immunoregulatory and anti-inflammatory properties in the airway process, which can help reduce the airway inflammatory response in chronic respiratory diseases (Kim *et al.,* 2018; Liu *et al.,* 2021).

The mean ± SD of serum CC16 levels in participants under 60 years old was significantly higher than that in participants aged 60 years and older (5.33 ± 4.24 vs 10.01 ± 6.91 ng/mL, $p < 0.001$). Interestingly, serum CC16 levels in participants aged 60 years and older were higher than those in participants aged under 60 years. Previous studies found that serum CC16 levels were correlated with age (Castro-Rodriguez *et al.,* 2018). Moreover, a previous study found that serum CC16 levels increased from birth through childhood and adulthood, respectively (Zhai *et al.,* 2018; Rong *et al.,* 2020). This study found that serum CC16 level were associated with PH, MH, and overall QoL. Importantly, after controlling for confounding variables, multiple linear regression analysis revealed that an increase in serum CC16 level was associated with a decrease in overall QoL. In addition, long-term exposure to air pollution has been associated with lower levels of serum CC16 and an increased risk of chronic respiratory diseases (Guerra *et al.,* 2015; Lam *et al.,* 2018; Zhai *et al.,* 2018; Zhang *et al.,* 2022). However, short-term exposure to air pollution has been associated with higher levels of serum CC16 (Madsen *et al.,* 2008; Zhang *et al.,* 2022). Previous studies found that a decrease in serum CC16 levels was associated with different chronic lung diseases, including a decline in lung function, severe COPD, and chronic asthma (Braido *et al.,* 2007; Van *et al.,*, 2012; Park *et al.,* 2013; Tiezzi *et al.,* 2022). Furthermore, reduction in QoL has been found to affect many risk factors (D'Souza *et al.,* 2013; Thongtip *et al.,* 2019). Thus, decreased serum CC16 levels can be used as indicators of disease progression and can be increased (Castro-Rodriguez *et al.,* 2018; Lam *et al.,* 2018; Rong *et al.,* 2020; Thongtip *et al.,* 2020; Zhang *et al.,* 2022). The limitations of this study were its a cross-sectional design, which did not describe a causal inference. Thus, further research is required to focus on a longitudinal analysis.

4. Conclusion

Overall, this study showed that air pollutants, especially PM_{10} and $PM_{2.5}$, may lead to health effects. Surprisingly, low levels of serum CC16 were discovered in people under the age of 60. Moreover, many factors may be linked to serum CC16 levels and QoL. Thus, concerned agencies should provide policymakers and health promotion interventions for reducing pollution exposure and self-protective behaviors to prevent airway inflammatory responses, chronic respiratory diseases, and poor QoL.

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