Socioeconomic impact of asthma, chronic obstructive pulmonary disease and asthma-COPD overlap syndrome

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Background: Asthma-chronic obstructive pulmonary disease (COPD) overlap syndrome (ACOS) is defined as having both features of asthma and COPD, which are airway hyper-responsiveness and incompletely reversible airway obstruction. However, socioeconomic impact of ACOS have not been well appreciated.

Methods: Adults with available wheezing history and acceptable spirometry were selected from the fourth Korean National Health and Nutrition Examination Survey (KNHANES IV) in 2007–2009. Their data were merged with the Korean National Health Insurance claim data. 'Asthma group' was defined as having self-reported wheezing history and $FEV_1/FVC \geq 0.7$, 'COPD group' was defined as having $FEV_1/FVC < 0.7$ and no wheezing, 'ACOS group' was defined as having both wheezing and $FEV_1/FVC < 0.7$, and 'no airway disease (NAD) group' was defined as having no wheezing and $FEV_1/FVC \geq 0.7$.

Results: Among a total of 11,656 subjects, ACOS comprise 2.2%; COPD, 8.4%; asthma, 5.8% and NAD, 83.6%. Total length of healthcare utilization and medical costs of ACOS group was the top among four groups (P<0.001), though inpatient medical cost was the highest in COPD group (P=0.025). Multiple linear regression analyses showed that ACOS group (β=12.63, P<0.001) and asthma group (β=6.14, P<0.001) were significantly associated with longer duration of healthcare utilization and ACOS group (β=350,475.88, P=0.008) and asthma group (β=386,876.81, P<0.001) were associated with higher medical costs.

Conclusions: This study demonstrated that ACOS independently influences healthcare utilization after adjusting several factors. In order to utilize limited medical resources efficiently, it may be necessary to find and manage ACOS patients.

Keywords: Asthma COPD overlap syndrome (ACOS); asthma; chronic obstructive pulmonary disease (COPD); epidemiology; medical cost

Introduction

Chronic airway disease is one of the most common chronic diseases, which is responsible for current and future socioeconomic burden (1). Asthma and chronic obstructive pulmonary disease (COPD) are major airway diseases and have unique distinctive features (2). However, clinicians often encounter patients presenting overlapping symptoms of both diseases. Now asthma-COPD overlap syndrome (ACOS) is widely used to describe such a condition sharing both features of asthma and COPD (3-5). ACOS is simply defined as coexistence of incompletely reversible airway obstruction and airway hyper-responsiveness. Subjects with ACOS tend to have increased risk of exacerbation and poor quality of life (6-8). High economic burden of ACOS was demonstrated compared to those of asthma and COPD (9-13). This study was to measure impact of ACOS particularly on healthcare utilization and medical cost using data from the fourth South Korean National Health and Nutrition Examination Survey (KNHANES IV) (14) and National Health Insurance claims (15,16).

Methods

Data source and ethical considerations

This study examined data from KNHANES IV and National Health Insurance claims.

KNHANES is a national survey performed every three years, which began in 1998. The purpose of KNHANES is to assist the establishment of a national health policy and to develop a knowledge base for the evaluation of health risk factors and health indicators. The fourth survey was later converted into a year-round investigation to improve weaknesses in survey areas and the quality of results gained. The first round [2007], the second round [2008], and the last round [2009] of the KNHANES IV have been conducted (14). KNHANES IV used stratified, multi-stage, clustered probability design to select a representative sample of non-institutionalized citizens from the Korean population (14). KNHANES IV consisted of Health Interviews, Health Behavior Surveys, Health Examination Studies, and Nutrition Surveys. More details on the research methodology used to gather and analyze the KNHANES IV data are available on the National Health and Nutrition Examination Survey website (https://knhanes.cdc.go.kr/knhanes/index.do).

The National Health Insurance claims data was provided by the Korean Health Insurance Review and Assessment Service (HIRA), which was established to review claims data and assess healthcare in Korea; it is under the responsibility of a single agency independent from insurers, providers, and other interested parties. All Koreans are covered under the national health insurance system, and the HIRA database contains all information regarding submitted claims and prescriptions.

This study analyzed respondents over the age of nineteen who participated in the spirometry test of the KNHANES IV and who provided responses to questions on whether they had experienced wheezing in the past year. Subjects who did not have missing covariates were selected, and their claims data, collected from January 1 to December 31 of the years when KNHANES IV was conducted, was examined in conjunction with the KNHANES IV data.

The Public Institutional Review Board approved the present study (PIRB11-025-2).

Study population selection

A total of 21,845 respondents, over the age of nineteen, participated in the KNHANES IV. This study examined a total of 11,940 subjects who had participated in the spirometry tests and had provided a response regarding experiences of wheezing during the one year prior to the survey. Two hundred-eighty four subjects with missing covariates were excluded from the final data set, and the remaining 11,656 respondents were analyzed for the study. *Figure 1* shows the details on the selection of the study population.

Measures

Definition of airway diseases
Subjects were categorized into four groups: ACOS group, COPD group, asthma group, and group with no airway disease (NAD). ACOS was defined as having FEV_1/FVC <0.7 and experiencing wheezing during the twelve months prior to the survey. COPD was defined as having FEV_1/FVC <0.7 and no wheezing during the twelve months prior to the survey. Asthma was defined as having FEV_1/FVC ≥0.7 and experiencing wheezing during the twelve months prior to the survey. NAD was defined as having FEV_1/FVC ≥0.7 and no wheezing.

Subjects' characteristics
The variables of the subjects' characteristics were age, gender, body mass index (BMI), spirometry, presence or
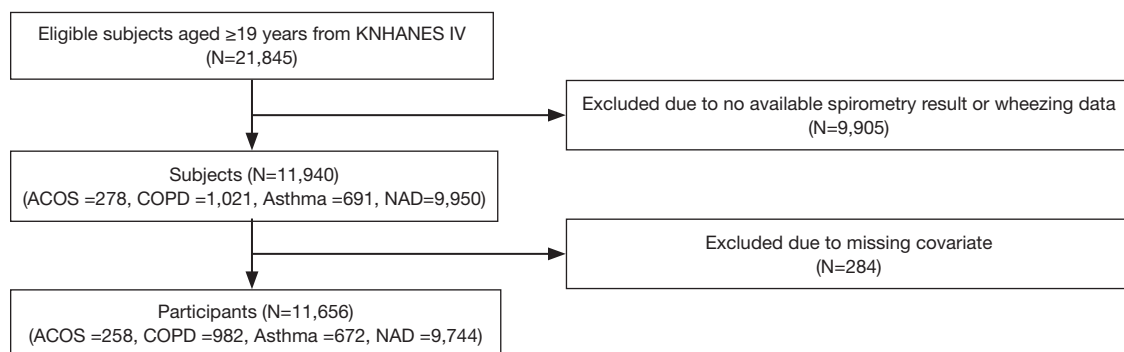
Figure 1 Flow diagram of the study selection process. KNHANES IV, fourth Korean National Health and Nutritional Examination Survey; ACOS, asthma-COPD overlap syndrome; COPD, chronic obstructive pulmonary disease; NAD, no airway disease.

absence of chronic bronchitis, smoking status, education, and household income level. BMI is obtained by dividing a subject's weight by the square of the subject's height, and this study divided subjects into three BMI groups: underweight (<18.5 kg/m²), normal (≥18.5 and <25 kg/m²), and overweight (≥25 kg/m²). Chronic bronchitis was defined as having cough or sputum production for over three months during the twelve months prior to the survey and had a cough or sputum that lasted over two years. Subjects' smoking status was divided into current smokers, former smokers, and never smokers. Subjects' education level was categorized as <12, 12, and >12 years. Household income level was divided into four groups based on their average total household income: 1st, 2nd, 3rd and the 4th quartile; the 1st quartile consisted of the lowest income group, while the 4th quartile was composed of subjects with the highest income.

Healthcare utilization

Healthcare utilization was measured by the medical cost and the duration (days) of medical service utilized per person. The medical cost was calculated as medical expenses (including insurance benefits and patients' copayments), including outpatient and hospitalization fees. The duration of medical service use included the hospitalization period (including intensive care unit hospitalization days and emergency room days) and number of outpatient visits.

Statistical analyses

Data was analyzed using the SAS statistical program [ver. 9.2 (SAS Institute)]; details of the analytical methods are listed below.

First, frequencies, percentages, and mean ± standard

deviation (SD) were calculated to enable comparison of subjects' baseline characteristics among four groups; the chi-squared test was used for categorical (discrete) variables and ANOVA was used for continuous variables.

Second, Chi-squared test was applied to assess differences in utilization or non-utilization of healthcare services among four groups; ANOVA was used to analyze differences in length of healthcare utilization (number of days) and medical costs.

Lastly, linear regression analysis was applied to assess the impact of airway diseases and subjects' characteristics on length of healthcare utilization and medical costs.

Results

Among a total of 11,656 subjects, ACOS comprise 2.2% [258]; COPD, 8.4% [982]; asthma, 5.8% [672] and NAD, 83.6% [9,744].

Four groups showed differences in age, gender, BMI, lung function, the presence or absence of chronic bronchitis, smoking status, education and household income level (P<0.001 respectively, *Table 1*). In terms of age, both ACOS and COPD groups were most common among those above sixty, while both asthma and NAD groups were most common among subjects between 40 and 60 (P<0.001). There were more males than females within both ACOS and COPD groups, and it was the opposite in both asthma and NAD groups (P<0.001). With regards to BMI, underweight is relatively common in both ACOS and COPD groups, and overweight is common in asthma group. Among four groups, ACOS group showed the worst lung function parameters as well as the highest smoking rate (68.2%). Moreover, current smoking rate was the highest. Although only 25 subjects had chronic bronchitis based on

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Table 1 Subjects' characteristics

Variables	ACOS (n=258)	COPD (n=982)	Asthma (n=672)	NAD (n=9,744)	P
Age (years), n (%)					
<40	14 (5.4)	89 (9.1)	191 (28.4)	3,201 (32.9)	<0.001[†]
≥40 and <60	75 (29.1)	246 (25.0)	247 (36.8)	4,273 (43.9)	
≥60	169 (65.5)	647 (65.9)	234 (34.8)	2,270 (23.3)	
Gender, n (%)					
Male	165 (64.0)	680 (69.2)	251 (37.4)	4,080 (41.9)	<0.001[†]
Female	93 (36.0)	302 (30.8)	421 (62.6)	5,664 (58.1)	
BMI, n (%)					
Underweight	15 (5.8)	46 (4.7)	16 (2.4)	261 (2.7)	<0.001[†]
Normal	165 (64.0)	697 (71.0)	351 (52.2)	6,017 (61.8)	
Overweight	78 (30.2)	239 (24.3)	305 (45.4)	3,466 (35.6)	
Lung function, mean ± SD or n (%)					
FVC % predicted	84.8±16.10	90.0±15.17	9.4±13.23	92.5±11.97	<0.001[‡]
FEV_1 % predicted	67.0±17.39	76.4±15.98	90.0±12.85	93.5±12.08	<0.001[‡]
FEV_1/FVC	0.59±0.11	0.63±0.07	0.80±0.06	0.82±0.06	<0.001[‡]
FEV_1 <50% predicted	43 (16.7)	55 (5.6)	4 (0.6)	12 (0.1)	<0.001[†]
FEV_1 ≥50% predicted	215 (83.3)	927 (94.0)	668 (99.4)	9,732 (99.9)	
Chronic bronchitis, n (%)					
No	247 (95.7)	974 (99.2)	671 (99.9)	9,739 (99.9)	<0.001[†]
Yes	11 (4.3)	8 (0.8)	1 (0.1)	5 (0.1)	
Smoking status, n (%)					
Current	109 (42.2)	308 (31.4)	254 (37.)	2,019 (20.7)	<0.001[†]
Former	67 (26.0)	352 (35.8)	66 (9.8)	1,892 (19.4)	
Never	82 (31.8)	322 (32.8)	352 (52.4)	5,833 (59.9)	
Education (years), n (%)					
<12	186 (72.1)	590 (60.1)	323 (48.1)	3,318 (34.1)	<0.001[†]
12	47 (18.2)	218 (22.2)	175 (26.0)	3,065 (31.5)	
>12	25 (9.7)	174 (17.7)	174 (25.9)	3,361 (34.5)	
Household income, n (%)					
1st quartile (lowest)	140 (54.3)	474 (48.3)	221 (32.9)	2,245 (23.0)	<0.001[†]
2nd quartile	43 (16.7)	193 (19.7)	139 (20.7)	2,142 (22.0)	
3rd quartile	54 (20.9)	194 (19.8)	180 (26.8)	3,230 (33.2)	
4th quartile (highest)	21 (8.1)	121 (12.3)	132 (19.6)	2,127 (21.8)	

[†], Chi-square test; [‡], ANOVA. ACOS, asthma COPD overlap syndrome; COPD, chronic obstructive pulmonary disease; NAD, no airway disease; BMI, body mass index; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second.

responses to questionnaires, most of them (n=19) belonged to both ACOS and COPD groups. ACOS group showed the lowest education levels, the next was COPD group and the third was asthma group (P<0.001). Household income showed similar trend to education level.

There were statistically significant differences among four groups in terms of the total number of days per person in healthcare utilization, outpatient care utilization, utilization of clinics, and utilization of tertiary medical centers from January 1 to December 31 of the year KNHANES IV was conducted (P<0.001, respectively, *Table 2*). While ACOS group recorded the top in both of total used days and total medical costs (P<0.001), inpatient medical cost was the highest in COPD group compared to the others (P=0.025).

When a univariate regression analysis was applied to know factors affecting the length of healthcare utilization, it revealed that the presence of airway disease, FEV_1 <50% predicted, the presence of chronic bronchitis, current smoking, overweight, lower education levels, lower household income levels, old age, and female gender are significantly associated with longer duration of health hare utilization (*Table 3*). To observe whether the type of airway disease had a specific impact on the length of healthcare utilization, all factors influencing the length of healthcare utilization from the univariate regression analysis were included in the multiple regression analysis; results showed that ACOS group (β=12.63, SE =2.21, P<0.001) and asthma group (β=6.14, SE =1.35, P<0.001) were significantly associated with higher number of days in healthcare utilization.

When the same approach was applied to the medical costs, univariate analyses showed that the type of airway disease, FEV_1 <50% predicted, the presence of chronic bronchitis, current and former smokers, overweight, lower education levels, lower household income levels, and old age were associated with higher medical costs (*Table 4*). To observe whether the type of airway disease had a specific impact on medical costs, all factors influencing medical costs from the univariate regression analysis were included in the multiple regression analysis; results showed that ACOS group (β=350,475.88, SE =131,289.38, P=0.008) and asthma group (β=386,876.81, SE =80,026.83, P<0.001) were associated with higher medical costs.

Discussion

This study clearly showed large impact of ACOS on

healthcare utilization, which existed independently after multiple adjustments with possible confounding factors. Although Rhee *et al.* (11) reported high medical utilization of ACOS in Korea, they used only the National Health Insurance claim data, which did not include spirometry data and history of smoking and chronic bronchitis. Therefore, their definitions of COPD and ACOS were not based on spirometry, but on diagnosis codes and medication records. Additionally Rhee *et al.* compared healthcare utilization of ACOS only with that of COPD, not with that of asthma. In contrast, our study applied spirometric criteria to define airway disease and used data from a representative sample of non-institutionalized citizens from the Korean population by stratified, multi-stage, clustered probability design. These support that our results could have representativeness.

ACOS is known to encompass severe asthma with airway remodeling and COPD with bronchial hyper-responsiveness. Naturally healthcare utilization and medical cost of ACOS group are expected to be higher than those of asthma and COPD. Accordingly, our study showed that all the medical cost and total length of healthcare utilization were the highest in ACOS group except inpatient medical cost, which was the highest in COPD group. Healthcare utilization and cost of COPD group were higher than those of asthma group, which is consistent with previous studies conducted in the other countries (9,10,17). However, our multiple regression analyses failed to show significant impact of COPD on health care utilization and medical cost though impacts of both ACOS and asthma kept significance. There were several possible reasons. Our definitions of ACOS, COPD, and asthma are not the same as those of previous studies. Bronchial hyper-responsiveness was based on self-reported wheezing and spirometry was not performed after bronchodilation, which made some heterogeneity even in the same group. Our definition of asthma might exclude subjects with recently well-controlled asthma, who were probably allocated to NAD group. Our asthma group presented wheezing in a previous year, which might make them to need healthcare utilization. Another reason is that these data were from national survey through representative sampling, which included subjects with relatively mild disease. Subjects with severe disease hardly participate survey. In our COPD group, only 5.6% had severe airflow limitation, defined as FEV_1 <50% predicted. In clinical practice, patients with FEV_1 ≥50% predicted rarely complain shortness of breath particularly if they are old and do not need physical activity. Maybe our asthma group represent recently poorly controlled

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Table 2 Healthcare utilization and medical cost according to the presence or absence of chronic airway disease

Variables	ACOS (n=258)	COPD (n=982)	Asthma (n=672)	NAD (n=9,744)	P
Used days					
Total					
Mean ± SD	60.2±50.77	44.5±41.68	43.3±41.25	32.7±35.45	<0.001[‡]
Yes, n (%)	253 (98.1)	947 (96.4)	652 (97.0)	9,293 (95.4)	0.020[†]
No, n (%)	5 (1.9)	35 (3.6)	20 (3.0)	451 (4.6)	
Outpatients					
Mean ± SD	57.1±49.06	42.5±40.29	40.8±38.63	31.4±33.99	<0.001[‡]
Yes, n (%)	253 (98.1)	945 (96.2)	651 (96.9)	9,290 (95.3)	0.034[†]
No, n (%)	5 (1.9)	37 (3.8)	21 (3.1)	454 (4.7)	
Inpatients*					
Mean ± SD	14.6±21.17	12.8±20.04	14.4±25.16	11.0±19.05	0.165[‡]
Yes, n (%)	54 (20.9)	155 (15.8)	120 (17.9)	1,100 (11.3)	<0.001[†]
No, n (%)	204 (79.1)	827 (84.2)	552 (82.1)	8,644 (88.7)	
Emergency room					
Mean ± SD	1.2±0.41	1.2±0.71	1.2±0.51	1.2±0.49	0.879[‡]
Yes, n (%)	24 (9.3)	71 (7.2)	44 (6.5)	502 (5.2)	0.001[†]
No, n (%)	234 (90.7)	911 (92.8)	628 (93.5)	9,242 (94.8)	
Hospital type					
Clinics					
Mean ± SD	57.4±49.16	42.6±40.29	41.0±38.74	31.6±5.02	<0.001[‡]
Yes, n (%)	253 (98.1)	947 (96.4)	652 (97.0)	9,293 (95.4)	0.020[†]
No, n (%)	5 (1.9)	35 (3.6)	20 (3.0)	451 (4.6)	
Tertiary medical center					
Mean ± SD	6.5±6.86	5.9±7.16	6.3±9.46	4.4±5.02	<0.001[‡]
Yes, n (%)	116 (45.0)	384 (39.1)	277 (41.2)	3,147 (32.3)	<0.001[†]
No, n (%)	142 (55.0)	598 (60.9)	395 (58.8)	6,597 (67.7)	
Medical cost: mean ± SD**					
Total	1,629±2,139	1,303±2,151	1,287±2,233	830±1,637	<0.001[‡]
Outpatients	1,221±1,162	953±1,314	951±1,644	645±1,123	<0.001[‡]
Inpatients*	1,909±2,582	2,154±2,881	1,834±2,615	1,561±2,339	0.025[‡]
Type of hospital (cost)					
Clinics	1,179±18,152	925±1,311	936±1,515	626±1,035	<0.001[‡]
Tertiary medical center	982±2,517	937±2,192	841±2,173	608±1,923	0.002[‡]

*, inpatients included the use of emergency room and hospitalization; **, unit, US dollar; [†], Chi-square test; [‡], ANOVA. ACOS, asthma COPD overlap syndrome; COPD, chronic obstructive pulmonary disease; NAD, no airway disease.

Table 3 Factors associated with total length of healthcare utilization (number of days)

Variables	Unadjusted				Adjusted*			
	β	SE	t	P	β	SE	t	P
Type of airway disease								
ACOS	27.52	2.34	11.74	<0.001	12.63	2.21	5.71	<0.001
COPD	11.77	1.25	9.38	<0.001	−1.24	1.20	−1.03	0.302
Asthma	10.65	1.49	7.15	<0.001	6.14	1.35	4.56	<0.001
NAD	Ref.				Ref.			
Lung function								
FEV$_1$ <50% predicted	17.41	3.61	4.82	<0.001	0.30	3.37	0.09	0.928
FEV$_1$ ≥50% predicted	Ref.				Ref.			
Chronic bronchitis								
Yes	37.01	7.59	4.87	<0.001	19.63	6.83	2.87	0.004
No	Ref.				Ref.			
Smoking status								
Current	−11.03	0.87	−12.61	<0.001	−2.44	1.04	−2.35	0.019
Former	1.06	0.90	1.18	0.238	3.93	1.03	3.81	0.000
Never	Ref.				Ref.			
BMI								
Underweight	−3.12	2.11	−1.48	0.140	−1.76	1.89	−0.93	0.351
Normal	Ref.				Ref.			
Overweight	4.18	0.74	5.62	<0.001	3.53	0.67	5.3	<0.001
Education (years)								
<12	30.00	0.79	37.89	<0.001	10.46	1.01	10.38	<0.001
12	7.64	0.84	9.07	<0.001	3.60	0.84	4.29	<0.001
>12	Ref.				Ref.			
Household income								
1st quartile (lowest)	22.78	1.00	22.84	<0.001	1.70	1.06	1.61	0.107
2nd quartile	6.59	1.05	6.28	<0.001	0.08	1.00	0.08	0.933
3rd quartile	−0.27	0.97	−0.28	<0.001	−1.39	0.90	−1.55	0.121
4th quartile (highest)	Ref.				Ref.			
Age (years)								
<40	Ref.				Ref.			
40≤ and <60	11.25	0.77	14.65	<0.001	6.68	0.84	7.99	<0.001
≥60	40.56	0.83	48.92	<0.001	30.62	1.10	27.76	<0.001
Gender								
Female	7.82	0.71	11.05	<0.001	7.03	0.93	7.59	<0.001
Male	Ref.				Ref.			

*, adjusted for all variables with P<0.05 in the univariate linear regression analysis. ACOS, asthma COPD overlap syndrome; COPD, chronic obstructive pulmonary disease; NAD, no airway disease; SE, standard error; Ref., reference; BMI, body mass index; FEV$_1$, forced expiratory volume in 1 second.

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Table 4 Factors associated with total medical cost

Variables	Unadjusted				Adjusted*			
	β	SE	t	P	β	SE	t	P
Type of airway disease								
ACOS	933,553.24	129,382.22	7.22	<0.001	350,475.88	131,289.38	2.67	0.008
COPD	553,231.80	69,262.66	7.99	<0.001	25,067.20	71,251.09	0.35	0.725
Asthma	533,882.13	82,262.66	6.49	<0.001	386,876.81	80,026.83	4.83	<0.001
NAD	Ref.				Ref.			
Lung function								
FEV$_1$ <50% predicted	877,653.78	198,306.72	4.43	<0.001	289,848.32	200,295.02	1.45	0.148
FEV$_1$ ≥50% predicted	Ref.				Ref.			
Chronic bronchitis								
Yes	895,468.57	417,434.82	2.15	0.032	143,891.92	405,598.49	0.35	0.723
No	Ref.				Ref.			
Smoking status								
Current	−225,061.98	48,320.27	−4.66	<0.001	−49,949.82	61,528.61	−0.81	0.417
Former	226,209.67	49,642.76	4.56	<0.001	200,141.83	61,224.73	3.27	0.001
Never	Ref.				Ref.			
BMI								
Underweight	−105,340.26	116,191.50	−0.91	0.365	−51,533.40	112,209.69	−0.46	0.646
Normal	Ref.				Ref.			
Overweight	188,403.67	40,877.17	4.61	<0.001	154,012.50	39,491.06	3.9	<0.001
Education (years)								
<12	960,013.64	45,498.42	21.1	<0.001	210,393.76	59,847.29	3.52	<0.001
12	245,945.79	48,438.97	−5.08	<0.001	86,052,12	49,894.53	1.72	0.085
>12	Ref.				Ref.			
Household income								
1st quartile (lowest)	811,547.90	55,932.25	14.51	<0.001	111,624.53	62,781.66	1.78	0.075
2nd quartile	327,677.47	58,834.63	5.57	<0.001	127,147.00	59,173.69	2.15	0.032
3rd quartile	6,555.30	54,255.24	0.12	0.904	−13,382.29	53,225.37	−0.25	0.802
4th quartile (highest)	Ref.				Ref.			
Age (years)								
<40	Ref.				Ref.			
40≤ and <60	403,062.96	44,895.38	8.98	<0.001	298,227.65	49,662.85	6.01	<0.001
≥60	1,457,803.02	48,486.99	30.07	<0.001	1,194,537.63	65,478.34	18.24	<0.001
Gender								
Female	67,447.10	39,062.99	1.73	0.084	100,054.13	54,972.58	1.82	0.069
Male	Ref.				Ref.			

*, adjusted for all variables with P<0.05 in the univariate linear regression analysis. ACOS, asthma COPD overlap syndrome; COPD, chronic obstructive pulmonary disease; NAD, no airway disease; SE, standard error; Ref., reference; BMI, body mass index; FEV$_1$, forced expiratory volume in 1 second.

asthma, and our COPD group mainly consists of subjects with mild to moderate airflow limitation and no symptoms. Furthermore, considering several features such as old age, high smoking rate, poor lung function, low education levels and low household income of ACOS group, most of them are likely to have severe COPD with frequent exacerbations or longstanding poorly-controlled asthma. Combination of low FEV_1 and airway hyper-responsiveness is likely to need medical attention. A previous study using the same definitions as those in our study also demonstrated that ACOS group reported the worst self-rated health status, but COPD group showed better than asthma group (8).

This study has several limitations. First, KNHANES was not exclusively intended to investigate chronic airway disease. Lung function was not measured in all participants, which contributes to selection bias. Total participation rate was not so high, and only participants with eligible spirometry results were included. Severely ill case could not be enrolled due to unsuitable data, though different sampling weights provided by KNHANES IV were applied to minimize the healthy worker effect (18). Second, bronchial hyper-responsiveness was defined only based on responses to questionnaires. This may result in misdiagnosis of an individual case and heterogeneity of subjects in the same group. Subjects with recent COPD exacerbations could have been misdiagnosed as having ACOS. Some asthmatics with poor compliance might have been misclassified to ACOS. Subjects with well-controlled mild asthma could have been considered to have NAD. COPD group may include subjects with well controlled ACOS. This sample bias might contribute to higher medical costs for the ACOS and asthma groups than those for the COPD. Nevertheless, self-assessment methods have been widely used in previous general population-based studies because of their feasibility (8,19,20). Although the definition of ACOS has been widely variable, the prevalence of ACOS in the current study is similar to that in previous studies (3,5), which estimated 15% to 45% of the population with obstructive airway disease. Our prevalence of ACOS was 21% [258/1,240] of subjects with airflow limitation. Additionally characteristics of our three groups are very consistent with previously described those of ACOS, asthma, and COPD. Third, only direct medical cost and length of healthcare utilization were shown, though indirect cost, loss of working days and mortality are very important to evaluate socioeconomic burden of disease.

Despite these limitations mentioned, this study clearly showed high impact of ACOS on healthcare utilization after multiple adjustments. Although our analysis was not complete, several important confounding factors such as age and socioeconomic factors were adjusted. These socioeconomic factors cannot be easily obtained in gathering clinical data, which was one of our strengths.

The current study highlights that the impact of ACOS on socioeconomic burden independently exists under multiple adjustments with other confounding factors. ACOS group needs appropriate socioeconomic supports as well as careful management by respiratory experts until evidence-based guidelines for management of ACOS will be developed.

Acknowledgements

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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