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ORIGINAL RESEARCH

Burden of Type 2 and Oral Corticosteroids Related Comorbidities in Severe Asthma Patients from the Gulf Countries: A Comparative Study from The ISAR Registry

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Background and Objectives: Comorbidities are common in severe asthma and can influence disease burden, and treatment outcomes. This study aimed to compare the prevalence and distribution of comorbidities potentially related to T2 inflammation and oral corticosteroid (OCS) use in severe asthma patients from Gulf countries using International Severe Asthma Registry (ISAR) data, and to assess their association with age, sex, and smoking status.

Methods: Data from severe asthma patients in Kuwait (n=494), Saudi Arabia (n=398), and the UAE (n=257) were extracted from ISAR (n=16,269). Comorbidities were categorized as T2–related or OCS–related. Comparative and subgroup analyses evaluated the prevalence and distribution of these comorbidities and their associations with age, sex, and smoking status.

Results: Gulf patients with severe asthma were significantly younger and had earlier disease onset compared to ISAR. T2-related comorbidities, especially allergic rhinitis and nasal polyposis were more prevalent in the Gulf, while OCS-related comorbidities such as osteoporosis, anxiety, and cardiovascular disease were markedly lower. Obesity was highly prevalent across all countries and subgroups. Significant associations were found between comorbidity types and age, sex, and smoking status, with T2 burden increasing in younger and male patients, and OCS burden remaining consistently low.

Conclusion: Severe asthma patients in the Gulf showed a high prevalence of T2-related comorbidities and obesity, with fewer OCS-related conditions. These patterns vary by age, sex, and smoking, highlighting the need for personalized management in this region.

Keywords: severe asthma, T2-related comorbidity, oral corticosteroid related comorbidity, Gulf countries, ISAR

Introduction

Asthma is a significant public health concern across Gulf countries, with prevalence varying widely by country: Saudi Arabia 4.7–24%, UAE 4.9–13.6%, and Kuwait 8.5–23%, with children generally exhibiting higher rates than adults.[1–3] Data on severe asthma are limited but align with international estimates of 5–10% among asthma patients, translating to approximately 0.5–2% of the total population.[4,5] Patients are classified as having severe asthma when their symptoms remain uncontrolled despite treatment with high-dose inhaled corticosteroids (ICS) combined with a controller bronchodilator.[6] These individuals often require frequent courses of systemic corticosteroids[7] and experience recurrent exacerbations along with multiple comorbidities, which collectively increase disease burden and complicate management.[8]

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More than half of all asthma patients have at least one comorbidity.[8] Conditions such as rhinitis and sinusitis, with or without nasal polyps, are commonly associated with poorer asthma control, increased exacerbation rates, and reduced quality of life.[9] These comorbidities are often linked to type 2 (T2) inflammation, which plays a central role in the pathophysiology of severe asthma.[10] T2 inflammation is driven by innate and adaptive immune responses, characterized by the production of IL-4, IL-5, and IL-13, leading to chronic airway inflammation, eosinophilia, mucus hypersecretion, and airway hyperresponsiveness.[10,11]

Additionally, some comorbidities arise as a consequence of long-term oral corticosteroid (LTOCS) therapy, which is used in 20–60% of severe asthma cases.[8] These include recurrent infections and metabolic, cardiovascular, musculoskeletal, and psychiatric complications. Collectively, these comorbidities contribute to worse clinical outcomes, increased healthcare utilization, and higher costs.[9] Targeted biologic therapies offer effective suppression of T2 inflammation, helping to minimize the need for oral corticosteroids (OCS), leading to reduced exacerbation rates, improved asthma control, and better quality of life.[12]

Previous analysis of ISAR highlight that 70% of patients have at least one T2-related comorbidity such as allergic rhinitis, which correlates with 1.12 to 1.29 times more annual exacerbations.[13] Additionally, about 67% experience OCS-related comorbidities (eg, diabetes, hypertension) linked to LTOCS use and uncontrolled asthma.[14] Multimorbidity is common, with 57% having three or more comorbidities, worsening outcomes, increasing healthcare use, and reducing quality of life.[15] Despite this, many patients with high OCS exposure do not receive biologics, missing an opportunity to reduce OCS reliance and mitigate associated risks.[16]

While global severe asthma registries provide valuable insights, specific analyses focusing on the Gulf region and its demographic variations are noticeably absent. Our study aimed to fill this gap by analyzing data from the ISAR. We conducted the first comprehensive assessment of T2- and OCS-related comorbidities in severe asthma patients from Kuwait, Saudi Arabia, and the United Arab Emirates. Additionally, we examined how demographic and behavioral factors, such as age, sex, and smoking status, were associated with the prevalence of these comorbidities.

Methods

Study Design and Data Source and Ethical Approval

This comparative observational study analyzed data from severe asthma patients enrolled in the ISAR up to 2024. Recruitment at participating centers in the Gulf region; Kuwait, the United Arab Emirates and Saudi Arabia, began in December 2018, April 2019 and May 2019 respectively, with data uploaded regularly to the ISAR online global system. These regional datasets were extracted and evaluated independently against the full ISAR dataset. The secondary analysis did not involve direct patient contact or access to identifiable information. The study was reviewed by the Ministries of Health Ethical Committees and Review Boards of Kuwait, Saudi Arabia, and the United Arab Emirates, which determined that it is exempt from further ethical review under national regulations governing research using de-identified data (Nos. 935/2018, 19-423, and DSREC-11/2019_10, respectively).

Patients and Case Definition

Patients included in the study were required to be at least 18 years old and have severe asthma. Severe asthma was defined as either receiving GINA 2018 Step 5 treatment or having uncontrolled asthma at GINA Step 4.[17]

T2-related comorbidities are medical conditions often seen with severe asthma, driven by T2 inflammation. Examples include allergic rhinitis, chronic rhinosinusitis with or without nasal polyps, and atopic dermatitis.[18] In contrast, OCS-related comorbidities are adverse health conditions resulting from prolonged or frequent use of OCS for asthma management. These can include, but are not limited to, diabetes mellitus, hypertension, osteoporosis, cataracts, and psychiatric disorders.[19]

Demographic and Clinical Characteristics

A wide array of demographic and clinical variables was collected for this study. This comprehensive dataset included specific information about asthma exacerbations, hospitalizations, and emergency department visits. We categorized

comorbidities into two distinct groups: those associated with T2 inflammation and those related to OCS use. The study also reported spirometry results and key clinical metrics including IgE, BEC, and FeNO. Finally, each patient's treatment regimen was detailed, covering long-term OCS use and any add-on therapies beyond ICS/LABA.

Statistical Analyses

All statistical analyses were performed using R version 4.3.2 (R Core Team, 2023). Patient characteristics were summarized by cohort using descriptive statistics means and standard deviations for normally distributed variables, medians and inter-quartile ranges for skewed variables, and frequencies and proportions for categorical variables. The prevalence of individual comorbidities at baseline was defined as the proportion of patients with documented diagnoses prior to the index date. The index date was defined as the date of ISAR enrollment or initiation of biologic therapy, whichever was applicable. Missing comorbidity data were addressed using a complete-case approach, with no imputation performed. Comorbidity prevalence and counts were calculated only for patients with non-missing data for at least three comorbidities within the relevant category to reduce potential bias from incomplete documentation. Associations between demographic factors (age, sex, smoking status) and clinical characteristics were explored using univariate comparisons, employing Kruskal–Wallis tests for continuous variables and Pearson's Chi-square tests for categorical variables.

Results

Table 1 showed that patients with severe asthma in the Gulf region (Kuwait, Saudi Arabia, and the UAE) were significantly younger and had an earlier onset of asthma compared to the international cohort from ISAR ($p<0.001$). Ethnic distribution varied, with Kuwait and the UAE being predominantly Caucasian, while Saudi Arabia included a more diverse population. Tobacco uses also differed markedly, with Kuwait showing more current smokers, while Saudi Arabia and UAE had more never smokers compared to ISAR.

Asthma control was poorer in Kuwait and Saudi Arabia, as reflected by a higher percentage of uncontrolled cases, while the UAE reported better asthma control compared to ISAR ($p<0.001$). LTOCS use was significantly lower in all Gulf countries ($p<0.001$), despite higher exacerbation rates in Kuwait and Saudi Arabia. Pulmonary function patterns varied: Kuwait showed reduced FEV1 but a higher FEV1/FVC ratio, Saudi Arabia demonstrated better overall lung function, and the UAE had preserved FEV1 with a higher FEV1/FVC ratio.

Biomarker analysis revealed Kuwait had significantly higher eosinophil counts and total IgE levels, yet lower FeNO. Saudi Arabia showed elevated IgE but normal eosinophils and lower FeNO, while the UAE demonstrated lower eosinophils and FeNO, but higher IgE. Allergen sensitization was more common in Kuwait and UAE, and less frequent in Saudi Arabia, compared to ISAR. Despite elevated T2 biomarkers, all three Gulf countries had a lower percentage of patients classified as "most likely eosinophilic," suggesting phenotypic variability.

Biologic treatment patterns differed substantially. UAE had the highest proportion of patients initiating biologics, while Kuwait and Saudi Arabia lagged behind ISAR. Kuwait showed a strong preference for Anti-IgE therapies (83.7%) over Anti-IL5/5R (10.9%), which may reflect higher rates of allergen sensitization in that population. In contrast, Saudi Arabia and UAE used more Anti-IL4R agents compared to ISAR, indicating regional variation in phenotype-driven treatment approaches.

In Table 2, T2-related comorbidities were clearly more prevalent in the Gulf, particularly allergic rhinitis, affecting 68–82% of patients in Kuwait, Saudi Arabia, and UAE (all $p<0.001$). Nasal polyposis was also significantly more frequent in Kuwait and Saudi Arabia, while chronic rhinosinusitis showed the highest rates in Saudi Arabia and the lowest in UAE. Conversely, eczema was most prevalent in Saudi Arabia but strangely less common in Kuwait and UAE.

OCS-related comorbidities revealed a different pattern. Obesity was consistently and significantly more prevalent in all Gulf countries (46–56%) compared to ISAR ($p<0.001$). However, other comorbidities typically associated with corticosteroid use, including osteoporosis, peptic ulcer, chronic kidney disease, cardiovascular disease, and psychiatric disorders, which were markedly less common in the Gulf. Anxiety and/or depression, for instance, were extraordinarily low, especially in Kuwait (0.4%), compared to ISAR (16.8%).

When stratifying the number of comorbidities, most Gulf patients had fewer than three, especially in Saudi Arabia. The burden of potentially OCS-related comorbidities was notably lower, while potentially T2-related comorbidities were

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Table 1 Basic Characteristics of Severe Asthma Patients

Patient Characteristics at Index Date	ISAR Overall (N=16,269)	Kuwait (n=494)	p	Saudi Arabia (n=398)	p	UAE (n=257)	p
Age (years)			<0.001		<0.001		<0.001
Mean (SD)	53.48 (15.17)	48.56 (14.91)		43.42 (13.96)		44.70 (15.70)	
Median (Q1, Q3)	55 (43.65)	48 (38.58)		42 (33.53)		44 (33.55)	
<40: n (%)	3087 (18.97)	132 (26.72)		162 (40.70)		107 (41.63)	
40-49: n (%)	2942 (18.08)	130 (26.32)		101 (5.38)		57 (22.18)	
50-59: n (%)	4107 (25.24)	114 (23.08)		86 (21.61)		43 (16.73)	
60-69: n (%)	3721 (22.87)	70 (14.17)		34 (8.54)		31 (12.06)	
70+: n (%)	2412 (14.83)	48 (9.72)		15 (3.77)		19 (7.39)	
Sex			0.301		0.002		0.165
Female: n (%)	10,111 (62.15)	318 (64.37)		277 (69.60)		149 (57.98)	
Ethnicity, N	14207	493	<0.001	379	<0.001	257	<0.001
Caucasian: n (%)	10,586 (75.47)	488 (98.99)		58 (15.30)		252 (98.05)	
North East Asian: n (%)	617 (4.40)	0 (0.00)		1 (0.26)		0 (0.00)	
South East Asian: n (%)	840 (5.99)	1 (0.20)		0 (0.00)		5 (1.95)	
African: n (%)	389 (2.77)	0 (0.00)		4 (1.06)		0 (0.00)	
Mixed: n (%)	336 (2.40)	1 (0.20)		0 (0.00)		0 (0.00)	
Other: n (%)	1259 (8.89)	3 (0.61)		316 (83.38)		0 (0.00)	
Tobacco use, N	13680	491	<0.001	391	<0.001	234	<0.001
Current smoker: n (%)	736 (5.38)	41 (8.35)		16 (4.09)		13 (5.56)	
Ex-smoker: n (%)	3727 (27.24)	34 (6.92)		17 (4.35)		12 (5.13)	
Never smoker: n (%)	9217 (67.38)	416 (84.73)		358 (91.56)		209 (89.32)	
Clinical characteristics							
Age at asthma onset (years), N	8662	484	<0.001	390	<0.001	218	<0.001
Mean (SD)	31.08 (18.54)	28.03 (15.25)		20.73 (14.09)		20.76 (15.75)	
Median (Q1, Q3)	31 (15.45)	27 (15.38)		20 (10.30)		20 (5.33)	
Number of asthma exacerbations in preceding year, N	9802	451	<0.001	313	<0.001	151	<0.001
Mean (SD)	1.83 (2.57)	2.70 (1.69)		2.69 (3.38)		0.58 (1.27)	
Median (Q1, Q3)	1 (0.2)	2 (2.4)		2 (1.3)		0 (0.1)	
0: n (%)	3210 (32.75)	6 (1.33)		58 (18.53)		102 (67.55)	
1: n (%)	2795 (28.51)	102 (22.62)		65 (20.77)		34 (22.52)	
2-5: n (%)	3118 (31.81)	312 (69.18)		157 (50.16)		13 (8.61)	
6+: n (%)	679 (6.93)	31 (6.87)		33 (10.54)		2 (1.32)	
LTOCS status, N	11793	473	<0.001	298	<0.001	198	<0.001
Yes: n (%)	2541 (21.55)	9 (1.90)		37 (12.42)		1 (0.51)	
LTOCS daily dose in users (mg/day), N	2325	8	0.685	34	0.585	1	0.222
Mean (SD)	11.03 (10.51)	9.91 (5.61)		10.71 (7.97)		20.00 (-)	
Median (Q1, Q3)	9.63 (5.00, 13.96)	10.00 (6.68, 11.33)		10.00 (5.00, 10.00)		20.00 (-)	

Asthma control, N	9280	492	<0.001	376	<0.001	254	<0.001
Uncontrolled: n (%)	5302 (57.13)	446 (90.65)		247 (65.69)		111 (43.70)	
Partly controlled: n (%)	2075 (22.36)	35 (7.11)		110 (29.26)		50 (19.69)	
Well controlled: n (%)	1903 (20.51)	11 (2.24)		19 (5.05)		93 (36.61)	
Percent predicted FEV1, N	11308	437	<0.001	224	0.035	149	0.398
Mean (SD)	74.5 (21.4)	66.0 (16.9)		77.1 (20.0)		75.7 (21.5)	
Median (Q1, Q3)	74.6 (60.0, 89.3)	65.6 (55.1, 77.3)		77.5 (63.7, 92.2)		77.5 (61.3, 89.5)	
FEV1/FVC ratio, N	11393	437	<0.001	224	<0.001	149	<0.001
Mean (SD)	0.70 (0.13)	0.77 (0.10)		0.74 (0.11)		0.79 (0.13)	
Median (Q1, Q3)	0.71 (0.62, 0.79)	0.78 (0.71, 0.84)		0.75 (0.66, 0.82)		0.82 (0.71, 0.88)	
Biomarkers							
Highest blood eosinophil count (cells/mcL), N	10211	418	<0.001	276	0.422	164	0.006
Mean (SD)	521 (635)	613 (524)		524 (588)		384 (390)	
Median (Q1, Q3)	350 (196, 670)	460 (260, 790)		350 (110, 720)		300 (200, 492)	
300+: n (%)	6109 (59.83)	293 (70.10)	<0.001	153 (55.43)	0.131	90 (54.88)	0.192
Latest serum total IgE concentration (IU/mL), N	9099	390	<0.001	278	<0.001	151	<0.001
Mean (SD)	441 (1299)	545 (760)		514 (830)		524 (902)	
Median (Q1, Q3)	148 (47, 412)	268 (122, 625)		202 (79, 568)		205 (113, 450)	
Latest FeNO concentration (ppb), N	6847	144	<0.001	85	<0.001	131	<0.001
Mean (SD)	44 (46)	29 (24)		15 (40)		20 (15)	
Median (Q1, Q3)	27 (14.56)	21 (10.41)		0 (0.0)		15 (11.23)	
Allergen test results, N	8236	455	<0.001	279	<0.001	111	<0.001
Positive: n (%)	5511 (66.91)	342 (75.16)		93 (33.33)		111 (100.00)	
Eosinophilic gradient, N	10071	407	<0.001	276	<0.001	149	<0.001
Unlikely/noneosinophilic: n (%)	61 (0.61)	5 (1.23)		3 (1.09)		10 (6.71)	
Least likely: n (%)	673 (6.68)	34 (8.35)		56 (20.29)		13 (8.72)	
Likely: n (%)	959 (9.52)	57 (14.00)		25 (9.06)		22 (14.77)	
Most likely: n (%)	8378 (83.19)	311 (76.41)		192 (69.57)		104 (69.80)	
Biologic initiation			0.089		0.008		0.040
Yes: n (%)	7890 (48.50)	221 (44.74)		167 (41.96)		141 (54.86)	
Biologic class in initiators, N	7889	221	<0.001	167	<0.001	141	<0.001
Anti-IgE: n (%)	3066 (38.86)	185 (83.71)		69 (41.32)		82 (58.16)	
Anti-IL5/5R: n (%)	4108 (52.07)	24 (10.86)		65 (38.92)		27 (19.15)	
Anti-IL4R alpha: n (%)	705 (8.94)	12 (5.43)		33 (19.76)		32 (22.70)	
Anti-TSLP	10 (0.13)	0 (0.00)		0 (0.00)		0 (0.00)	

Notes: P-values compare patients characteristics in a specific country vs all other countries in ISAR. Kruskal Wallis test was used for continuous variables and Pearson Chi-squared test was used for categorical variables. When only one p-value is provided, it relates to the continuous variable. P value less than 0.05 considered significant.

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Table 2 Prevalence of Potentially T2-Related or OCS-Related Comorbidities in Severe Asthma Patients

Comorbidity	ISAR overall (N=16269)			Kuwait (N=494)				Saudi Arabia (N=398)				UAE (N=257)			
	Sample Size	n	Prevalence	Sample Size	n	Prevalence	p	Sample Size	n	Prevalence	p	Sample Size	n	Prevalence	p
Potentially T2-related comorbidities															
Allergic rhinitis	14397	7668	53.26%	494	376	76.11%	<0.001	316	259	81.96%	<0.001	257	176	68.48%	<0.001
Chronic rhinosinusitis	15149	7317	48.30%	493	236	47.87%	0.846	376	249	66.22%	<0.001	257	56	21.79%	<0.001
Nasal polyposis	15208	3257	21.42%	493	167	33.87%	<0.001	397	214	53.90%	<0.001	257	34	13.23%	0.001
Eczema/atopic dermatitis	15546	1688	10.86%	493	34	6.90%	0.004	397	91	22.92%	<0.001	257	9	3.50%	<0.001
Potentially OCS-related comorbidities															
Obesity	15932	5517	34.63%	493	274	55.58%	<0.001	395	196	49.62%	<0.001	257	120	46.69%	<0.001
Osteoporosis	14181	1061	7.48%	493	19	3.85%	0.002	395	9	2.28%	<0.001	257	5	1.95%	<0.001
Diabetes	13585	1437	10.58%	493	42	8.52%	0.130	395	52	13.16%	0.090	257	32	12.45%	0.324
Sleep apnea	15126	2143	14.17%	493	8	1.62%	<0.001	316	18	5.70%	<0.001	257	35	13.62%	0.799
Anxiety and/or depression	14259	2443	16.81%	493	2	0.41%	<0.001	393	12	3.05%	<0.001	257	4	1.56%	<0.001
Heart failure	12327	257	2.08%	493	0	0.00%	-	366	2	0.55%	0.037	257	0	0.00%	-
Myocardial infarction	12060	160	1.33%	493	2	0.41%	0.068	366	7	1.91%	0.320	257	2	0.78%	0.437
Cerebrovascular accident	12060	155	1.29%	493	0	0.00%	-	366	2	0.55%	0.203	257	0	0.00%	-
Pulmonary embolism and/or venous thromboembolism	12060	202	1.67%	493	2	0.41%	0.025	366	5	1.37%	0.640	257	1	0.39%	0.104
Peptic ulcer	12806	386	3.01%	493	4	0.81%	0.004	395	1	0.25%	0.001	257	0	0.00%	-
Chronic kidney disease	12765	156	1.22%	493	0	0.00%	-	395	2	0.51%	0.188	257	2	0.78%	0.513
Cataract	12461	358	2.87%	493	0	0.00%	-	396	0	0.00%	-	257	1	0.39%	0.016
Glaucoma	12725	159	1.25%	493	0	0.00%	-	396	0	0.00%	-	257	0	0.00%	-
Pneumonia	13438	1065	7.93%	493	6	1.22%	<0.001	395	5	1.27%	<0.001	257	12	4.67%	0.051

Notes: P-values compare patients characteristics in a specific country vs all other countries in ISAR. Pearson Chi-squared test was used for categorical variables. P value less than 0.05 considered significant.

more prevalent. Kuwait and Saudi Arabia, in particular, had a higher proportion of patients with multiple T2-related conditions but fewer OCS-related issues (Supplementary Tables 1 and 2).

Age and sex analysis confirmed these patterns. Obesity was highly prevalent in all age groups, especially among older patients in Kuwait and Saudi Arabia (Supplementary Table 3) Meanwhile, anxiety and depression remained consistently low across sexes and age ranges (Supplementary Table 3 and Supplementary Table 4). Markedly, diabetes prevalence was higher in older Gulf patients (eg, 42.9% in Saudi patients ≥70) compared to ISAR (17.6%, $p<0.001$). Other OCS-related comorbidities, such as heart failure and kidney disease, remained rare in both younger and older groups in the Gulf (Supplementary Table 4)

Lastly, comorbidity profiles also varied by smoking status (Supplementary Table 5). Obesity remained significantly more common across all smoking categories in the Gulf, while osteoporosis, anxiety/depression, and cardiovascular comorbidities were again less prevalent than in ISAR. Allergic rhinitis remained the most consistently elevated T2 comorbidity across groups, particularly in Kuwait and Saudi Arabia. This highlights a distinct Gulf phenotype characterized by a high T2-inflammatory burden, high obesity rates, and low prevalence of severe systemic comorbidities.

Discussion

Severe asthma poses a major challenge in the Gulf region, marked by diverse phenotypes and frequent comorbidities, especially upper airway diseases.[1] Asthma prevalence in the region is 7.6%, with severe asthma significantly contributing to the burden; country-specific rates range from 8% to 9.5% in the UAE, Kuwait, and Saudi Arabia.[2] In our cohort, patients from Gulf countries were significantly younger and demonstrated earlier recorded asthma onset compared with the ISAR population, where the mean age at onset is 30.7 years.[3,20] This trend may reflect heightened environmental exposures including desert dust, urban air pollution, and elevated allergen load, as well as a higher baseline atopy burden in the region. Atopic diseases are common in Gulf populations, with atopic dermatitis reported in up to 66% of children in Saudi Arabia[21] and 36.4% in the UAE,[22] and allergic rhinitis and hay fever affecting 46.5% and 22.1% of children in the UAE, respectively.[3] Environmental exposures further compound this risk; air pollution and recurrent dust storms are strongly linked to increased asthma incidence and exacerbations in the Gulf,[23,24] with surges in PM2.5, nitrogen dioxide, and airborne dust associated with emergency visits and symptom worsening.[25] These pollutants contribute to asthma heterogeneity by driving airway inflammation, oxidative stress, and immune dysregulation, influencing both atopic and non-atopic phenotypes; a relationship confirmed in local studies from Kuwait.[26] While improved healthcare access and structured screening programs in the region likely facilitate earlier detection rather than earlier biological development of asthma, timely identification may support prompt intervention and potentially improve long-term disease control and outcomes.

Our cohort demonstrated prominent regional variation in smoking status, with Kuwait showing a higher proportion of current smokers among severe asthma patients compared with Saudi Arabia and the UAE. While this finding reflects severe asthma population, it should be interpreted within the broader context that smoking remains a significant public health issue in the Gulf, with adult smoking prevalence ranging from 9.6% in Oman to 25.1% in Bahrain, and significant rates in other member states.[27] This sustained tobacco use greatly contributes to morbidity, mortality, and a multi-billion-dollar economic burden.[28]

Cigarette smoking is a well-established contributor to asthma development and severity, particularly with early-life exposure, and is associated with accelerated lung function decline and poorer asthma control.[29,30] The higher proportion of never-smokers observed in Saudi and UAE patients in our cohort may relate to local cultural patterns, healthcare messaging, and demographic characteristics of patients referred for biologic therapy, rather than lower national smoking rates. International cohorts such as ISAR frequently report higher smoking rates among severe asthma patients,[31] and our findings highlight that regional and sociocultural factors may shape smoking behaviors and exposure patterns within these populations. Clarifying these traits is important when comparing Gulf asthma phenotypes to global studies.

Our study found poorer asthma control in Kuwait and Saudi Arabia, with a higher proportion of uncontrolled cases, while the UAE showed better control, even outperforming ISAR outcomes. This aligns with Gulf-wide studies: the ESMAA study showed only 43% of patients had controlled asthma, and the SNAPSHOT study reported 38.2% had uncontrolled symptoms, contributing to higher hospitalizations and healthcare costs.[32,33] Key barriers include poor adherence, limited education, and medication access.[33]

Despite national efforts like the Saudi Initiative for Asthma (SINA), real-world data show persistent control issues in Saudi Arabia. The AIM study reported only 3% of patients achieving well-controlled asthma, highlighting significant implementation gaps.[1,34] In contrast, recent UAE data from ESMAA and AIM indicate improvement, with up to 66% reporting-controlled asthma, likely due to better access, guideline adherence, and consistent controller use.[1,35] Kuwait and Saudi Arabia still struggle, despite updated protocols, due to systemic issues like limited access, low awareness, and poor adherence.[35] Compared to ISAR, which shows lower rates of uncontrolled asthma in high-income countries, Kuwait and Saudi Arabia remain disproportionately affected.[1,33–35] This highlights a need for targeted Gulf-specific interventions to bridge the gap between guidelines and real-world outcomes.

LTOCS use was low across Gulf countries despite high exacerbation rates in Kuwait and Saudi Arabia, reflecting a regional preference to minimize systemic steroid exposure.[36] This differs from international trends where frequent exacerbations often lead to increased LTOCS use. In the GCC, treatment mainly involves fixed-dose ICS/LABA combinations, with LTOCS reserved for severe, refractory cases.[36,37] Treatment choices are shaped by education, demographics, comorbidities, and environmental factors, with a strong focus on limiting steroid side effects and promoting alternatives like biologics.[37,38]

Despite lower LTOCS use, Kuwait and Saudi Arabia report more exacerbations, suggesting factors like poor adherence, environmental triggers, or limited use of biologics contribute to poor control.[36,38] ISAR data show higher LTOCS use among severe asthma patients with frequent exacerbations, though biologics like mepolizumab have helped reduce this globally.[39] Notably, Gulf countries already had lower baseline LTOCS use, possibly due to conservative prescribing habits. The NEST study confirmed a drop in LTOCS use post-biologic therapy in the GCC.[37]

Our study highlighted distinct biomarker and allergen sensitization patterns among severe asthma patients in the Gulf, differing from international data. In Kuwait, patients had significantly higher eosinophil counts and total IgE, with lower FeNO levels, which suggesting strong IgE-mediated inflammation and possibly atypical airway involvement. The low FeNO likely reflected corticosteroid use, while environmental and genetic factors may have contributed to this profile.[40] In contrast, patients in Saudi Arabia and the UAE showed elevated IgE but normal or low eosinophils and FeNO. Saudi patients had normal eosinophils and reduced FeNO, while UAE patients had low levels of both. These findings indicated allergic asthma with limited eosinophilic inflammation, possibly due to early ICS use, environmental exposures, or genetic factors. Allergen sensitization was higher in Kuwait and the UAE compared to ISAR, consistent with high atopy rates in the Gulf, especially among younger populations. Saudi Arabia showed lower sensitization, potentially due to environmental or diagnostic differences.[40]

Emerging evidence from the COVID-19 period supports the role of indoor environmental conditions in shaping allergic responses; factors such as limited ventilation, dampness, and household fuel type were associated with respiratory risk and heightened indoor allergen exposure.[41] This aligns with our observation of increased dust-mite sensitization during the pandemic era, whereas pet-related sensitization showed a more stable trend, likely reflecting differences in exposure dynamics.

Despite elevated T2 biomarkers, fewer patients were classified as "most likely eosinophilic," suggesting phenotypic diversity and highlighting the limitations of using single biomarkers in this region. This aligned with global evidence that called for combined or longitudinal assessments to better define asthma endotypes.[42,43] Environmental triggers and early steroid exposure likely influenced these discordant biomarker profiles, unlike Western cohorts where eosinophils, FeNO, and IgE often overlapped.[42,43] Although atopy was generally common in the Gulf, allergen sensitization varied. In particular, some Saudi cohorts showed unexpectedly low sensitization rates, warranting further investigation.[43]

Biologic therapy usage varied across the Gulf region and may reflect both clinical and system-level factors. The UAE demonstrated the highest uptake of biologics, likely supported by broader insurance coverage and earlier adoption pathways. Kuwait showed a predominant use of anti-IgE therapy (83.7%) with limited anti-IL5/5R prescription (10.9%), consistent with a strong allergic phenotype profile and high sensitization rates.[26] Saudi Arabia displayed a more balanced biologic distribution, with increased use of anti-IL4R in patients with CRSwNP, aligning with disease characteristics and supporting precision selection.[44–46] Compared with the ISAR cohort, biologic utilization in parts of the Gulf remains relatively lower, and this may contribute to the higher exacerbation burden and lower asthma control seen in regional populations. In addition to phenotype-driven practice, access dynamics including variable reimbursement criteria, formulary restrictions, and timing of local approvals, also influence prescribing patterns. All currently available biologics

are approved across Kuwait, Saudi Arabia, and the UAE; however, differences in healthcare funding and eligibility pathways may limit equitable access. These structural variations complement clinical factors in shaping treatment decisions, underscoring that regional trends reflect both disease biology and healthcare system context. Our findings add granularity to global ISAR observations by highlighting how biologic availability, affordability, and policy frameworks intersect with phenotype in Gulf severe asthma management.[44–52]

The comorbidity profile also differed from ISAR. T2-related conditions were common across the Gulf, while atopic dermatitis was less prevalent in Kuwait and the UAE. Obesity was consistently high, while OCS-related and psychiatric comorbidities such as anxiety and depression were markedly low, possibly due to underdiagnosis, cultural stigma, or reporting differences. Most patients had fewer than three comorbidities, primarily T2-related, consistent with previous regional reports.[53,54] These findings emphasized the unique inflammatory and clinical profiles in Gulf severe asthma patients and underscored the need for tailored, region-specific treatment strategies.

Our analysis of age and sex correlations with comorbidity types showed that obesity was highly prevalent across all age groups, with increased rates in older patients in Kuwait and Saudi Arabia. This aligned with regional data indicating some of the world's highest obesity rates in the Gulf, particularly among older adults.[55,56] Contributing factors likely included sedentary lifestyles, high-calorie diets, and genetic predisposition.[55] Diabetes was also more common in older Gulf patients compared to the ISAR cohort, consistent with epidemiological data highlighting exceptionally high diabetes rates in Saudi Arabia and Kuwait.[57]

In contrast, rates of anxiety and depression remained low across all age and sex groups, echoing other Gulf studies where psychiatric comorbidities were underreported, possibly due to cultural stigma, underdiagnosis, or limited mental health screening.[58] This differed from international cohorts like ISAR, where psychiatric comorbidities in severe asthma patients reached up to 16–17%.[59] Similarly, comorbidities associated with long-term OCS use, such as heart failure and chronic kidney disease, were rare in both younger and older Gulf patients, possibly due to better asthma control, younger population demographics, or underreporting.[59,60]

Comorbidity profiles also varied by smoking status. Obesity remained significantly more common across all smoking categories in the Gulf, in line with regional studies showing persistently high obesity rates regardless of smoking habits.[55,56,61] This contrasted with Western populations, where smoking is often linked to lower body weight. In the Gulf, lifestyle and genetic factors appeared to outweigh smoking-related metabolic effects.[56]

Other OCS- and smoking-associated comorbidities, like osteoporosis, anxiety, depression, and cardiovascular disease, remained less common in the Gulf than in ISAR, regardless of smoking status. This may reflect the region's younger demographic structure, or underdiagnosis of chronic and psychiatric conditions.[58,60] ISAR and other international studies typically reported higher rates of these comorbidities among smokers with severe asthma, reflecting known risks from both smoking and corticosteroids exposure.[59]

Allergic rhinitis was the most consistently elevated T2-related comorbidity across all smoking groups, especially in Kuwait and Saudi Arabia. This aligned with regional data showing high rates of allergic rhinitis among asthma patients, likely driven by environmental allergen exposure and genetic predisposition to atopy.[62] These findings contrast with international cohorts, where smokers with severe asthma often had higher rates of osteoporosis, cardiovascular disease, and psychiatric illness, and obesity was less common due to nicotine's weight-suppressing effects.[59,63]

In a previous work,[64] another aspect of the objective showed that severe asthma exacerbation rates varied substantially across 17 countries, even after adjusting for patient and disease characteristics, highlighting the impact of health system and contextual factors on acute outcomes. While that study provides valuable insights into acute exacerbation risk and informs country-specific management strategies, our findings focus on the chronic disease burden in a regional population, offering complementary knowledge to support personalized management approaches.

Overall, while previous studies have focused on global severe asthma outcomes, including acute exacerbation rates, biologic effectiveness, and OCS use, our study uniquely provides the first real-world, region-specific characterization of Type 2– and OCS-related comorbidities in severe asthma patients from the Gulf countries. By detailing the prevalence, distribution, and demographic associations of these comorbidities, our findings complement existing evidence on acute and treatment-related outcomes, offering critical insights to inform personalized management and targeted OCS-sparing strategies. Moreover, the observed comorbidity patterns highlight a distinct profile in Gulf patients, shaped by region-specific lifestyle, environmental, and cultural factors.

Conclusion

This study highlights key regional differences in severe asthma across the Gulf. Patients exhibited earlier disease onset, high allergic sensitization, and diverse biomarker profiles, underscoring the limitations of single-marker classification. Asthma control remained suboptimal in Kuwait and Saudi Arabia, whereas the UAE showed better outcomes and higher biologic use. Obesity and diabetes were common, particularly among older patients, while psychiatric and steroid-related comorbidities were less frequent. Allergic rhinitis emerged as the most consistent Type 2 comorbidity. These findings reinforce the need for phenotype-driven, region-specific asthma management strategies tailored to local clinical and healthcare factors. A practical implication is the importance of routine screening and early, proactive management of Type 2 comorbidities and obesity in severe asthma patients in the Gulf region, which may support better disease control and improve long-term outcomes.

Abbreviations

ISAR, International Severe Asthma Registry; CS, Oral Corticosteroid(s); T2, Type 2 inflammation; UAE, United Arab Emirates; ICS, Inhaled Corticosteroids; IL-4, IL-5, IL-13, Interleukin 4, 5, and 13; LTOCS, Long-Term Oral Corticosteroid therapy; GINA, Global Initiative for Asthma; IgE, Immunoglobulin E; BEC, Blood Eosinophil Count; FeNO, Fractional Exhaled Nitric Oxide; LABA, Long-Acting Beta-Agonist; FEV1, Forced Expiratory Volume in 1 second; FVC, Forced Vital Capacity; Anti-IL5/5R, Anti-Interleukin 5/5 Receptor; Anti-IL4R, Anti-Interleukin 4 Receptor; SINA, Saudi Initiative for Asthma; GCC, Gulf Cooperation Council; CRSwNP, Chronic Rhinosinusitis with Nasal Polyps; OPC, Optimum Patient Care; OPRI, Observational and Pragmatic Research Institute; OPCG, Optimum Patient Care Global.

Data Sharing Statement

The datasets used during the current study are available from corresponding author Dr. Mona Al-Ahmad on reasonable request.

Ethics Approval and Consent to Participate

This study involved secondary analysis of fully anonymized data from the International Severe Asthma Registry (ISAR). All participating ISAR centers obtained ethics approval and written informed consent from enrolled patients in accordance with local regulations and the Declaration of Helsinki. The current analysis did not involve direct patient contact or access to identifiable information. The study was reviewed by the Ministries of Health Ethical Committees and Review Boards of Kuwait, Saudi Arabia, and the United Arab Emirates, which determined that it is exempt from further ethical review under national regulations governing research using de-identified data (Nos. 935/2018, 19-423, and DSREC-11/2019_10, respectively).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, took part in drafting, revising the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Mona Al-Ahmad has received advisory board and speaker fees from AstraZeneca, Sanofi, Novartis, and GlaxoSmithKline. Riyad Al-Lehebi has given lectures at meetings supported by AstraZeneca, Boehringer Ingelheim, Novartis, GlaxoSmithKline, and Sanofi, and participated in advisory board fees from GlaxoSmithKline, AstraZeneca, Novartis, and Abbott. Dominic A. Friston is an employee of Optimum Patient Care (OPC). OPC is a co-funder of the International Severe Asthma Registry. Victoria Carter is an employee of Optimum Patient Care (OPC). OPC is a co-funder of the International Severe Asthma Registry. Ghislaine Scelo is a consultant for Observational and Pragmatic Research Institute (OPRI). OPRI conducted this study in collaboration with Optimum Patient Care, a co-funder of the International Severe Asthma Registry. Lakmini Bulathsinhala is an employee of the Observational and Pragmatic Research Institute (OPRI). OPRI conducted this study in collaboration with Optimum Patient Care, a co-funder of the International Severe Asthma Registry. Aaron Beastall is an employee of Optimum Patient Care Global, a co-funder of the International Severe Asthma Registry. David B. Price has advisory board membership with AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Viatris, Teva Pharmaceuticals; consultancy agreements with AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Viatris, Teva Pharmaceuticals; grants and unrestricted funding for investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd) from AstraZeneca, Chiesi, Viatris, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, and UK National Health Service; payment for lectures/speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Inside Practice, GlaxoSmithKline, Medscape, Viatris, Novartis, Regeneron Pharmaceuticals and Sanofi Genzyme, Teva Pharmaceuticals; payment for travel/accommodation/meeting expenses from AstraZeneca, Boehringer Ingelheim, Novartis, Medscape, Teva Pharmaceuticals.; owns 74% of the social enterprise Optimum Patient Care Ltd (Australia and UK) and 92.61% of Observational and Pragmatic Research Institute Pte Ltd (Singapore); is peer reviewer for grant committees of the UK Efficacy and Mechanism Evaluation Programme, and Health Technology Assessment; and he was an expert witness for GlaxoSmithKline. The authors report no conflicts of interest in this work.

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