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RESEARCH ARTICLE

Uncovering the Burden of Influenza-Associated Illness across Levels of Severity in the Kingdom of Saudi Arabia Across Three Seasons

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Abstract

Background Influenza imposes a substantial global health burden, particularly among high-risk populations such as the elderly, young children, and individuals with chronic conditions. In Saudi Arabia, a national influenza sentinel surveillance program was established in 2017 to monitor respiratory virus trends, yet comprehensive estimates of the influenza-associated burden remain limited. This study aims to address this gap by quantifying influenza-associated severe acute respiratory infection (SARI) hospitalization rates and estimating the broader influenza burden across severity levels.

Methods Data from four sentinel hospitals in three regions of Saudi Arabia were analyzed across three influenza seasons: 2017–2018, 2018–2019, and 2022–2023. Weekly SARI case counts were combined with census population data to calculate SARI hospitalization rates per 100,000 population. Influenza positivity rates, derived from laboratory-confirmed cases, were used to estimate influenza-associated SARI hospitalization rates, stratified by age and season. The John Hopkins University/WHO Seasonal Influenza Burden Disease Estimator (Flutool) was employed to extrapolate national estimates of influenza-associated hospitalizations, deaths, and mild/moderate cases. Confidence intervals and age-specific stratifications were computed to enhance precision and comparability.

Results The average annual SARI hospitalization rate was 294 per 100,000 population (95% CI: 288–300). Influenza-associated SARI hospitalization rates averaged 48 per 100,000 population (95% CI: 45–50), with the highest burden observed in individuals aged 65 years and older (269 per 100,000, 95% CI: 240–301) and children aged 0–4 years (118 per 100,000, 95% CI: 107–131). Seasonal variation was noted, with the highest rates in the 2017–2018 season. National estimates suggested a substantial burden, with influenza-associated hospitalizations totaling 17,678 in 2017–2018, 7,683 in 2018–2019, and 13,982 in 2022–2023. The flutool analysis estimated annual influenza-associated deaths ranging from 30 to 4,441 and mild/moderate cases reaching up to 6.3 million in the most severe season.

Conclusions This study demonstrates a significant burden of influenza-associated SARI hospitalizations in Saudi Arabia, with the highest rates observed in the elderly and young children. Seasonal variation was evident, highlighting the urgent need to enhance influenza vaccination coverage, particularly among high-risk groups such as the elderly and young children, to reduce severe outcomes. Expanding sentinel surveillance to more regions and incorporating detailed clinical and economic data are recommended to better inform public health policies. Strengthening pandemic preparedness and tailoring vaccination campaigns based on seasonality and age-specific risk will be critical for mitigating the influenza burden in Saudi Arabia.

Keywords Influenza · SARI · Sentinel surveillance · Burden · Respiratory · Saudi arabia

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1 Introduction

Influenza is a viral disease that poses a significant economic and social burden globally [1–4]. The World Health Organization (WHO) estimates that up to 10% of the global population is infected by seasonal influenza annually, resulting in as many as 650,000 deaths [5]. While influenza impacts individuals of all age groups, the burden falls disproportionately on high-risk populations, including infants, the elderly, and those with chronic medical conditions or compromised immune systems. Around two-thirds of influenza-related deaths occur among those aged 65 years and older [6]. These high-risk individuals exhibit an increased susceptibility to influenza-related complications, including secondary infections and the exacerbation of pre-existing medical conditions, often necessitating hospitalization [6]. Consequently, precise estimation of the influenza burden is critical for the development and implementation of evidence-based public health interventions.

The Kingdom of Saudi Arabia (KSA), the largest country in the Middle East, has a population exceeding 32 million as of 2022, with a significant proportion of expatriates. Its unique demographic structure and climatic diversity provide an important context for understanding the burden of influenza and guiding public health interventions tailored to this region. A national influenza sentinel surveillance program was established in January 2017 through a collaboration between the Ministry of Health of KSA and the WHO Regional Office for the Eastern Mediterranean (EMRO). The program aims to characterize circulating respiratory viruses and identify their novel strains, monitor disease trends and seasonality distributions, including the establishment of thresholds to assess seasonal severity and timing, and estimate the morbidity and mortality associated with influenza. The insights gleaned from surveillance programs play a pivotal role in shaping targeted vaccination strategies and enhancing pandemic preparedness efforts [7]. Despite this, comprehensive assessments of the influenza burden in KSA remain scarce, highlighting a critical gap in public health data.

This study aims to address this knowledge gap by estimating the number and rates of influenza-associated illness across three recent influenza seasons (2017–2018, 2018–2019, and 2022–2023) using data from four national sentinel influenza surveillance sites to infer the burden of influenza in KSA across a spectrum of severity (i.e., mild/moderate cases, hospitalizations, and deaths). This study aims to estimate the burden of influenza in KSA by analyzing data from sentinel surveillance systems established across diverse regions of the country. Using detailed age-stratified and seasonal estimates, it seeks to calculate influenza-associated SARI hospitalization rates and assess demographic and clinical characteristics of affected individuals. These findings will provide robust evidence to inform public health decision-making, including optimizing vaccination programs, tailoring mitigation strategies, and strengthening pandemic preparedness initiatives.

2 Methods

2.1 Study Settings

KSA, situated in West Asia and the Middle East, covers an area of approximately 2,150,000 square kilometers. The population consists of roughly 60% Saudi nationals and 40% expatriates, primarily originating from South Asia, West Asia, and North Africa [8]. The climate is predominantly desert, characterized by hot and arid conditions, with the southwestern region experiencing subtropical highland and semi-desert climates.

2.2 Influenza Sentinel Surveillance

Sentinel surveillance in KSA was established in 2017 with 15 sites among 6 regions, including 9 hospitals conducting severe acute respiratory infection (SARI) surveillance and 6 primary care clinics conducting influenza-like illness surveillance. By 2022, the system had expanded to 100 sites in all 13 regions, including 30 sentinel hospitals and 70 sentinel primary care clinics [9].

SARI sentinel surveillance in KSA uses the WHO recommended case definition: "Any case with a history of fever≥38° C and cough within the last 10 days and requiring hospitalization" [10]. Patients of any age admitted to a sentinel hospital meeting the SARI case definition were recruited into the surveillance.

This study utilized data collected from four strategically selected SARI sentinel hospital sites to ensure a robust representation of the population's diverse characteristics, including regional and demographic variability. These sentinel hospitals function as key healthcare providers within their respective regions, offering valuable insights into local healthcare patterns. The provincial population covered by these sentinel sites numbered approximately 3.3 million in 2022 or about one-tenth the total population. Geographically distributed across the country, the selected sites included Hospitals A and B in the southwestern Jazan region, Hospital C in the central Al-Qaseem region, and Hospital D in the northern Al-Jouf region, capturing a wide spectrum of population dynamics and healthcare utilization trends (Fig. 1).

A standardized questionnaire was employed to collect essential patient information, including symptoms, date of symptom onset, presence of high-risk conditions, and

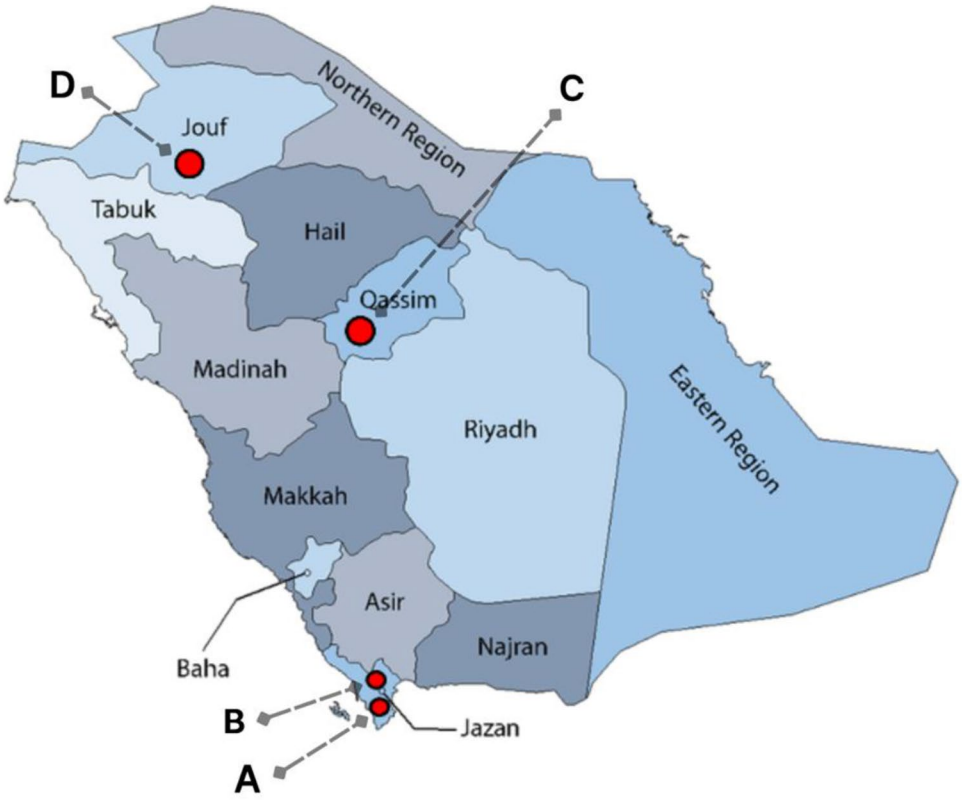

Fig. 1 Map of the Kingdom of Saudi Arabia showing the locations of the four sentinel influenza surveillance sites used in this analysis

vaccination status. Nasopharyngeal swabs were also collected for influenza testing, with residual samples forwarded to the public health laboratory in Riyadh for confirmatory testing, influenza subtyping, and genetic sequencing. These data and samples were further shared with WHO Collaborating Centers for Influenza, aligning with global influenza surveillance initiatives [11].

2.3 Calculation of SARI Hospitalization Rates, Percent Positive and Influenza-Associated SARI Hospitalization Rates

Influenza-associated SARI hospitalization rates were derived from data spanning three distinct influenza seasons: 2017–2018, 2018–2019, and 2022–2023. Each seasonal period was defined as starting in July and ending in June of the following year. Notably, the 2019–2020, 2020–2021, and 2021–2022 seasons were excluded from the analysis due to the significant confounding impact of the COVID-19 pandemic, which could compromise the validity of estimates [12]. The analysis was further stratified into five predefined age categories: 0–4 years, 5–14 years, 15–49 years, 50–64 years, and 65 years and above, to ensure age-specific precision in the estimation process. Estimates were also calculated for the 5+years age group, consistent with WHO recommendations [13].

SARI hospitalization rates were calculated using weekly SARI case counts from hospitals in three regions covered the four sentinel sites, based on Ministry of Health data. The populations of these regions, obtained from the General Authority for Statistics, were used as denominators and expressed per 100,000 population [14].

$$\text{SARI Hospitalization Rate} = \frac{\text{Total SARI Cases}}{\text{Population}} \times 100,000$$

Standard errors and confidence intervals were computed using standard formulas and assuming a Poisson distribution [15].

$$SE = \exp(1.96\sqrt{1/d})$$

Where the d is the number of SARI cases; these were converted to *upper* (rate × SE) and *lower* (rate/SE) confidence intervals.

To estimate the number of influenza-positive cases among all SARI cases, we first calculated the percentage of specimens testing positive (% positive) as the number of test-positive specimens divided by the total number of specimens tested multiplied by 100 for each age group. Influenza-associated SARI hospitalization rates were then calculated by multiplying the SARI hospitalization rate by the percent positive for each age group [13]. Seasonal and

age-stratified rates were applied to national census data to estimate total influenza-associated respiratory hospitalization counts, with all rates reported per 100,000 population along with their confidence intervals (calculated assuming a Poisson distribution [15]).

2.4 Estimation of National Influenza Burden across Levels of Severity

To aid interpretation of the overall burden of influenza across levels of severity in KSA, we entered the influenza-associated hospitalization counts into the John Hopkins University (JHU)/WHO Seasonal Influenza Burden Disease Estimator or "Flutool" (https://www.flutool.org/). The flutool uses a multiplier-based approach to estimate the influenza-associated disease burden across levels of severity (from mild illness to death). The multipliers were derived from a review of the literature reporting estimates across multiple burden levels (e.g., hospitalizations and deaths) from all six WHO regions. The tool takes as inputs the total number of influenza-associated respiratory hospitalizations in a given season, as calculated above, and applies the multipliers to extrapolate the estimated total number of deaths, critically-ill cases and mild/moderate cases in that season. The distribution of cases across each severity level is assumed to be stable across seasons. Options are available to adjust for any known or suspected under-estimation of the counts; however, we assumed no under-estimation. Further details of the estimation methods used can be found in the methodology section of the flutool website [16]. Confidence intervals were calculated assuming a Poisson distribution as above [15].

2.5 Ethical Approval

The influenza surveillance program and data collection activities were considered routine public health functions by the Ministry of Health of KSA. Therefore, the study did not require a formal ethical review process. Nevertheless, patients were made aware of their participation in the surveillance and provided their verbal consent to have their samples collected for the influenza surveillance efforts.

3 Results

Counts of SARI hospitalizations in each of the three regions and the estimated SARI hospitalization rates by season and age group are shown in Table 1. The total number of SARI cases admitted in the three regions was 9,885, 8,716, and 9,682 during the 2017–2018, 2018–2019, and 2022–2023 seasons, respectively. These counts corresponded to SARI hospitalization rates of 312 per 100,000 population (95% CI: 306 - 318) in 2017–2018, 279 per 100,000 (95% CI: 273 - 285) in 2018–2019, and 290 per 100,000 (95% CI: 284 - 296) in 2022–2023. Across the three seasons, the average SARI hospitalization rate was 294 per 100,000 (95% CI: 288 - 300). The highest hospitalization rates were observed in individuals aged 65 years and above, followed by children aged 0–4 years (see Table 1).

A total of 4,891 of these SARI cases were enrolled in sentinel surveillance and tested for influenza at the four sentinel sites. Of these, 792 (16%) tested positive for influenza. The numbers tested and the percent positive by month are shown in Fig. 2. Percent positivity peaked in November 2017, while the lowest was recorded in July 2018. Estimated positivity varied by age group across seasons (see Table 1).

Estimates of the influenza-associated SARI hospitalization rate for the three regions, based on the SARI hospitalization rates and percent positive, are shown in Table 1. The overall influenza-associated SARI hospitalization rate was 48 per 100,000 persons (95% CI: 45 - 50). The overall rate was higher among children < 5 years (118 per 100,000 persons; 95% CI: 107 - 131) compared with those aged over 5 years (39 per 100,000 persons; 95% CI: 37 - 41), but rates were highest for those age 65 years and older (269 per 100,000 persons; 95% CI: 240 - 301). By season, the overall rate was highest in 2017–2018 at 65 per 100,000 persons (95% CI: 62 - 68), and lowest in 2018–2019 at 29 per 100,000 (95% CI: 27 - 31).

The estimated rates were used to estimate the total number of influenza-associated respiratory admissions in the Kingdom for each age group (Table 2). Overall, admissions were estimated to total 17,678 in 2017–2018, 7,683 in 2018–2019, and 13,982 in 2022–2023. In all seasons the counts were highest for the 15–49 years age group (the largest age group), followed by the 0–4 years group in 2017-18 and 2022-24 and the 65 + years group in 2018-19.

3.1 Estimated Influenza-Associated Burden at All Levels of Severity Using the Flutool

The estimated number of hospitalizations for each age group across the whole nation was input to the flutool to estimate the annual number of deaths, critically ill cases, and mild/moderate cases. Results are shown in Table 2. The number of deaths was estimated at 1,298 in 2017–2018 (4.2 per 100,000), 819 in 2018–2019 (2.7 per 100,000) and 1,527 in 2022–2023 (4.7 per 100,000). The corresponding numbers and rates of critically ill cases were 4,146 (rate: 13 per 100,000) in 2017–2018, 1,988 (rate: 6.6 per 100,000) in 2018–2019 and 3,466 (rate: 11 per 100,000) in 2022–2023. The estimated number of mild/moderately ill cases was estimated to be 7,888,929 (rate: 25,467 per 100,000)

Table 1 Estimates of the influenza-associated SARI hospitalization rates in 4 Sentinel sites, by season and age group

Season / Age group	Total SARI admissions	Estimated catchment population[1]	Estimated SARI hospitalization rate/100,000 population (95% CI)	Test-positive	Total tested	% positive	Estimated number of influenza-positive SARI admissions	Estimated influenza-associated SARI hospitalization rate per 100,000 population (95% CI)
2017–2018								
0–4	2,521	290,324	868 (835 - 903)	58	333	17%	439	151 (138 - 166)
5–14	1,510	541,954	279 (265 - 293)	48	176	27%	412	76 (69 - 84)
15–49	2,209	1,904,602	116 (111 - 121)	104	427	24%	538	28 (26 - 31)
50–64	1,405	314,597	447 (424 - 471)	22	116	19%	266	85 (75 - 96)
65+	2,240	119,325	1,877 (1,801 - 1,957)	22	170	13%	290	243 (217 - 273)
5+	7,364	2,880,478	256 (250 - 262)	196	889	22%	1,624	56 (54 - 59)
All ages	9,885	3,170,802	312 (306 - 318)	254	1,222	21%	2,055	65 (62 - 68)
2018–2019								
0–4	2,164	284,337	761 (730 - 794)	23	375	6%	133	47 (39 - 55)
5–14	872	531,219	164 (154 - 175)	26	158	16%	143	27 (23 - 32)
15–49	1,985	1,883,761	105 (101 - 110)	76	671	11%	225	12 (10 - 14)
50–64	1,244	310,573	401 (379 - 423)	22	191	12%	143	46 (39 - 54)
65+	2,451	116,627	2,102 (2,020 - 2,186)	38	389	10%	239	205 (181 - 233)
5+	6,552	2,842,181	231 (225 - 236)	162	1,409	11%	753	27 (25 - 28)
All ages	8,716	3,126,518	279 (273 - 285)	185	1,784	10%	904	29 (27 - 31)
2022–2023								
0–4	4,850	315,616	1,537 (1,494 - 1,581)	63	595	11%	514	163 (149 - 177)
5–14	896	644,816	139 (130 - 148)	35	220	16%	143	22 (19 - 26)
15–49	1,467	1,997,247	73 (70 - 77)	164	551	30%	437	22 (20 - 24)
50–64	704	279,837	252 (234 - 271)	32	225	14%	100	36 (29 - 44)
65+	1,765	99,482	1,774 (1,693 - 1,859)	59	294	20%	354	356 (321 - 395)
5+	4,832	3,021,382	160 (155 - 165)	290	1,290	22%	1,086	36 (34 - 38)
All ages	9,682	3,336,998	290 (284 - 296)	353	1,885	19%	1,813	54 (52 - 57)
Overall[3]								
0–4	3,178	296,759	1,071 (1,034 - 1,109)	144	1,303	11%	351	118 (107 - 131)
5–14	1,093	572,663	191 (180 - 202)	109	554	20%	215	38 (33 - 43)
15–49	1,887	1,928,537	98 (94 - 102)	344	1,649	21%	394	20 (18 - 23)
50–64	1,118	301,669	370 (349 - 393)	76	532	14%	160	53 (45 - 62)
65+	2,152	111,811	1,925 (1,845 - 2,008)	119	853	14%	300	269 (240 - 301)
5+	6,249	2,914,680	214 (209 - 220)	648	3,588	18%	1,129	39 (37 - 41)
All ages	9,428	3,211,439	294 (288 - 300)	792	4,891	16%	1,527	48 (45 - 50)

95% CI: 95% confidence interval

Source: The General Authority for Statistics (GAStat) https://www.stats.gov.sa/en [14]

Overall estimates are calculated based on the average across the three seasons studied

in 2017–2018, 3,028,723 (rate: 10,030 per 100,000) in 2018–2019 and 4,886,834 (rate: 15,188 per 100,000) in 2022–2023. Estimates by age group and season are shown in Table 2. Estimates for death and critically ill cases tended to be highest among the oldest age group.

4 Discussion

The influenza sentinel surveillance data from the four sentinel sites across the three study seasons estimated that, on average, there were 48 (95% CI: 45 - 50) influenza-associated hospitalizations per 100,000 population per year in KSA. This is the first published estimate of the influenza-associated hospitalization burden in KSA and contributes to

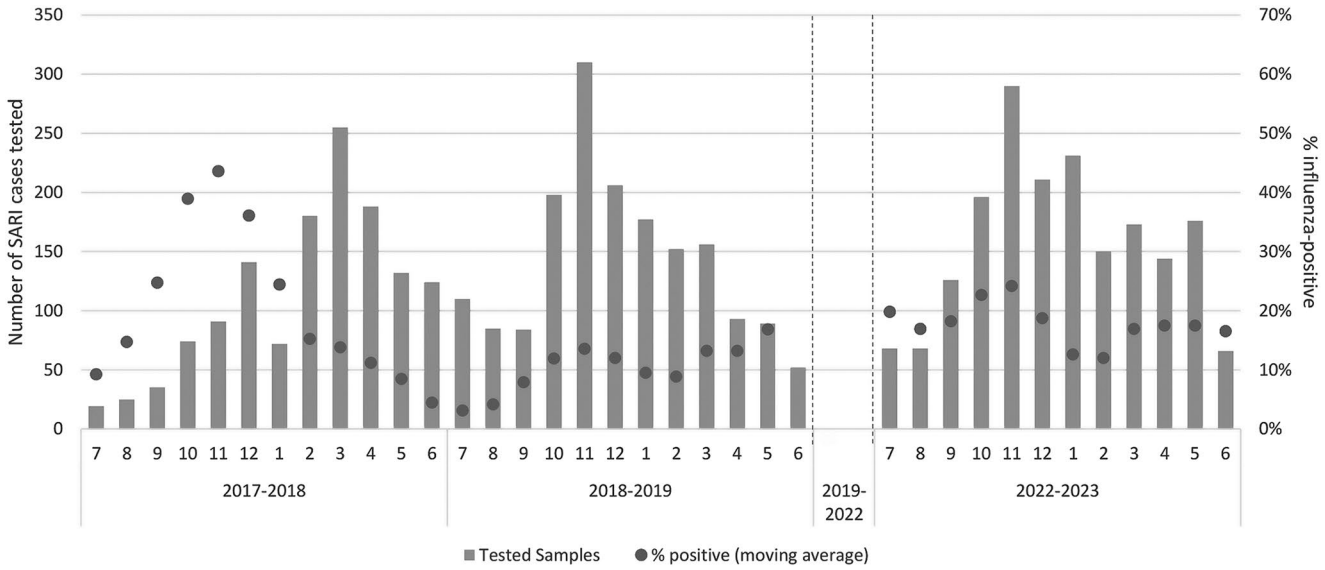

Fig. 2 Number of SARI cases tested by month at four SARI sentinel sites (bars, left axis) and the percentage of these tests positive for influenza (points, right axis)

the growing awareness of influenza burden regionally and globally.

Our estimate of the average annual influenza-associated hospitalization rate in KSA is somewhat comparable to previous findings from the region. In Egypt, estimates from three hospitals in Damanhour district in 2013 suggested an annual influenza-associated SARI rate of 44 cases per 100,000 person-years (95% CI: 39 to 48) [17]. A study from Oman, which used ICD-10 codes to identify respiratory hospitalization, reported a lower average influenza-associated hospitalization rate across 2012–2015 of 21 per 100,000 population (95% CI: 20 to 21) [18]. Studies from Africa have also reported slightly lower estimates than ours or the Egyptian study. For example, the estimate reported from Uganda for 2013–2016 was 34 per 100,000 persons (95% CI: 23 to 48) [19], while a Kenyan study from 2012 to 2014 reported a lower estimate of 21 per 100,000 population (95% CI: 19 to 23) [20]. Each of these studies has used slightly different approaches to the burden estimation and estimated the burden for earlier seasons than used in our study. Moreover, the surveillance systems differ somewhat among countries. For example, in KSA, all SARI cases are tested, whereas in most other countries testing is performed for a subset of SARI patients.

As observed in previous influenza burden studies [21], our data indicate a high influenza-associated hospitalization burden among adults aged 65 years and older (269, 95% CI: 240 - 301 per 100,000 persons) and children under 5 years (118, 95% CI: 107 - 131 per 100,000). Our estimate for children less than 5 years is comparable with estimates reported from Uganda (116 per 100,000, 95% CI: 78 - 165 [15] and Kenya (101 per 100,000, 95% CI: 92 - 110) [20]. However, estimates for influenza hospitalization for elderly adults aged 65 years and older in Uganda were much lower at 25 per 100,000 (95% CI: 9 - 41), possibly reflecting the different age structures and healthcare-seeking behavior in the two countries. In contrast, Pakistan estimated a very high influenza-associated SARI hospitalization rate among its elderly of 716 per 100,000 population [22]. These discrepancies remind us why country-specific estimates are important for local public health decision-making.

Counter to the hospitalization burden, the highest positivity rates from the laboratory testing data were among patients aged 15–49 years (21%), followed by the 5–14 years age group (20%). Higher positivity in working-age adults may be due to the greater specificity of the SARI case definition in this age group as well as lower viral shedding in older age groups [23]; while higher positivity rates in the younger, more socially active age groups may be due to increased mixing in these populations [24], as well as higher viral load and longer durations of shedding [23].

We observed seasonal variations in all our estimates. Influenza epidemic timing and intensity are expected to vary across seasons. Rates were highest in the 2017–2018 season, which was a season characterized by antigenically drifted A(H3N2) and B/Victora viruses [25]. In contrast, a study from Lebanon [26], which relied on ICD-10 codes, rather than SARI surveillance, reported a higher hospitalization rate in 2018–2019 (82.3 influenza-associated respiratory hospitalizations per 100,000 (79.9–84.6)) compared with 2017–2018 (31.1 per 100,000 population (95%CI: 29.6–32.5)). This reflects observations from elsewhere that influenza seasonal activity can vary within and among regions and countries [27]. The apparent lack of seasonal activity in

Table 2 Summary of National influenza-associated SARI hospitalization burden and extrapolation to all levels of severity using the WHO/JHU flutool

Season / Age group	Total Population[1]	Influenza-associated SARI hospitalisation rate per 100,000 (95% CI)[2]	Estimated influenza-associated SARI hospitalizations, nationally (95% CI)	Deaths[3]		Critically ill cases[3]		Hospitalizations[3]		Mild/moderate illness[3]	
				Count (95% CI)	Rate (95% CI)	Count (95% CI)	Rate (95% CI)	Count (95% CI)	Rate (95% CI)	Count (95% CI)	Rate (95% CI)
2017–2018											
0–4	2,859,199	151 (138 - 166)	4,324 (3,938 - 4,748)	42 (30 - 57)	1.5 (0.025 - 5.6)	649 (600 - 701)	23 (14- 34)	4,324 (4,196 - 4,455)	151 (128 - 177)	635,283 (633,722 - 636,847)	22,219 (21,927 - 22,513)
5–14	4,900,917	76 (69 - 84)	3,724 (3,381 - 4,102)	107 (88 - 129)	2.2 (0.24 - 7.2)	663 (613 - 715)	14 (7.3 - 23)	3,724 (3,605 - 3,846)	76 (59 - 95)	3,028,581 (3,025,171 - 3,031,994)	61,796 (61,310 - 62,285)
15–49	19,747,744	28 (26 - 31)	5,578 (5,126 - 6,070)	370 (333 - 410)	1.9 (0.11 - 6.4)	1417 (1,344 - 1,493)	7.2 (2.8 - 14)	5,578 (5,433 - 5,726)	28 (19 - 41)	3,982,358 (3,978,448 - 3,986,271)	20,166 (19,889 - 20,446)
50–64	2,766,129	85 (75 - 96)	2,343 (2,078 - 2,642)	181 (156 - 209)	6.5 (2.5 - 14)	788 (734 - 845)	28.5 (18.6 - 41)	2,343 (2,249 - 2,440)	85 (67 - 105)	227,787 (226,853 - 228,724)	8235 (8,058 - 8,414)
65+	703,366	243 (217 - 273)	1,709 (1,523 - 1,917)	598 (551 - 648)	85 (68 - 105)	629 (581 - 680)	89 (71 - 110)	1,709 (1,629 - 1,792)	243 (213 - 275)	14,920 (14,682 - 15,161)	2121 (2,032 - 2,213)
5+	28,118,156	56 (54 - 59)	15,849 (15,096 - 16,639)	1256 (1,187 - 1,327)	4.5 (1.1 - 10)	3497 (3,382 - 3,615)	12 (6.2 - 21)	13,354 (13,128 - 13,582)	47 (35 - 63)	7,253,646 (7,248,368 - 7,258,927)	25,797 (25,483 - 26,114)
All ages	30,977,355	65 (62 - 68)	20,073 (19,206 - 21,065)	1298 (1,228 - 1,371)	4.2 (1.1 - 10)	4146 (4,021 - 4,274)	13 (6.9 - 22)	17,678 (17,418 - 17,941)	57 (43 - 74)	7,888,929 (7,883,425 - 7,894,436)	25,467 (25,155 - 25,781)
2018–2019											
0–4	2,847,159	47 (39 - 55)	1,329 (1,121 - 1,576)	13 (7 - 22)	0.46 (0.00049 - 4.7)	200 (173 - 230)	7.0 (2.8 - 14)	1,329 (1,259 - 1,402)	47 (34 - 62)	195,257 (194,392 - 196,125)	6858 (6,696 - 7,022)
5–14	4,937,621	27 (23 - 32)	1,334 (1,132 - 1,571)	39 (28 - 53)	0.79 (0.0 - 4.7)	238 (209 - 270)	4.8 (1.4 - 11)	1,334 (1,263 - 1,408)	27 (18 - 39)	1,084,889 (1,082,848 - 1,086,932)	21,972 (21,682 - 22,264)
15–49	18,904,230	12 (10 - 14)	2,256 (1,980 - 2,571)	150 (127 - 176)	0.79 (0.0 - 4.7)	573 (527 - 622)	3.0 (0.62 - 8.8)	2,256 (2,164 - 2,351)	12 (6 - 20)	1,610,649 (1,608,163 - 1,613,138)	8520 (8,340 - 8,703)
50–64	2,787,241	46 (39 - 54)	1,286 (1,092 - 1,515)	100 (81 - 122)	3.6 (0.84 - 10)	433 (393 - 476)	15.5 (8.8 - 25)	1,286 (1,217 - 1,358)	46 (34 - 61)	125,025 (124,333 - 125,720)	4486 (4,355 - 4,619)
65+	720,030	205 (181 - 233)	1,478 (1,302 - 1,678)	517 (473 - 564)	72 (56 - 90)	544 (499 - 592)	76 (59 - 95)	1,478 (1,404 - 1,555)	205 (178 - 235)	12,903 (12,681 - 13,128)	1792 (1,710 - 1,877)
5+	27,349,122	27 (25 - 28)	7,249 (6,837 - 7,658)	806 (751 - 864)	2.9 (0.42 - 8.0)	1788 (1,706 - 1,873)	6.5 (2.5 - 14)	6,354 (6,199 - 6,512)	23 (15 - 35)	2,833,466 (2,830,168 - 2,836,767)	10,360 (10,161 - 10,561)

Table 2 (continued)

Season / Age group	Total Population[1]	Influenza-associated SARI hospitalisation rate per 100,000 (95% CI)[2]	Estimated influenza-associated SARI hospitalizations, nationally (95% CI)	Deaths[3]		Critically ill cases[3]		Hospitalizations[3]		Mild/moderate illness[3]	
				Count (95% CI)	Rate (95% CI)	Count (95% CI)	Rate (95% CI)	Count (95% CI)	Rate (95% CI)	Count (95% CI)	Rate (95% CI)
All ages	30,196,281	29 (27 - 31)	8,729 (8,153 - 9,361)	819 (764 - 877)	2.7 (0.42 - 8.0)	1988 (1,902 - 2,077)	6.6 (2.5 - 14)	7,683 (7,512 - 7,857)	25 (16 - 37)	3,028,723 (3,025,313 - 3,032,136)	10,030 (9,835 - 10,228)
2022–2023											
0–4	2,578,159	163 (149 - 177)	4,195 (3,847 - 4,574)	40 (29 - 54)	1.6 (0.11 - 6.4)	630 (582 - 681)	24 (15 - 36)	4,195 (4,069 - 4,324)	163 (138 - 190)	616,330 (614,792 - 617,871)	23,906 (23,603 - 24,211)
5–14	5,308,731	22 (19 - 26)	1,174 (996 - 1,383)	34 (24 - 48)	0.64 (0.00 - 4.7)	209 (182 - 239)	4 (0.84 - 10)	1,174 (1,108 - 1,243)	22 (14 - 33)	954,768 (952,854 - 956,685)	17,985 (17,723 - 18,249)
15–49	20,395,242	22 (20 - 24)	4,459 (4,060 - 4,897)	296 (263 - 332)	1.5 (0.030 - 5.6)	1133 (1,068 - 1,201)	5.6 (1.9 - 12)	4,459 (4,329 - 4,592)	22 (13 - 33)	3,183,459 (3,179,963 - 3,186,958)	15,609 (15,365 - 15,855)
50–64	3,031,243	36 (29 - 44)	1,085 (892 - 1,319)	84 (67 - 104)	2.8 (0.42 - 8.0)	365 (329 - 404)	12. (6.2 - 21)	1,085 (1,021 - 1,152)	36 (25 - 49)	105,484 (104,848 - 106,123)	3480 (3,365 - 3,597)
65+	861,849	356 (321 - 395)	3,069 (2,765 - 3,405)	1073 (1,010 - 1,139)	124 (103 - 148)	1129 (1,064 - 1,197)	131 (109 - 155)	3,069 (2,961 - 3,180)	356 (320 - 395)	26,793 (26,473- 27,116)	3109 (3,000 - 3,220)
5+	29,597,065	36 (34 - 38)	10,641 (10,063 - 11,247)	1487 (1,412 - 1,565)	5.0 (1.6 - 12)	2836 (2,733 - 2,942)	10 (4.5 - 18)	9,787 (9,594 - 9,983)	33 (23 - 46)	4,270,504 (4,266,455 - 4,274,556)	14,429 (14,194 - 14,666)
All ages	32,175,224	54 (52 - 57)	17,482 (16,731 - 18,340)	1527 (1,451 - 1,606)	4.7 (1.4 - 11)	3466 (3,352 - 3,583)	11 (5.1 - 19)	13,982 (13,751 - 14,216)	43 (31 - 58)	4,886,834 (4,882,502 - 4,891,169)	15,188 (14,947 - 15,432)
Overall[4]											
0–4	2,761,506	118 (107 - 131)	3,269 (2,955 - 3,618)	32 (21 - 45)	1.1 (0.03 - 5.6)	493 (450 - 539)	18 (10 - 28)	3,283 (3,171 - 3,397)	119 (98 - 142)	482,290 (480,930 - 483,653)	17,465 (17,206 - 17,726)
5–14	5,049,090	38 (33 - 43)	1,895 (1,666 - 2,171)	60 (46 - 77)	1.19 (0.0300 - 5.6)	370 (333 - 410)	7 (2.81 - 14)	2,077 (1,989 - 2,168)	41 (29 - 56)	1,689,413 (1,686,866 - 1,691,962)	33,460 (33,102 - 33,820)
15–49	19,682,405	20 (18 - 23)	4,018 (3,543 - 4,527)	272 (241 - 306)	1.4 (0.030 - 5.6)	1,041 (979 - 1,106)	5.3 (1.6 - 12)	4,098 (3,973 - 4,225)	21 (13 - 32)	2,925,489 (2,922,137 - 2,928,843)	14,863 (14,625 - 15,104)
50–64	2,861,538	53 (45 - 62)	1,515 (1,288 - 1,774)	122 (101 - 145)	4.3 (1.09 - 10.20)	529 (484 - 576)	18.5 (10.7 - 28)	1,571 (1,494 - 1,651)	55 (41 - 71)	152,765 (152,000 - 153,533)	5,339 (5,196 - 5,484)
65+	761,748	269 (240 - 301)	2,045 (1,828 - 2,293)	729 (677 - 784)	96 (77 - 117)	767 (714 - 823)	101 (82 - 122)	2,085 (1,996 - 2,176)	274 (242 - 308)	18,205 (17,941 - 18,471)	2,390 (2,295 - 2,487)

Table 2 (continued)

Season / Age group	Total Population[1]	Influenza-associated SARI hospitalisation rate per 100,000 (95% CI)[2]	Estimated influenza-associated SARI hospitalizations, nationally (95% CI)	Deaths[3]		Critically ill cases[3]		Hospitalizations[3]		Mild/moderate illness[3]	
				Count (95% CI)	Rate (95% CI)	Count (95% CI)	Rate (95% CI)	Count (95% CI)	Rate (95% CI)	Count (95% CI)	Rate (95% CI)
5+	28,354,781	39 (37 - 41)	107,574 (10,491 - 11,625)	1,183 (1,117 - 1,252)	4.2 (1.1 - 10)	2,707 (2,606 - 2,811)	10 (4.5 - 18)	9,832 (9,638 - 10,028)	35 (24 - 48)	4,785,872 (4,781,585 - 4,790,162)	16,879 (16,625 - 17,135)
All ages	31,116,287	48 (45 - 50)	154,881 (14,002 - 15,558)	1,215 (1,147 - 1,285)	3.9 (0.8 - 10)	3,200 (3,090 - 3,313)	10 (4.8 - 18)	13,114 (12,891 - 13,340)	42 (30 - 57)	5,268,162 (5,263,664 - 5,272,663)	16,931 (16,676 - 17,188)

95% CI: 95% confidence interval

Influenza-associated SARI hospitalization rates are those estimated from the 4 sentinel sites and are repeated from Table 1

Source: The General Authority for Statistics (GAStat) https://www.stats.gov.sa/en [14]

Estimated counts for Death, Critically-ill and Mild/moderate cases are calculated in the flutool, https://www.flutool.org

Overall estimates are calculated based on the average across the three seasons studied

2022 may be associated with disruptions to influenza seasonality seen globally after the COVID-19 pandemic.

Using the flutool, we estimated a substantial burden of influenza across levels of severity, with one-quarter of the population estimated to have experienced mild or moderate influenza in 2017 and an excess of 1,500 deaths in 2022–2023. The very large number of mild and moderate cases represents a substantial burden on the primary care health system. For those who do not seek care, illness may still be associated with significant economic costs such as presenteeism and care duties for parents and children who care for parents. Going forward, expansion of surveillance and leveraging of the electronic medical records systems available in KSA will enable better estimation of influenza-associated deaths as well as mild and moderate disease.

Notwithstanding the appreciable burden of influenza leading to hospitalizations in KSA, our study has also identified a considerable burden of SARI hospitalizations per se, many of which may be attributable to other respiratory viruses, such as RSV, pneumococcal, and, more recently SARS-CoV-2. SARI hospitalization rates averaged 393 to 403 per 100,000 population, representing a considerable burden on our hospitals. The availability of testing for non-influenza pathogens in this surveillance system will enable estimation of the burden of RSV, MERS, and SARS-CoV-2 and may be able to inform estimates of the impact of new vaccination programs against these diseases.

Our study did not undertake a hospital utilization survey to estimate the size of the catchment population because the hospitals from which SARI cases were derived had clear catchment populations. This simplified the exercise for KSA compared with many other countries (e.g. Cambodia, Indonesia, Kenya [20, 28, 29], for which surveillance systems have less clear denominators. It may also explain some of the discrepancies in influenza-associated hospitalization rates observed between our study and other studies that have used the WHO method. Additionally, healthcare-seeking behavior likely varies among countries which may further explain differences in the observed burden.

We also did not strictly follow the WHO approach to estimate the hospitalization burden where the SARI incidence is calculated for each sentinel site using the sentinel catchment population then combined. Instead, we combined data across four sentinel sites in three regions to estimate the rate of influenza-associated hospitalizations and extrapolate to estimate the national average number of cases per season. This approach assumes homogeneity among regions, which we acknowledge may be a tenuous assumption. For example, in the regions included, a lower proportion are non-Saudi nationals (26-31% non-Saudi) than the national average (42% non-Saudi) [14]. However, data were insufficient to reliably estimate rates per site. As a result, there

would have been greater imprecision in our estimates and the heterogeneity observed among sites could be the result of sparse and small samples rather than true heterogeneity. Indeed, we did encounter 0 counts of influenza-positive SARI cases for some combinations of age group-site-season, motivating our aggregated approach.

This study had several limitations that should be considered when interpreting the findings. Firstly, the surveillance data lacked information on patient comorbidities and clinical status at the time of hospital admission (e.g., whether admitted to the general ward or ICU). This additional clinical data could have provided valuable insights into the underlying risk factors and severity of illness associated with the SARI and influenza cases. Absence of these data also precluded any stratification of our estimates by high-risk group.

Furthermore, the study did not capture data on the duration of hospital stay for the SARI patients. This information would have allowed for a more comprehensive assessment of the healthcare utilization and economic impact associated with influenza-related severe illnesses in the region.

Additionally, the surveillance data used were restricted to four sentinel sites, which may not be fully representative of the broader epidemiology in the country. Surveillance in KSA has expanded to include more diverse geographic locations and healthcare facilities, which will enhance the generalizability of the findings in future studies.

For the youngest age group, we used 0–4 years to be consistent with WHO guidance, rather than assessing finer age bands. Given the high burden of disease in this age group and differences in treatment and preventive options available for infants and children, estimates for younger age groups could be helpful for public health decision-making. For example, a study from Iran found that the highest influenza hospitalization burden was among children aged less than 6 months, followed by those aged 6–11 months, than those aged 1 year [30]. Hospitalization rates in these young cohorts were each higher than the rate for elderly adults aged 65 years and older, suggesting a need to consider treatment and prevention options among infants.

Despite these limitations, the study has provided important epidemiological data on the burden of SARI and influenza-associated illness in the Kingdom. The results support current Ministry of Health recommendations for annual influenza vaccination among the elderly and young children. Continued efforts to improve vaccine uptake and access in these vulnerable groups are crucial to mitigate the severe outcomes associated with influenza infections.

Further research is warranted to comprehensively estimate the direct and indirect healthcare costs and economic burden associated with influenza-related illnesses in the region. Detailed investigations into the risk factors for severe disease outcomes would also help inform evidence-based strategies for reducing the influenza burden. Additionally, conducting knowledge, attitude, and practice (KAP) studies on influenza vaccine acceptance could provide valuable insights to guide public health messaging and address any barriers to vaccination uptake. Such multifaceted approaches, combining robust surveillance, health economic analyses, and behavioral research, will be essential for developing a more holistic understanding of the influenza landscape and designing effective interventions to protect the population.

In conclusion, this analysis of sentinel surveillance data has provided valuable insights into the burden of SARI and influenza-associated illness in KSA. The consistently high rates observed in the elderly and young children underscore the importance of targeted prevention and control measures for these high-risk groups. Variations in incidence and positivity rates across sites and seasons highlight the need for ongoing, robust surveillance to guide public health decision-making and resource allocation. Addressing the identified gaps, such as incorporating more comprehensive clinical data and expanding the surveillance system, could strengthen future investigations and inform more targeted public health interventions.

Author Contributions A.M.A., S.G.S., and S.T. conceptualized the study and designed the methodology. A.M.A., A.B., H.A.N., A.A., and O.H. collected and curated the data. E.O., M.M., S.F.B., G.A., R.A., N.A., and L.A. contributed to data validation and formal analysis. N.Z.A. and H.A. provided critical revisions and oversight. A.M.A., E.O., and S.G.S. drafted the initial draft, with contributions from all authors. All authors reviewed and approved the final manuscript.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Ethical Approval The influenza surveillance program and data collection activities were classified as routine public health functions by the Ministry of Health of Saudi Arabia.

Patient Consent Patients were informed about the purpose of the SARI surveillance and provided verbal consent to participate.

Consent for Publication The Deputyship of Population Health, Ministry of Health provided consent for the publication of this study.

Competing Interests The authors declare no conflicts of interests.

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