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Syndromic surveillance of respiratory infections during protracted conflict: experiences from northern Syria 2016-2021

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ABSTRACT

Objective: Northern Syria faces a large burden of influenza-like illness (ILI) and severe acute respiratory illness (SARI). This study aimed to investigate the trends of Early Warning and Response Network (EWARN) reported ILI and SARI in northern Syria between 2016 and 2021 and the potential impact of SARS-CoV-2.

Methods: We extracted weekly EWARN data on ILI/ SARI and aggregated cases and consultations into 4-week intervals to calculate case positivity. We conducted a seasonal-trend decomposition to assess case trends in the presence of seasonal fluctuations.

Results: It was observed that 4-week aggregates of ILI cases (n = 5,942,012), SARI cases (n = 114,939), ILI case positivity, and SARI case positivity exhibited seasonal fluctuations with peaks in the winter months. ILI and SARI cases in individuals aged $\geq$5 years surpassed those in individuals aged $<$5 years in late 2019. ILI cases clustered primarily in Aleppo and Idlib, whereas SARI cases clustered in Aleppo, Idlib, Deir Ezzor, and Hassakeh. SARI cases increased sharply in 2021, corresponding with a severe SARS-CoV-2 wave, compared with the steady increase in ILI cases over time.

Conclusion: Respiratory infections cause widespread morbidity and mortality throughout northern Syria, particularly with the emergence of SARS-CoV-2. Strengthened surveillance and access to testing and treatment are critical to manage outbreaks among conflict-affected populations.

Background

Influenza-like illnesses (ILIs) and severe acute respiratory infections (SARIs) surveillance in conflict-related humanitarian settings remain understudied despite the high burden of disease (Al Amad and Almoayed, 2022). In Syria, where uprisings in March 2011 descended into a protracted conflict, the public health infrastructure has been severely damaged (Muzzall et al., 2021; Abbara and Ekzayez, 2021; Fouad et al., 2017; Haar et al., 2018). Violence, including against healthcare, has been especially concentrated in northern Syria, where competing warring parties retain tenuous strongholds and control over governorates (Kieny et al., 2022). The gap left by the death and forced exodus of the healthcare workforce and damage to infrastructure have left Syria particularly vulnerable to the emergence and re-emergence of infectious disease outbreaks, including cutaneous leishmaniasis, measles, diarrheal infections, polio, and other vaccine-preventable diseases (Ozaras et al., 2016; Abbara et al., 2021).

Early warning systems for communicable disease outbreaks in such settings are critical for early detection and response. In resource-constrained settings, this is often done through syndromic surveillance to provide rapid detection of potential infec-

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tious disease outbreaks (Hope et al., 2006). This approach relies on the reporting of key clinical syndromes, with clusters of symptoms in space or time potentially indicating outbreaks of infectious diseases (Ismail et al., 2016; Colón-González et al., 2018; Connolly et al., 2004).

In Syria, there are two parallel syndromic surveillance systems. The Early Warning, Alert and Response System (EWARS) was established by the World Health Organization (WHO) with the Syrian Ministry of Health in 2013 and mainly operates in government-controlled areas. The Assistance Coordination Unit established the Early Warning, Alert and Response Network (EWARN) in 2014, which primarily serves areas outside of government control because of the withdrawal of the Ministry of Health (Abbara et al., 2021; Ismail et al., 2016). Data from EWARS and EWARN have been used to analyze disease trends in Syria previously, although early work has focused primarily on diseases related to water, sanitation, and hygiene (Abbara et al., 2021; Ismail et al., 2016). Since March 2020, both EWARS and EWARN established monitoring for suspected and confirmed COVID-19 cases across Syria.

In Syria, where more than half the preconflict population of 22 million has been forcibly displaced, millions live in inadequate or unfinished shelters; this leaves them susceptible to environmental hazards (including freezing temperatures), overcrowding, and poor ventilation (United Nations High Commission for Refugees, 2022; Abbara et al., 2020; Almhawish et al., 2021; Basha et al., 2021). Across all age groups in northern Syria, respiratory infections are the most prevalent infectious diseases in individuals seeking healthcare (Basha et al., 2021; van Berlaer et al., 2017; Alhaffar and Janos, 2021). Despite the extensive disease burden of respiratory infections in northern Syria, previous studies have not used EWARN surveillance data to analyze historical and granular infection trends in the region during conflict. In this study, we aimed to investigate trends in EWARN-reported ILI and SARI in northern Syria between week 1, 2016, and week 43, 2021, including an analysis of the likely association of COVID-19 with these trends.

Methods

We conducted a retrospective analysis to identify trends in ILI, SARI, and COVID-19 cases in northern Syria as reported in EWARN between week 1, 2016, and week 43, 2021. Northern Syria was selected because of its vulnerability to disease outbreaks and the availability of EWARN data. We also used data on confirmed COVID-19 cases to assess the likely impact of COVID-19 on ILI and SARI trends.

Setting

Northern Syria is comprised of northwest and northeast Syria. Northwest Syria is under opposition control and has a population of 4.17 million, half of whom are internally displaced (Abbara et al., 2020). A total of 1.4 million people in this area remain in tented settlements, with many others in inadequate shelter. The last remaining governorates in northwest Syria are Idlib and parts of Aleppo governorate, although Hama was included in the region until early 2019. Northeast Syria contains around 3 million people and falls under *de facto* Syrian Defense Force control (Balanche, 2020; Syria Public Health, 2020). Raqqa, Deir Ezzor, Hassakeh, and parts of Aleppo fall under northeast Syria. After the closure of the Yaroubieh border crossing in January 2020, this area has been reliant on access to aid flow through Damascus and areas under government control (Marzouk et al., 2020). This includes SARS-CoV-2 polymerase chain reaction (PCR) testing, which is intermittently available in Qamishli, Hassakeh. The first case of COVID-19 was reported in government areas of Syria on March 22, 2020, in northeast Syria on April 16, 2020, and in northwest Syria in July 2020 (Marzouk et al., 2020). In northern Syria, there are 480 total EWARN sentinel sites as of week 43, 2021, with the most in Aleppo (n = 133) and Idlib (n = 110). Figure 1 shows a map of northern Syria.

Data Sources

EWARN reports weekly data at the governorate level, although weeks may have incomplete data for several reasons, including conflict events or safety concerns (Abbara et al., 2021; Sparrow et al., 2016). However, data are backfilled to the appropriate week when received. Conflict-related volatility and quick changeover of governorate control between warring parties also contribute to missing weeks of data for individual, or clusters of, governorates (Ismail et al., 2016; Sparrow et al., 2016). EWARN follows the WHO's global influenza surveillance standard definitions for ILI and SARI. An ILI case is defined as an acute respiratory infection beginning in the last 10 days with a fever of ≥38°C (100.4°F) and cough. A SARI case is an acute respiratory infection requiring hospitalization that began in the last 10 days with a history of fever or measured fever of ≥38°C and cough (World Health Organization, 2014)

COVID-19 cases are reported on two dashboards, separated by northwest Syria and northeast Syria. The COVID-19 Response Tracking Dashboard for Northwest Syria is administered by the Health Cluster and WHO (Abbara et al., 2020). COVID-19 cases, confirmed by PCR, are reported weekly at the governorate level for Idlib and parts of Aleppo, with data sourced from EWARN, the Health Information System Unit, and the COVID-19 Task Force. The dashboard also reports several other COVID-19-related metrics, including vaccinations, logistical measures, and deaths. The Northeast Syria COVID-19 Dashboard is updated by the Kurdish Red Crescent using SARS-CoV-2 PCR laboratory data from northeast Syria. Similarly, confirmed COVID-19 cases are reported daily at the governorate level, and the dashboard includes other relevant metrics. This dashboard covers COVID-19 cases in Hassakeh, Raqqa, Deir Ezzor, and parts of Aleppo.

Data extraction

We manually extracted the weekly number of ILI cases, SARI cases, and total consultations for Aleppo, Idlib, Hama, Deir Ezzor, Hassakeh, and Raqqa governorates from EWARN between week 1, 2016, and through week 43, 2021. Weeks without reports were treated as missing data. For aggregated analyses, cases in individuals aged ≥5 and <5 years were combined. Otherwise, data were separated by age. Similarly, we manually extracted weekly COVID-19 cases from the COVID-19 Response Tracking Dashboard for Northwest Syria. Weeks without reports were treated as missing data. Daily cases were extracted from the Northeast Syria COVID-19 Dashboard and aggregated into weeks that aligned temporally with the epidemiological weeks used by EWARN and the COVID-19 Response Tracking Dashboard. Because each COVID-19 dashboard covers different parts of Aleppo, we combined the number of cases reported in each database for Aleppo to produce a total number. For all data sources, it is possible to differentiate between weeks with missing data and weeks with few-to-no cases by incorporating the number of consultations in the weekly data.

Data analysis

ILI, SARI, and COVID-19 cases were aggregated into 4-week intervals to account for variability in reporting. Aggregated ILI and SARI cases were divided by the total number of consultations for a 4-week interval to calculate the number of cases per 100 (for ILI) or 100,000 (for SARI) consultations, hereafter referred to as

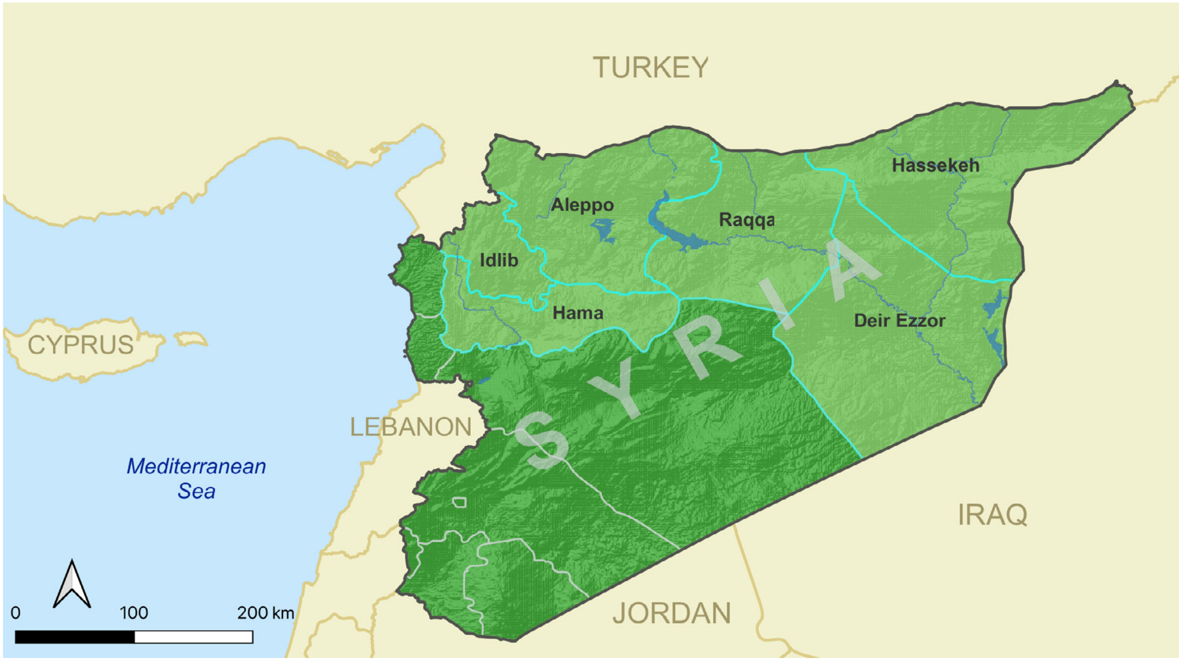

Figure 1. Map of Syria with the study area highlighted.

case positivity. Annual and average seasonal peak timing were calculated through time series plots of the 4-week case aggregates for ILI and SARI. Annual SARI and ILI cases were used to create governorate-level maps of cases.

To assess trends in ILI and SARI cases in the presence of seasonal fluctuations, we conducted a seasonal-trend decomposition with locally estimated scatterplot smoothing (LOESS) using weekly case data. This method decomposes a time series with seasonal fluctuation into three components, as expressed by:

$$D_t = S_t + T_t + R_t$$

where D is the complete time series data, S is the seasonal component of the data, T is the trend component or the long-term change over time, and R is the variation remaining outside of the seasonal and trend components (Cleveland et al., 1990).

Microsoft Excel and R (R Foundation for Statistical Computing, 2021, Version 4.0.4) was used for statistical analysis and figures. QGIS (Version 3.16.11, Hannover) was also used for the figures.

Results

ILI and SARI case trends

Between week 1, 2016, and week 43, 2021, EWARN reported 5,942,012 ILI cases and 114,939 SARI cases. Aleppo (n = 2,047,811) and Idlib (n = 1,750,631) reported the highest number of ILI cases which increased over the period of study. Annual reporting of SARI cases increased annually across all included governorates, particularly in Hassakeh (total n = 30,746), Idlib (total n = 28,002), and Aleppo (total n = 18,003) (Figure 2b). All governorates were missing data for week 49, 2018. Hama left EWARN coverage in week 18, 2019, because of a change in governorate control. Because of this, Hama data only includes week 1, 2016, to week 18, 2019. However, reporting of SARI increased during this period.

The 4-week aggregates of ILI cases, SARI cases, ILI case positivity, and SARI case positivity all exhibited clear seasonal fluctuations, with peaks in the winter months and nadirs in the summer months (Figure 3a-d). The seasonal peaks between 2016-2020 occurred annually on average in weeks 4.5 and 5 for ILI and SARI, respectively. The peaks for the 2020-2021 season were not included in calculating averages because of potential delays from COVID-19, although they occurred in week 52 of 2020 and week 17 of 2021 for ILI and SARI, respectively. However, ILI and SARI both exhibited delayed peaks in the 2019-2020 season. As seen in Figure 3d, Hassakeh experienced a spike in SARI case positivity in early 2019. This was primarily because of a spike in cases in the Qamishli district, located primarily at the National Hospital and a private hospital.

After seasonal-trend decomposition with LOESS, the trend component for ILI cases increased steadily over the study period, with an increase in slope beginning in late 2020. In 2021, ILI cases reached a maximum of 121,085 in weeks 40-43, 2021. Previous maximums for that time period were 85,968 (2019), 81,310 (2020), and 70,373 (2018). The trend component for ILI case positivity decreased through 2019, at which point the trend began increasing. The slope of the trend line increased in early 2021 (Figures 4a and 4c). The case positivity for ILI in weeks 40-43, 2021 was 12.80 per 100 consultations compared with 9.94 in 2020, 10.57 in 2019, and 8.61 in 2018. The trend components of both SARI cases and SARI case positivity fluctuated between 2016 and early 2020, with a clear upward trend beginning in mid-2020 (Figures 4b and 4d). In 2021, SARI cases also hit a maximum in weeks 40-43 (n = 4,053); previous case numbers for that time period were 1,496 (2018), 1,273 (2019), and 929 (2020). SARI case positivity in weeks 40-43, 2021 was 428.61 per 100,000 consultations compared with 113.66 in 2020, 156.50 in 2019, and 183.08 in 2018.

COVID-19 trends

Between week 28, 2020, and week 42, 2021, 119,398 COVID-19 cases were reported in northern Syria. Cases in Hama were not included as the governorate was no longer in coverage by the beginning of the COVID-19 pandemic. Case data are missing for Hassakeh during weeks 28-29, 2020, Raqqa during weeks 28-30, 2020, and Deir Ezzor during weeks 28-30, 2020, and weeks 39-40, 2020. Idlib (n = 51,196), Aleppo (n = 37,574), and Hassakeh (n = 21,372) reported the highest number of COVID-19 cases. Northern Syria experienced its third and largest wave of COVID-19 cases beginning

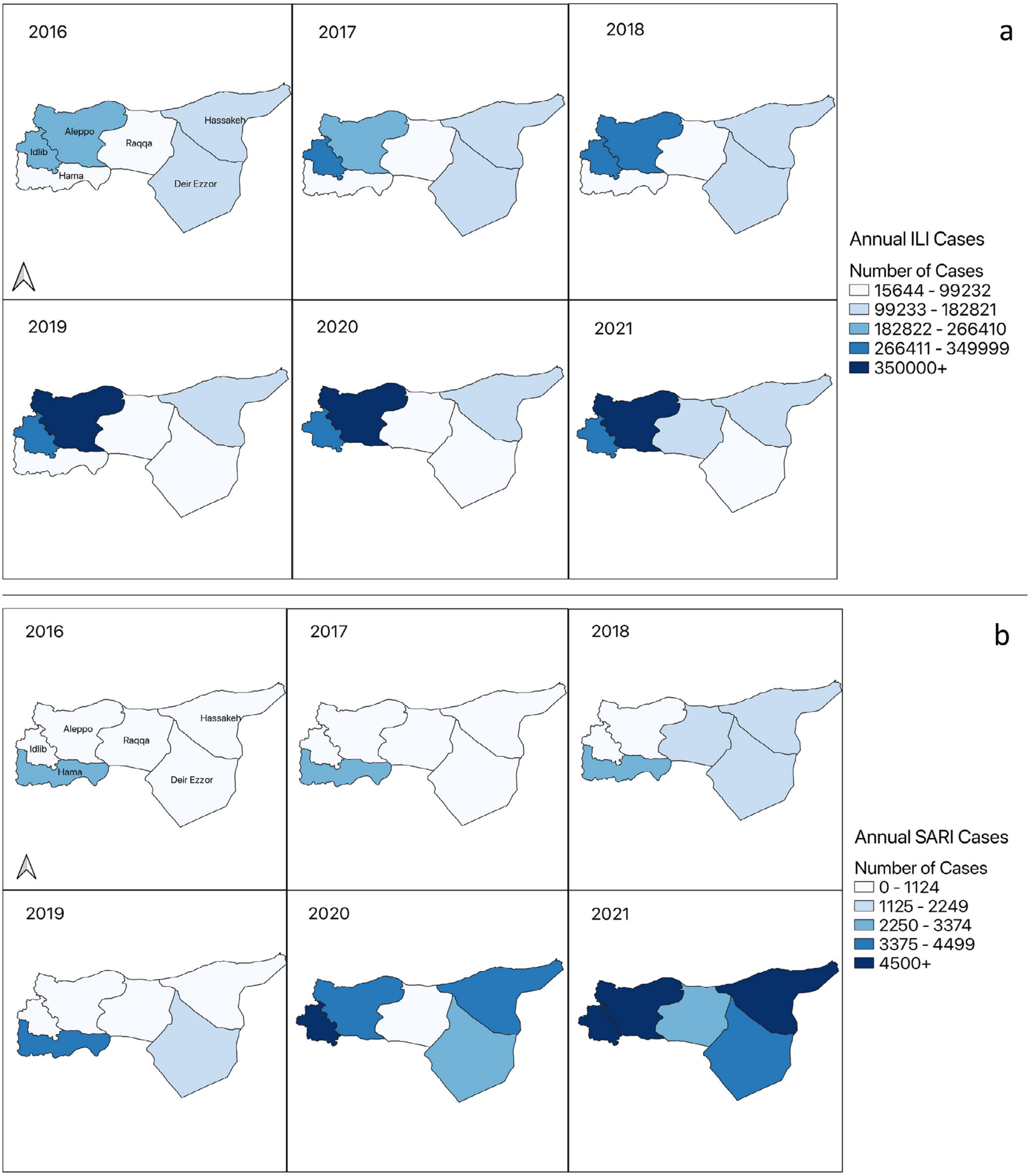

Figure 2. Maps of northern Syria showing annual case numbers of ILI (a) and SARI (b). ILI = influenza-like illness; SARI = severe acute respiratory infection.

in July 2021, and it remains ongoing. COVID-19, ILI, and SARI cases began increasing on week 31, 2021. Seasonal decomposition with LOESS was not conducted for COVID-19 cases because of the outbreak's limited duration.

Crossover events

Throughout the beginning of the study period, there were more reported cases of ILI in individuals aged <5 years than in individuals aged ≥5 years, excluding a brief crossover in mid-2016. However, in early to mid-2020 and after mid-2021, ILI cases in individuals aged ≥5 years surpassed the number of cases in individuals aged <5 years (Figure 5a). This crossover is even more prominent in SARI cases. Between early 2016 to late 2019, the number of SARI cases in individuals aged <5 years was far greater than that in individuals aged ≥5 years. After the crossover in late 2019, there were more SARI cases in individuals aged ≥5 years for the remainder of the study period, excluding a brief period in early 2021 (Figure 5b). These crossovers are also seen in the ratios of ILI and SARI cases in individuals aged ≥5 years to individuals aged

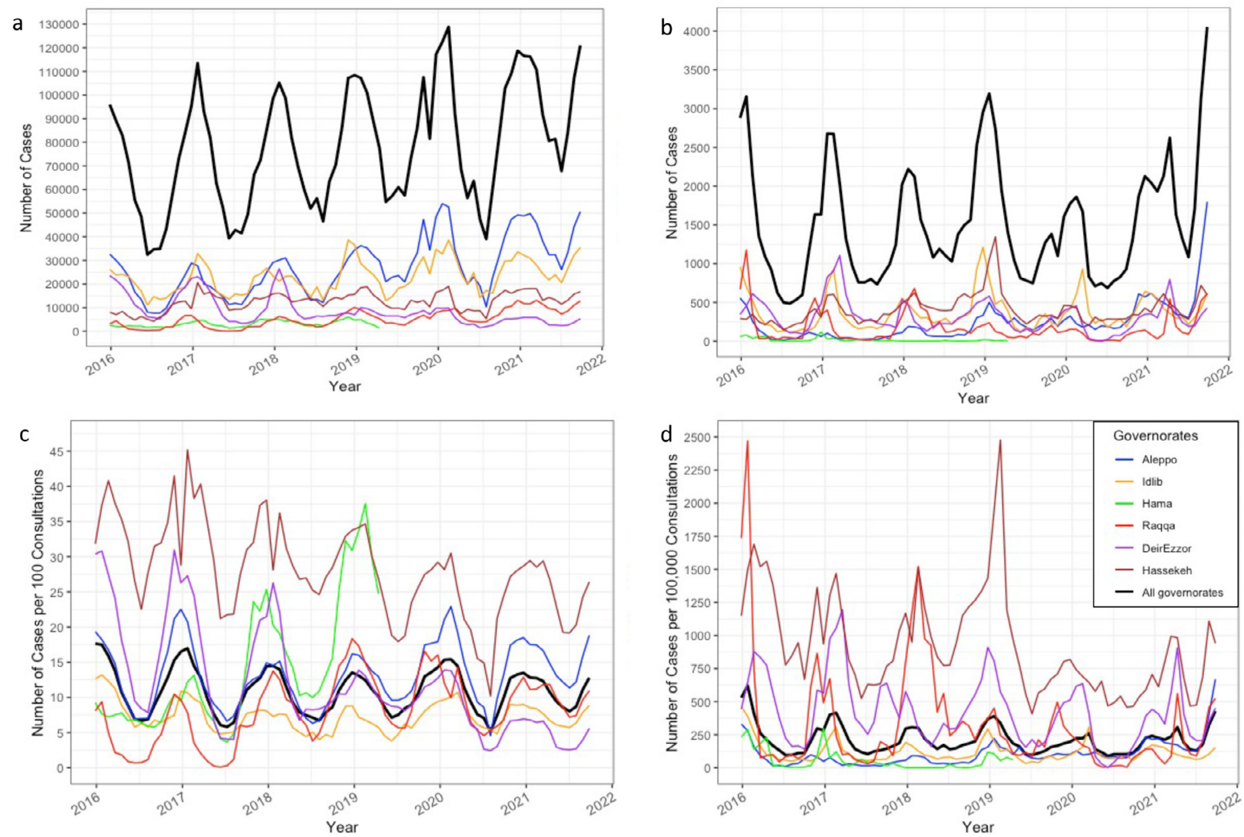

Figure 3. Time series showing number of ILI cases (a) and SARI cases (b) reported in EWARN between 2016-2021 by governorate. The number of ILI cases per 100 consultations is shown in (c), and the number of SARI cases per 100,000 consultations is shown in (d), both by governorate.
EWARN = early warning and response network; ILI = influenza-like illness; SARI = severe acute respiratory infection.

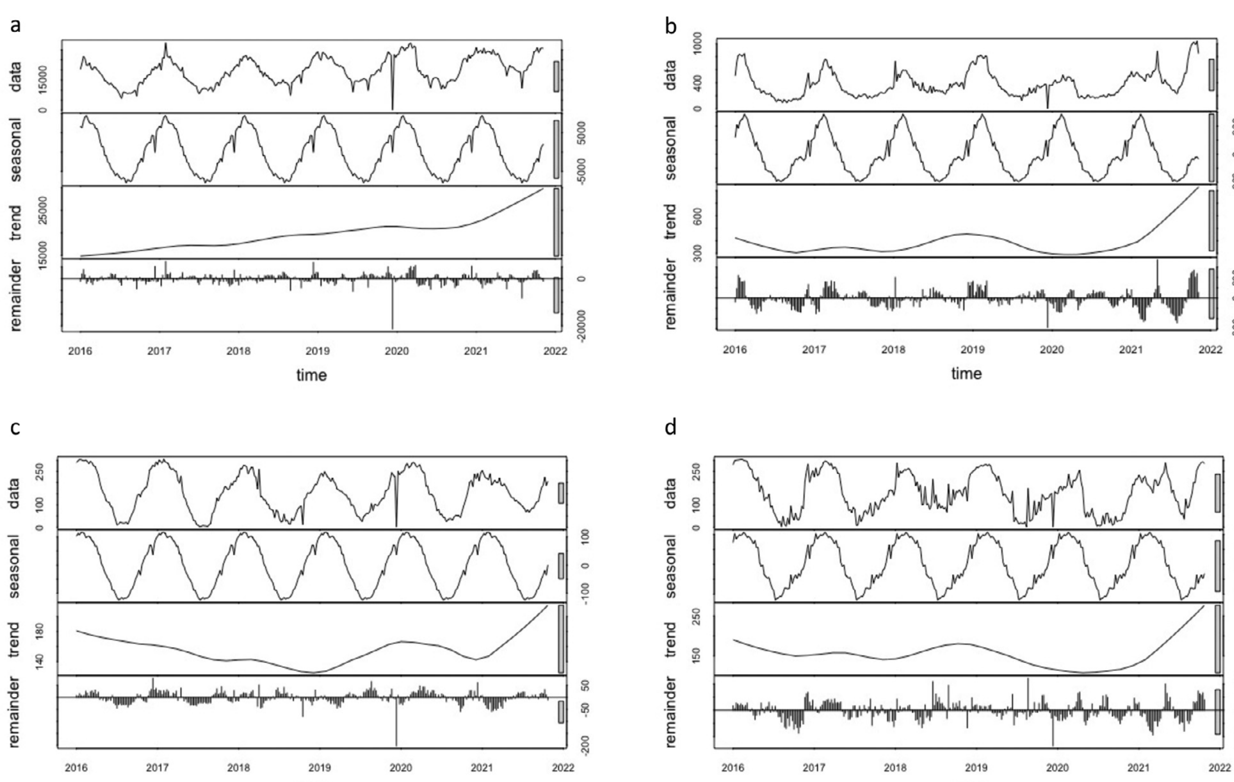

Figure 4. Seasonal-trend decomposition with LOESS plots of ILI cases (a), SARI cases (b), ILI case positivity (c), and SARI case positivity (d).
ILI = influenza-like illness; LOESS = locally estimated scatterplot smoothing; SARI = severe acute respiratory infection.

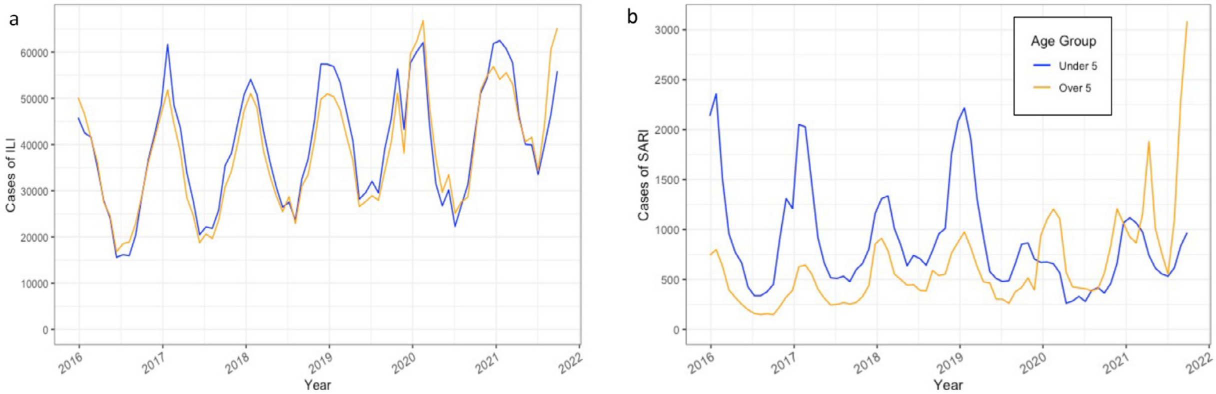

Figure 5. Time series of ILI (a) and SARI (b) cases by age group.
ILI = influenza-like illness; SARI = severe acute respiratory infection.

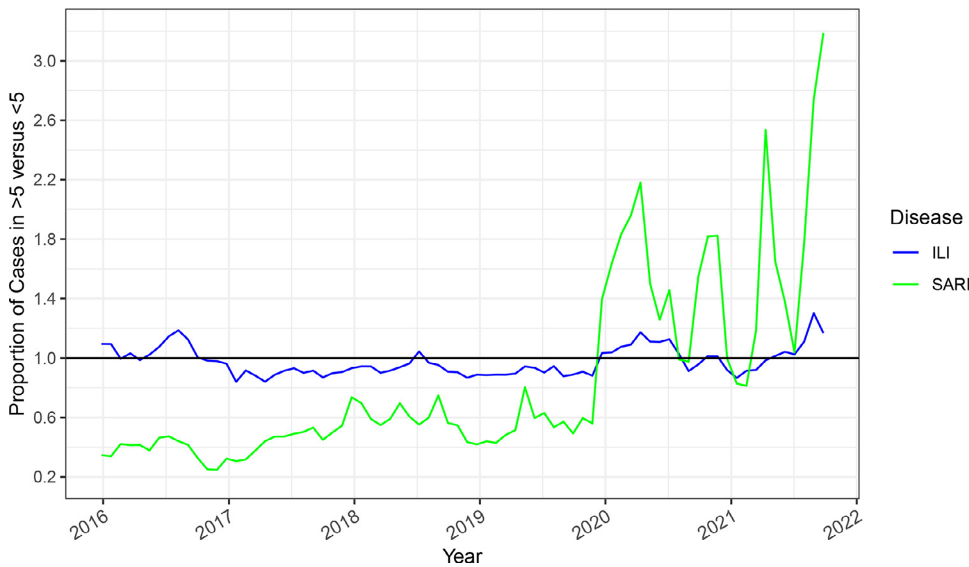

Figure 6. Time series of cases in individuals ≥5 years old to individuals <5 years old by disease type.

<5 years. The time periods during which the trend lines are above 1.0 indicate periods where the case ratio inverted (i.e., when there are more cases in individuals aged ≥5 than <5 years), as seen primarily after 2020 (Figure 6).

Discussion

This study uses available data from EWARN and COVID-19 dashboards to report trends in ILI, SARI, and SARS-CoV-2 in northern Syria, an area of protracted conflict. We noted increases in both ILI and SARI trends over the time period studied; this is consistent with other studies from Syria, which report increases in emerging and reemerging infectious diseases during the conflict (Mowafi, 2011; Doganay and Demiraslan, 2016; Nimer, 2018; Raad et al., 2018; Tarnas et al., 2021). These findings support previous work in other settings where respiratory infections are important causes of excess morbidity, mortality, and case fatality among populations affected by protracted conflict (Goniewicz et al., 2021; Moradi-Lakeh et al., 2018; Guha-Sapir and van Panhuis, 2004; Bellos et al., 2010). This can be attributed to many factors, including the general breakdown of health and public health infrastructure, interruption of vaccination coverage, migration, forced displacement, and camp settings conducive to increased transmission. The increases in ILI over the study time period and SARI in mid-2020 could also have been influenced by improved reporting, population growth, or population movements rather than reflecting a true increase in cases. However, we attempt to control for the former by standardizing the case counts by the number of consultations for both ILI and SARI. As an early warning system, EWARN has a history of responding to observed epidemiological trends such as these with public health action focused primarily on scaling up testing capabilities, laboratory training, activation of rapid response teams, contact tracing, triaging at health facilities, and risk mapping (Office for the Coordination of Humanitarian Affairs, 2020a; Ekzayez et al., 2020). For example, EWARN was responsible for scaling up COVID-19 testing capabilities in northwest Syria throughout 2020; tests were processed inside Syria because of EWARN's laboratory capacity building in response to SARI and ILI trends in 2017 (Ekzayez et al., 2020).

The seasonality in ILI and SARI cases is consistent with established seasonal trends in respiratory infections (Moriyama et al., 2020). Both ILI and SARI experienced delayed peaks in weeks 9 and 7, respectively, during the 2019-2020 season, as seen in Figures 3a-d. This may be attributable, at least in part, to the northwestern offensive launched by the Syrian government and allied forces in Idlib governorate in late 2019. This escalated to a major offensive by mid-December 2019, during which government forces captured territory in southern Idlib and forced almost a million people from their homes to northern areas (Office for the Coordination of Humanitarian Affairs, 2020b; United Nations, 2020; King, 2020). The stark decline in SARI and ILI cases (Figures 3a-d) in late 2019 may correspond with the increase in violence and destruction of healthcare infrastructure during this period. As a result, the delayed peak in the 2019-2020 season may be due to delays in seeking care, an increase in cases because of the influx of displaced individuals in camp settings, or a combination of the two.

In Figures 4c and 4d, we see declines in both ILI and SARI case positivity throughout most of 2020, which is likely because of the impact of COVID-19–related lockdown policies. This is consistent with the association of COVID-19 response measures, and potential viral interference with influenza and other ILI observed in other countries (Feng et al., 2021; Galli et al., 2021). Initial lockdown measures in northwest Syria included border closures, self-isolation advisories, and the closing of schools, mosques, and markets for nonfood items. In northeast Syria, restaurants, cafes, markets, and private clinics were closed in late March 2020, in addition to restrictions on public gatherings and the implementation of a mandatory curfew (Marzouk et al., 2020). These lockdown measures may have aided in decreasing the spread of ILI and SARI during this initial time period, as has been the case in other settings (Sullivan et al., 2020; Feng et al., 2021).

Crossover in the distribution of ILI and SARI cases between individuals aged <5 and ≥5 years in the last week of 2019 are of particular interest. Based on first-hand contextual knowledge of testing results from author NA, we hypothesize that this early crossover may be in part because of an increase in influenza A cases among adults. It is also possible that early cases of COVID-19 entered Syria through Turkey, which hosts a large number of visitors from China, thus potentially creating a pathway for SARS-CoV-2 to spread from China to Syria (Republic of Türkiye, 2022). As COVID-19 cases are more likely to result in hospital admission among adults, the inversion of the SARI case proportions may be a signature of the COVID-19 outbreak in the region and reflect an increase in hospitalizations in individuals aged ≥5 years because of COVID-19 (Romero Starke et al., 2020). This may indicate the presence of undiagnosed COVID-19 cases in northern Syria before the first official cases were detected (April 2020 in northeast Syria and July 2020 in northwest Syria). This was particularly the case in northeast Syria (and remains so), where there was inadequate capacity for SARS-CoV-2 PCR testing, which could lead to delays in case identification, isolation, and contact tracing (Human Rights Watch, 2020).

Limitations and strengths

The data used for this study are likely affected by underreporting because of inadequate testing, movement restriction, political pressures, and weak reporting infrastructure in northern Syria (Almhawish et al., 2021). Mass population movement can also result in uncertainties in population denominators which leads to imprecision in estimates of disease incidence or prevalence. Population movement can also lead to fluctuations in cases even when case incidence or prevalence remains constant. We aimed to mitigate this by calculating case positivity per governorate and aggregating data over four-week periods. Because of insufficient testing capacity for SARS-CoV-2, particularly in northeast Syria, the true number of cases is unlikely to be reflected in reports as the numbers of cases may vary with testing availability in each governorate (Lau et al., 2021). Although we can demonstrate trends in ILI, SARI, and COVID-19 and suggest etiologies for these, we are unable to establish any causal relationships. Conversely, having time series data (including total consultations) allows us to assess trends over time and to assess whether disruptions in consultations were associated with those trends. The data and our analyses are also strengthened by the inclusion of demographic data, which can be valuable for detecting outbreaks of disease that impact age groups differentially.

Conclusion

Respiratory infections continue to be a source of widespread morbidity and mortality throughout northern Syria, particularly with the emergence of SARS-CoV-2. Analyzing trends in reported cases is a necessary precursor to understanding the extent of the association of conflict with respiratory infections and the use of syndromic surveillance during the conflict. By extracting trend data from expected seasonal fluctuations and mapping annual case data, we can elucidate changes in reported ILI and SARI at governorate-level granularity. We can also leverage EWARN data while analyzing reported COVID-19 cases to hypothesize underreporting of COVID-19 throughout the region. Through this study, we hope to shed light on the reported magnitude of the respiratory infection burden in northern Syria and the importance of disease surveillance during the conflict. This work may have implications for future respiratory infection monitoring in northern Syria and provides important foundational knowledge for responses to ongoing and emerging respiratory infections during protracted conflict. Given the recent emergence of several novel human coronaviruses, this is an area on which increased public health attention should be focused.

Conflicts of interests

The authors have no competing interests to declare.

Funding

This research did not receive any funding from agencies in public, commercial, or not-for-profit sectors.

Ethical approval

This study was a secondary data analysis that used publicly available data from EWARN, the COVID-19 Response Tracking Dashboard for Northwest Syria, and the Northeast Syria COVID-19 Dashboard. No patient-level or identifiable patient data were used. Therefore, ethics approval was not sought.

Availability of data and materials

The datasets analyzed during the current study are available from ACU-EWARN (https://acu-sy.org/ewarn/), the COVID-19 Response Tracking Dashboard for Northwest Syria, and the Northeast Syria COVID-19 Dashboard.

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