Epidemiological Analysis of Acute Flaccid Paralysis (AFP) Surveillance in Conflict-Affected Syria

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ABSTRACT

Syria has been polio-free since 1999; however, due to factors including mass displacement, insecurity, and the decreasing functionality of public health infrastructure, poliomyelitis (polio) reemerged in 2013-2014 and 2017. The aims of this study were to describe trends in the incidence and surveillance of the clinical diagnosis of polio, acute flaccid paralysis (AFP), in northern Syria over a three-year period during the ongoing conflict. We conducted a retrospective analysis of reported AFP incidence and surveillance among AFP cases in people under the age of 15 years from January 2018 to December 2020. We utilized data collected from the Early Warning Alert and Response Network (EWARN) operated by the Assistance Coordination Unit (ACU). A total of 1124 cases of AFP were reported in northern Syria during the study period. More than half of the children were under five years of age (n= 837, 68.9%) and 57.7% (n= 701) were male. All cases were classified as non-polio cases based on serology, with one case classified as polio compatible. Surveillance indicators were constantly above the minimum targets on a national level, with a significant increase in the adequacy of stool specimens and rank of reporter over the period studied. AFP surveillance data are the final measure of a country's progress towards polio eradication. While the ACU has strengthened the sensitivity and quality of the AFP surveillance system in northern Syria over time, additional efforts are needed to strengthen subnational sensitivity.

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INTRODUCTION

Since the Syrian civil war began in 2011, the country's health care system has suffered due to destruction of health facilities, an exodus of health professionals, shortages of medical supplies, disruption of preventative services, and mass displacement.[1-5] In the first year of conflict, disease surveillance broke down. It was not until 18 months after the beginning of the crisis that this deficit began to be addressed.[6] The conflict has led to a drop in vaccination rates and the re-emergence of poliomyelitis (polio) in mid-2013.[7] The spread of infectious diseases is attributable, among many other factors, to uncoordinated and delayed response efforts caused by mass displacement. Nationwide acute flaccid paralysis (AFP) surveillance is the gold standard for detecting cases of polio, and only one in two hundred non-immune infected individuals develop the condition.[14,17,18] Therefore, the great majority of those infected with poliovirus (90- 95%) are asymptomatic and do not exhibit paralysis.[1,11] This underscores the need for early warning and intervention, effective management of infectious disease, and timely information systems.[12]

In this study, we use a disease surveillance dataset focused on case reporting for AFP, the clinical case description for suspected polio, and describe the characteristics of cases in conflict affected northern Syria based on epidemiological surveillance indicators. Although many studies have been conducted on the causes of AFP and its surveillance in different countries, few aim to describe the incidence, distribution, and surveillance performance of AFP in Syria.[1,10,13–15] We hope that this data will contribute to a broader understanding of outbreak vulnerabilities in regions affected by conflict and highlight the need for robust early warning surveillance systems in complex emergencies.

METHODS

Study Design and Period

We conducted a retrospective time-series analysis of AFP surveillance data in conflict affected northern Syria between January 1st, 2018, and December 31st, 2020. This data was collected by the Early Warning Alert and Response Network (EWARN) and operated by the Assistance Coordination Unit (ACU), a national Syrian non-governmental and non-profit organization. We describe EWARN data and AFP surveillance indicators and then review the statistical analysis.

EWARN Surveillance

The re-emergence of polio in 2013 takes place in the context of an increased incidence in AFP documented by both the EWARN operated by the ACU; and the Early Warning and Response System (EWARS) operated by the World Health Organization (WHO). These two surveillance systems operate independently within Syria but are seen as complementary, providing a full profile of epidemic-prone disease burden.[19,21,22] The immediate reporting and weekly reporting components of these systems emphasize effectiveness and proactiveness–an essential method for the early detection of polio where clinical illness (AFP) is documented only in a minority of infected individuals.[6]

Study Setting

For this study, the complex landscape was split into two categories of authority within Syria: areas under control of the Syrian government (government-controlled areas), and those not in control of the Syrian government (non-state-controlled areas).[18] This retrospective analysis focused on data routinely collected by the EWARN in non-state-controlled areas of northern Syria. The EWARS is a similar system but focuses on government-controlled areas and is jointly administered by the WHO and the Syrian Ministry of Health.6 Areas that are phased out of the coverage region after the Syrian government regained control are reported as having missing case reports. We do not report on data from EWARS.

As of 2020, Syria's population is estimated at about 17 million people according to UN data.[19] The country's administration is divided by 14 regional governorates (muhafazat), which are further

divided into 61 districts (manatiq) which in turn are subdivided into subdistricts (nawahi).[20] The EWARN collects data on 13 infectious diseases from more than 480 health facilities and covers a population of about 12 million.[21]

AFP Surveillance Indicators

The ACU defines an AFP case as a child less than 15 years of age presenting with recent or sudden onset of floppy paralysis or muscle weakness due to any cause, or any person of any age with paralytic illness if polio is suspected by a clinician. The alert threshold is one suspected case, while the outbreak threshold is one confirmed case (including laboratory confirmation) of polio.[6,22,23]

The WHO has established surveillance indicators that ensure the quality and sensitivity of the AFP surveillance system is achieved and maintained. For this analysis, we focused on the following indicators: non-polio acute flaccid paralysis rate (NP-AFP rate), early detection, rank of reporter, and stool adequacy.

Non-Polio Acute Flaccid Paralysis (NP-AFP) rate

The sensitivity of the AFP surveillance system is reflected by the annualized non-polio AFP rate.[9,15] The NP-AFP rate is the incidence of AFP cases due to conditions other than polio. It measures the number of non-polio AFP cases in a population aged under 15 years that should be detected over one year. An NP-AFP of at least 2 per 100,000 aged under 15 is considered sensitive in endemic regions and is the minimum target.[9]

Districts	2018	POPL15	2019	POPL15	2020	POPL15	Total Cases
Aleppo Total:	107	871,322	122	822,029	107	1,385,803	336
A'zaz	16	171,371	18	179,426	9	288,011	43
Afrin	8	137,913	7	87,584	31	175,647	46
Ain Al Arab	9	60,417	7	66,588	3	65,982	19
Al Bab	7	79,626	13	72,996	5	217,419	25
Jarablus	8	41,361	42	39,604	25	90,553	75
Jebel Saman	37	183,556	29	217,313	25	399,905	91
Menbij	22	177,327	6	158,518	9	148,286	37
Al-Hasakeh Total:	45	516,321	56	446,353	58	429,405	159
Al-Hasakeh	23	252,050	26	183,010	31	200,651	80
Al-Malikeyyeh	5	56,073	5	62,117	2	62,503	12
Quamishli	2	155,111	7	158,133	16	153,019	25
Ras Al Ain	15	53,087	18	43,093	9	13,232	42
Ar-Raqqa Total:	38	255,080	23	285,378	39	269,396	100
Ar-Raqqa	21	102,969	13	167,444	25	189,144	59
Ath-Thawrah	5	77,012	6	66,071	10	51,602	21
Tell Abiad	12	75,099	4	51,863	4	28,650	20
Dar'a Total:	6	412,218	NA	NA	NA	NA	6
As-Sanamayn	1	80,685	NA	NA	NA	NA	1
Dar'a	5	214,528	NA	NA	NA	NA	5
Izra'	NA	117,005	NA	NA	NA	NA	NA
Deir-ez-Zor Total:	62	246,539	65	194,183	75	242,085	202
Abu Kamal	2	105,092	8	69,169	6	52,843	16
Al Mayadin	11	33,166	12	23,124	4	22,747	27
Deir-ez-Zor	49	108,281	45	101,890	65	166,495	159
Hama Total:	6	66,227	1	72,103	NA	NA	7
As-Suqaylabiyah	6	66,227	1	67,433	NA	NA	7
Hama	NA	NA	NA	4,670	NA	NA	NA
Homs Total:	6	295,610	NA	NA	NA	NA	6
Ar-Rastan	NA	79,931	NA	NA	NA	NA	NA
Homs	6	215,679	NA	NA	NA	NA	6
Idleb Total:	128	964,297	162	1,051,574	107	1,448,147	397
Al Ma'ra	29	224,496	33	193,931	1	131,135	63
Ariha	12	83,100	9	108,693	5	171,930	26
Harim	45	296,144	60	357,301	76	570,440	181
Idleb	32	258,015	47	279,323	17	436,647	96
Jisr-Ash-Shugur	10	102,542	13	112,326	8	137,995	31
Quneitra Total:	1	42,892	NA	NA	NA	NA	1
Quneitra	1	42,892	NA	NA	NA	NA	1
Total	399	3,670,506	429	2,871,620	386	3,774,836	1214

Table 1: Reported AFP cases and population under 15 by district and year, northern Syria, January 2018 to December 2020. **POPL15 = Population under 15 years of age within the area by year.*

Early Detection

Timely reporting is crucial. Within seven days of the onset of paralysis, the case should be reported to the health system, which classifies it as early detection. The minimum target of early detection is 80% of all AFP cases.[9]

Rank of Reporter

Another characteristic of detection is the rank of the reporter–the order of the individual who notified the suspected case to EWARN. A ranking of "1" is considered best in terms of early detection, implying that the first person who observed the AFP case notified EWARN; a ranking of "2" signifies that the second person who observed the case reported to EWARN (signifying that one person prior detected the case and did not report), and so on. The rank was coded as "1, 2, and 3+," with the "3+" category being from "3" to "5."

Stool Adequacy

Stool adequacy is the collection of adequate specimens collected from AFP patients and helps determine the quality of the sample submission process to the lab and resulting confidence in lab results. Adequate stools are defined as two stool specimens collected from an AFP pattern person 24 to 48 hours apart, within 14 days of onset of symptoms, and in good condition. A stool specimen is said to have arrived in such condition if ice packs in stool carrier still have frozen water, specimen is of adequate quantity (8-10 g), presents no leakage or desiccation, and with complete documentation.[14] At least 80% of all AFP cases should have adequate stool specimens.[9]

Furthermore, an AFP case is classified as polio compatible if the stool specimens were not adequate to rule out poliovirus and the case had developed residual paralysis after 60 days follow up, died within 60 days or was last to follow. These cases were presented to an independent Expert Review Committee (ERC) to provide the classification of whether the specimens were compatible or discarded.[14]

Data Analysis

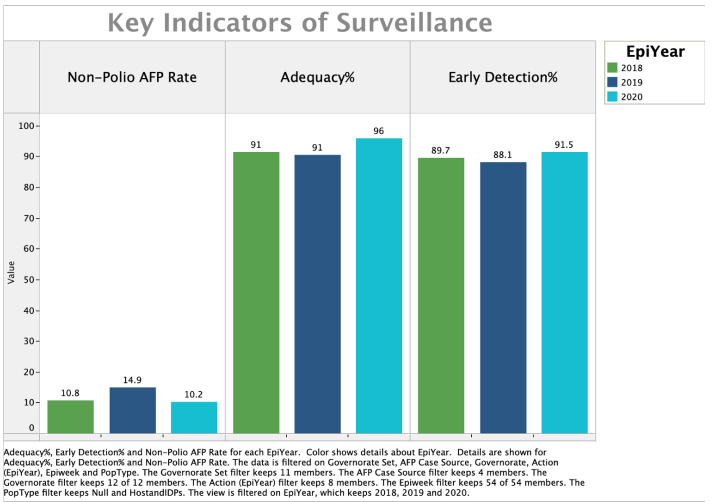

Figure 2: Surveillance indicators, northern Syria, January 2018 to December 2020.

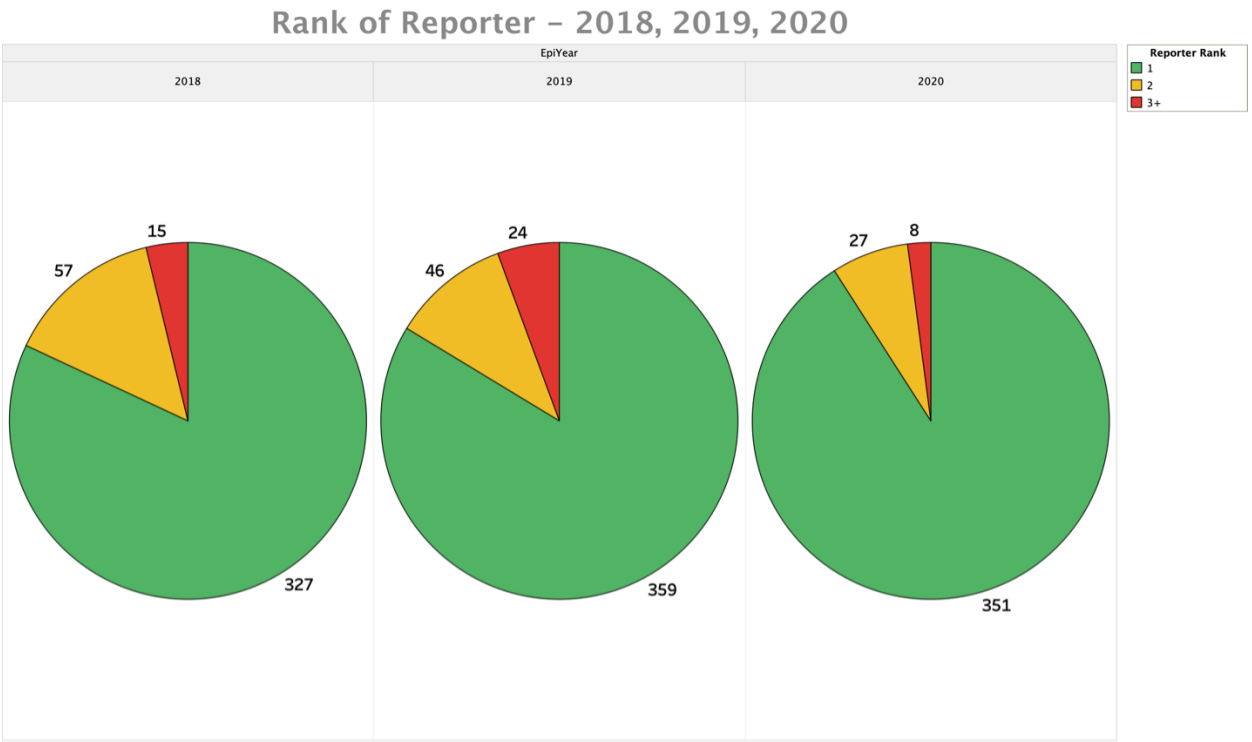

Figure 3: Rank of reporter, northern Syria, January 2018 to December 2020.

Descriptive analysis was performed to describe the epidemiology of reported AFP cases in conflict-affected Syria, and statistics based on the WHO recommended surveillance indicators for AFP surveillance were generated. Mapping was performed to visualize the distribution of AFP cases by location and year.

We conducted a statistical analysis of surveillance data to report on the study population characteristics, which included variables for age, sex, and geographic district. The study aimed to analyze the rank of reporter and adequacy over time to examine whether there were significant improvements of these variables over the three-year study period. Linear regression analysis was used with the year being considered the explanatory variable, with a reference year of 2018 and p-value of <0.05 chosen as the threshold for significance.

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RESULTS

Descriptive Analysis of Reported AFP Epidemiology

From January 2018 to December 2020, EWARN identified a total of 1214 cases of AFP from children under 15 years of age reported in conflict-affected northern Syria. Table 1 shows the governorate of Idleb (n= 397, 32.7% of cases) had the highest numbers of total AFP cases, followed by Aleppo (n= 336, 27.7% of cases) and Deir-ez-Zor (n= 202, 16.6% of cases) (Figure 1). None of the reported cases classified as polio; however, the ERC classified one AFP case as polio compatible in 2018 (located in the district of Menbij, Aleppo).

The study population included a total of 1214 individuals between the ages of 0-15. Within the coverage region, the average age of children was 4.24 years (±3.23). Children under five years of age accounted for 68.9% (n= 837) of the total population; the average age of children in this age group (≤ 5 years) was 2.39 years (±1.18). There was no significant difference between males and females under the age of 15 years (p-value = 0.845): males accounted for 701 of the 1214 total cases (57.7%) and females accounted for 513 (42.3%).

The mean NP-AFP rate during the study period was 12 per 100,000 children under 15 years: 10.8/ 100,000 in 2018, 14.9/ 100,000 in 2019 and 10.2/ 100,000 in 2020. These rates consistently exceeded the recommended benchmark of 2/ 100,000. The proportion of AFP cases with two stool specimens collected within 14 days after paralysis onset, 24-48 hours apart, and in "good condition" (adequacy) remained stable from 2018 to 2019 (91%) and increased to 96% in 2020. Lastly, the proportion of AFP cases notified to the health system within 7 days after paralysis onset (early detection), was 89.7% in 2018, 88.1% in 2019 and 91.5% in 2020.

Overall, reporters ranked "1" for 85% of total cases (n= 1037),

Year	*Estimates*	*Std. Error*	*p-value*
(Intercept)	1.24	0.03	<0.001
2019	0	0.04	0.907
2020	-0.11	0.04	**0.004**

Figure 4: Simple Linear Regression comparing rank of reporter between each year.

Year	*Estimates*	*Std. Error*	*p-value*
(Intercept)	0.91	0.01	<0.001
2019	-0.01	0.02	0.659
2020	0.04	0.02	**0.019**

Figure 5: Simple Linear Regression comparing stool adequacy (%) between each year.

"2" for 11% of cases (n= 130) and "3+" for 4% of cases (n= 47). Doctors reported the most cases (n= 963, 79.3%), followed by nurses (n= 90, 7.4%) and pharmacists (n= 41, 3.4%).

In 2018, 82% (n= 327) of reporters ranked as "1"; in 2019, 84% (n= 359); and in 2020, 91% (n= 351) (Figure 3). Linear regression was done to compare each year to 2018, and the analysis had 1211 degrees of freedom and yielded a p-value of 0.003. There was a significant difference between 2018 and 2020 in terms of rank of reporter–the order of the individual who notified the suspected case to EWARN (p-value = 0.004). The year 2019 was not statistically different from 2018.

The proportion of AFP cases with two stool specimens collected within 14 days after paralysis onset, 24-48 hours apart, and in "good condition" between the years was compared using simple linear regression analysis. The analysis had 1211 degrees of freedom and yielded a p-value of 0.011. In 2018 and 2019, adequacy was 91% and increased to 96% in 2020. The year 2019 was not statistically different from 2018. However, 2020 was statistically different from 2018 (p value = 0.019).

DISCUSSION

The present study focused on descriptive and statistical analyses of reported AFP based on surveillance indicators in northern Syria over a three-year study period using data obtained from EWARN. The Syrian humanitarian crisis has left much of the population vulnerable to disease outbreaks. Throughout the first three years of conflict (2011-2013), a decrease in vaccination coverage occurred, along with disruptions in previously well-functioning disease surveillance systems and poor sanitation.[24] Vaccination coverage dropped across the country from 90% before the crisis to 50% in December 2013.24 Throughout the years 2014 to 2017, health services suffered, civilian violence exponentially increased, and disease surveillance was low. Among children born during the war, the estimated proportion of unvaccinated children with non-polio AFP (NP-AFP) increased from 3% in 2015 to 6% by the end of 2016.[25]

Wild poliovirus, which had been eliminated in Syria since 1999, had a resurgence in 2013-2014, occurring against the backdrop of declining routine vaccination coverage and in one of the most contested areas of the country.25,26 Surveillance systems were established and multiple rounds of supplementary immunization activities (SIAs) were implemented in response to the outbreak in 2013-2014. However, the frequency and quality of SIAs lessened after the outbreak was declared over in early 2014.[25] The disease resurged in 2017 partly due to a lack of treatment and control, with the first cases reported in the governorate of Deir-ez-Zor. An 18-month long intensive vaccination campaign successfully halted this outbreak, despite large-scale population movement and accessibility issues.26 Following the outbreak, a strengthened response during 2018 and onwards has contributed to an increase in reporting and surveillance performance, even amidst the 2020 COVID-19 pandemic.

Nonetheless, the viral strain responsible for the outbreak in 2017 was circulating for approximately a year before the isolation of cVDPV. This delay in reporting, along with gaps in AFP surveillance performance and the ongoing conflict, contributed to the inability to earlier detect of the outbreak.[25] Non-governmental organizations continually strengthen data collection methods and efforts to enhance surveillance for polioviruses and immunization programs.[26,27]

Out of the 1214 total AFP cases, no cases of polio were reported from 2018 through 2020, with one case classified as polio compatible by the Expert Review Committee. The high numbers of reported AFP cases in the governorates of Idleb (n= 397, 32.7% of total cases) and Aleppo (n= 336, 27.7% of total cases) can be explained by the high population of children under 15 years of age in these areas. As for Deir-ez-Zor (n= 202, 16.6% of total cases), experiencing two outbreaks within five years may have resulted in high sensitivity among healthcare providers and led to high reporting. The EWARN coverage region phased out of the governorates of Dar'a, Homs, Rural Damascus, and Quneitra once the Syrian government regained control, therefore there were little to none reported cases due to the lack of reporting.

Our findings showed that 68.9% of AFP cases occurred in children under five old, confirming that young age was a risk factor, as shown in previous literature.[10,14,15,28] Although the differences in reported AFP by sex was not statistically significant, our findings indicate that the majority (57.7%) of AFP cases involved males. This is also consistent with previous literature and may be explained by sex differences in the susceptibility to infectious agents.[10,14,15,28]

The minimum NP-AFP, early detection, and stool adequacy targets set by the WHO were surpassed at the national level in all three years analyzed. When looking at the mean NP-AFP by governorates, all met the recommended NP-AFP goal of 2/ 100,000 and all governorates exceeded the early detection target of 80%. The success of an AFP surveillance system not only depends on the detection of AFP cases, but also on the investigation and reporting of the cases. The mean proportion of AFP cases with adequate specimens collected within 14 days of onset of paralysis exceeded the target of 80% throughout the study period. Results showed disparities in adequacy performance among governorates, as the governorate of Homs (50%) did not meet the minimum target. This may have been accounted for by the changing coverage region; as the Syrian government regained control of the area, the EWARN lost half of collected specimens.

While surveillance indicators increased over the three-year study period, we found significant increases in the rank of reporter and adequacy in 2020 compared to the reference year of 2018. The rank of reporter signifies the order of the individual who notified the suspected case to EWARN. Our findings indicate a gradual increase of the rank of reporter being "1" throughout the study period, signifying a statistical increase in reporting methods. Additionally, adequacy significantly increased in 2020, signifying increased quality of AFP surveillance.

Nonetheless, challenges still exist in terms of AFP surveillance activities, especially throughout the COVID-19 pandemic. These challenges include: the partial closures of a considerable number of private physicians' practices; the inability to conduct supplementary AFP surveillance activities such as Area Coverage Survey and out-of-household contact sampling; delay in lab results; lack of PPEs with the field staff; and inability to conduct in-person Expert Review Committee sessions as a precaution measure against COVID-19. Mitigation efforts should be made to address such challenges. These efforts include communicating with surveillance focal points on a regular basis to ensure immediate notifications of AFP cases, maintaining communication channels with the reference laboratory to

ensure timely feedback, and looking into alternative laboratories to run needed tests.[33,34]

Active surveillance for AFP depends, above all, on early detection and timely action. Staying ahead of the virus requires a well-managed system for detecting AFP cases that entails immediate investigation. EWARN has helped detect epidemic-prone diseases in Syria, where the risk of disease outbreaks is greatly increased by cross-border movements of highly mobile populations.[24] This paper is unique in analyzing the rank of reporter as a surveillance indicator over time, along with assessing the WHO recommended surveillance indicators in conflict affected Syria.

The most recent polio outbreak occurred in 2017. Although Syria maintained a three year period (2018-2020) without any confirmed polio cases throughout the country, the resurgence of poliovirus remains a potential threat; therefore, it is essential to maintain high quality AFP surveillance, supplemented by mitigation measures.[29] The recent outbreaks in Syria emphasize the significance of increasing financial and logistical support for immunization efforts, especially in complex emergencies where epidemic-prone diseases can reemerge. Furthermore, the gradual disintegration of the Syrian public health system has led to a greater reliance on NGOs.[24] Although Syrian NGOs provide 75% of the support in Syria currently, these NGOs receive less than 1% of the international funding.[30] It is critical to resolve the Syrian conflict, continue the surveillance of infectious diseases, and further support NGOs.

Limitations

Limitations include the changing coverage region based on the political situation–territories starting off as non-state-controlled areas that later fall out of the coverage region after becoming government-controlled areas were reported as having missing case reports and therefore excluded from this analysis. Additionally, analysis was done by aggregating for the entire coverage region by year. National performance can obscure the subnational performance and prevent early detection of AFP cases, which can occur at the sub-county level.[15] Therefore, surveillance indicators should be analyzed at the governorate and district level to uncover underperformance that might be concealed by country level analyses.

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