

Systematic Review of Reported HIV Outbreaks, Pakistan, 2000–2019

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Learning Objectives

Upon completion of this activity, participants will be able to:

- Distinguish groups at highest risk for HIV infection in Pakistan
- Analyze causes of outbreaks of HIV infection in Pakistan
- Assess factors which might promote unsafe injection practices in Pakistan

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Unsafe injection practices and injection drug use have been linked to multiple HIV outbreaks in Pakistan since 2003; however, few studies have systematically analyzed the causes of these outbreaks. We conducted a systematic review of published English-language literature indexed in bibliographic databases and search engines and a focused gray literature review to collate and analyze all reported HIV outbreaks in Pakistan during 2000–2019. Of 774 unique publications reviewed, we identified 25 eligible publications describing 7 outbreaks. More than half occurred during 2016–2019. The primary sources of transmission were iatrogenic transmission, affecting children, persons with chronic medical conditions, and the general population (4 outbreaks); injection drug use (2 outbreaks); and a combination of both (1 outbreak). In the absence of robust HIV testing and surveillance in Pakistan, timely and detailed outbreak reporting is important to understand the epidemiology of HIV in the country.

The first cases of HIV in Pakistan were reported in 1987, with epidemiologic evidence supporting the importation of cases by migrant workers from the Gulf States (1–3). Since that time, noncontinuous surveillance assessments have noted high prevalence of HIV in certain populations; the most recent 2016–2017 prevalence estimates were 38.4% among persons who inject drugs (PWID), 7.2% among transgender persons, and 5.6% among men who have sex with men (4–8). By comparison, the prevalence in the general population is 0.1%, representing ≈190,000 persons living with HIV (PLHIV), including 6,100 children <15 years of age, according to 2019 Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates (8,9). Approximately 44,758 (24%) PLHIV were registered with the National AIDS Control Programme with a known diagnosis as of December 2020, and of these, only 24,362 (54%) were receiving antiretroviral therapy (ART) (10). These statistics are far below the UNAIDS 90–90–90 HIV treatment targets (90% of HIV-positive persons being aware of their status; of those, 90% receiving ART; and of those, 90% being virally suppressed) aimed at controlling the AIDS epidemic; most PLHIV (87%) in Pakistan are not receiving treatment (11).

In April 2019, a major HIV outbreak in Larkana District in Pakistan was identified by local and provincial public health officials (12). After several ill children with HIV-negative parents tested positive for HIV, the provincial Sindh AIDS Control Program began a voluntary district-wide testing campaign. During April 25–June 28, 2019, a total of 30,192 persons were tested for HIV; 876 (2.9%) were HIV positive, and 82% of those were children <15 years

of age. A World Health Organization (WHO) report cited unsafe medical practices and poor infection control programs as key risk factors for infection (12) and noted that this outbreak was the fourth HIV outbreak in Larkana since 2003. A cursory review of the literature, however, did not identify peer-reviewed publications on all of these referenced outbreaks. The objective of our systematic review was to identify and collate data from all reported HIV outbreaks in Pakistan to describe overarching themes and aid in future prevention efforts.

Methods

We followed the PRISMA statement and the Cochrane Handbook to conduct this systematic review (Appendix Table 1, <https://wwwnc.cdc.gov/EID/article/27/4/20-4205-App1.pdf>) (13). We searched Medline, Embase, CAB Abstracts, Global Health, PsycInfo, Cochrane Library, Scopus, Academic Search Complete, Cumulative Index to Nursing and Allied Health Literature, ProQuest Central, PubMed Central, Virtual Health Library, and Google Scholar to identify English-language publications on reported HIV outbreaks in Pakistan during January 1, 2000–December 31, 2019. We limited the search to studies published after January 1, 2000, because the earliest reported HIV outbreak in Pakistan occurred in 2003 (14). To complement the published literature search, we conducted a comprehensive search of the gray literature (i.e., publications not published in indexed peer-reviewed journals), including UNAIDS reports, WHO reports, and International AIDS Society conference abstracts. In addition, we manually reviewed Pakistan's provincial and national Ministry of Health websites. The following search strategy was used for database and gray literature searches: (HIV or AIDS, any associated synonyms, or both) AND (outbreak, epidemic, pandemic, or cluster) AND (Pakistan [or all subnational units]). We omitted location criteria for manual review of Pakistan governmental websites. The full search strategy is detailed in Appendix Table 2. We used Endnote X9 (Clarivate Analytics, <https://endnote.com>) to import and manage retrieved records. To identify duplicate reports, we used the EndNote automated “find duplicates” function, with preferences set to match by title, author, and year; a second round of manual de-duplication was performed by using the same matching criteria. We grouped the remaining reports by database, search engine, and source, and authors reviewed these independently. We used a shared database to track the progress of the reviews.

We systematically screened and reviewed results from the published and gray literature search (Figure). We screened titles and abstracts, and we defaulted to reviewing the abstract if the title had an unclear focus and reviewing the full report if no abstract was available, counting it among the number of abstracts reviewed. We included publications that reported data on outbreaks of HIV or sudden increases in cases in Pakistan. For the purpose of this systematic review, we defined an outbreak as an unexpected number of HIV cases identified through targeted testing or key population surveillance, labeled and reported as an outbreak, and leading to an evaluation or investigation. We excluded abstracts without published final reports (unless identified in the gray literature), reports that provided prevalence or incidence data only (including key population surveys), opinion pieces without mention of a specific outbreak, mathematical modeling studies, epidemiologic analyses, reports without quantitative data, and preprint reports. We also excluded reports where the author did not define the described cases as an outbreak or did not provide a discrete geographic, temporal, or epidemiologic link. If identical reports were published in ≥ 1 journal, the earliest publication was included. Similarly, if identical or nearly identical reports were published in a journal and also included as a conference abstract, we included only the published report. If a report included outbreak data as well as a subset of data in a case control, cohort, or cross-sectional investigation, we included data on the larger outbreak and the study. We reviewed journal submission guidelines to determine whether a publication was peer-reviewed.

We organized eligible publications, gray literature, and government reports by geographic location and year of the reported outbreak. We included reports describing multiple outbreaks under each appropriate outbreak heading. We extracted year and type of report, investigating agency and source or reference for primary data, number of persons tested and diagnosed with HIV, case positivity rate (defined as the percentage of persons positive among the number tested within the period defined by the authors of the publication), notable demographic and behavioral characteristics of case-patients, major risk factors, and other relevant information (Appendix Table 3). We noted instances where articles used media reports as their primary citation. One author independently reviewed initial data extraction of all eligible reports for concurrence. If necessary, we reached out to corresponding authors of individual reports for clarification.

Results

Our initial search identified 1,653 records published during January 2000–December 2019. We removed 879 (53%) duplicate reports identified across multiple databases or search engines through automated and manual processes (Figure). Of the remaining 774 de-duplicated reports, 625 (81%) were excluded after review of the title and 108 (14%) were excluded after review of the abstract. We excluded 16 reports upon review of the full article, gray literature, or government report, leaving 25 (3%) reports eligible for inclusion.

The 25 reports identified by our search strategy described 7 outbreaks: 4 in Punjab Province (Sargodha, Sargodha District [2007]; Kot Imrana, Sargodha District [2018]; Jalalpur Jattan, Gujrat District [2008]; and Faisalabad, Faisalabad District [2019]) and 3 in Sindh Province (Larkana, Larkana District [2003 and 2016] and Ratodero, Larkana District [2019]) (Appendix Table 3). Six (24%) reports described ≥ 2 outbreaks.

Case-positivity rates ranged from 1.3% to 51.8%, varying in part because of sampling methods. The potential source of 4 of the 7 outbreaks was reported as iatrogenic transmission through unsafe healthcare practices at clinics, hospitals, and dialysis centers; 2 outbreaks were attributed to injection drug use, and 1 outbreak was attributed to both. Several reports described a potential association with unqualified healthcare providers (frequently designated as quacks in Pakistan [15]), in general, or with a specific provider. Some reports also reported cultural practices as a contributing factor to transmission. Populations most affected by the outbreaks varied by proposed etiology; iatrogenic causes affected the general community, including women and children, as well as persons living with specific medical conditions, such as end-stage renal disease. Recreational drug use affected primarily PWID, most frequently men.

Our review identified 5 reports in peer-reviewed literature, with the remaining reports published as letters to the editor or correspondence, nongovernmental organization and government reports, and conference abstracts. National or provincial AIDS control programs led the initial investigations of 4 of the 7 outbreaks; the National Institutes of Health–Pakistan and Field Epidemiology Training Program–Pakistan and district health departments provided data for the other 3 outbreaks. The Ratodero (2019) outbreak had additional support from WHO, other United Nations agencies, local universities, and other international and local partners. Of the

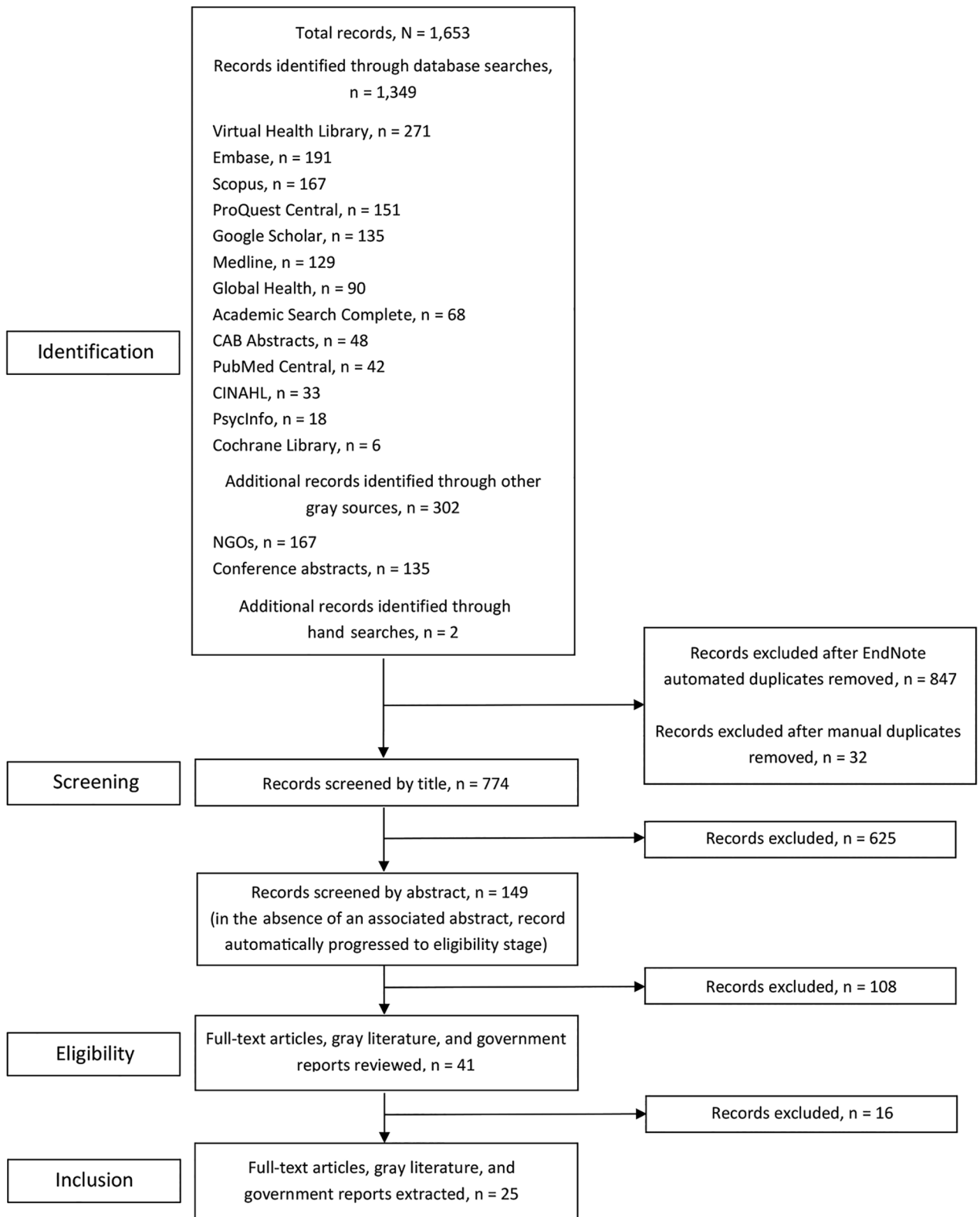


Figure. Identification and selection of studies reporting HIV outbreaks in Pakistan, January 2000–September 2019. CINAHL, Cumulative Index to Nursing and Allied Health Literature; NGOs, nongovernmental organizations.

25 reports, 17 (68%) describe this single outbreak. Other outbreaks had more limited data, often limited to case counts and affected population. Authors were often not directly affiliated with the primary data but rather briefly described testing statistics, demographic information, and risk factors obtained from investigations from government entities, media reports, and other sources. Some discrepancies were noted across reports pertaining to the same outbreak, and many reports did not provide complete information on case-positivity rates, study period, or method of data collection. Authors occasionally (4 [16%]) used media reports as the primary source of information. Though most outbreaks had at least 1 article citing primary data or data directly from a testing program, the single report found for the Faisalabad (2019) outbreak cited only a newspaper article. Of the 25 reports describing the 7 outbreaks, only 5 reports provided detailed outbreak investigation information. Despite more extensive investigations, these reports still had limited ability to draw conclusions or conduct statistical comparisons because of study design (e.g., no comparison group [16] or small sample size [17]). Only 1 of the 25 reports, describing an outbreak investigation in Jalalpur Jattan (2008), included phylogenetic information (16), which demonstrated that transmission likely occurred over a decade, reflecting endemic disease rather than an outbreak.

Discussion

Our review identified 25 reports describing 7 HIV outbreaks during 2000–2019 in Pakistan: 3 in Sindh Province and 4 in Punjab Province. Of these, 4 were identified during 2016–2019. In 2019, two outbreaks were reported: a large outbreak primarily affecting children in Ratodero in Larkana, a district with multiple prior outbreaks, and an outbreak in Faisalabad, primarily infecting PWID. Case-positivity rates ranged from 1.3% to 51.8%, and populations most affected varied by outbreak but included PWID; persons living with specific medical conditions; and the general population, including women and children. The level of detail pertaining to the description of data collection and investigation methods varied across the publications, and much of the data provided were collected not by authors but by national, provincial, and district health departments and other government entities. Iatrogenic transmission (57%), injection drug use (29%), or both (14%) were identified as the potential sources of the outbreaks; no outbreak solely attributable to sexual transmission was reported.

Iatrogenic transmission from unsafe healthcare practices and poor infection prevention and control was identified as the primary or contributing risk factor in 5 of the 7 HIV outbreaks (Jalalpur Jattan [2008], Kot Imrana [2018], Larkana [2016], Ratodero [2019], and Faisalabad [2019]). From a recent survey in Pakistan, researchers estimated that ≈38% of surveyed physicians likely reused syringes (18). Data from the latest Demographic Health Survey indicate that ≈9% of injections given to patients in Pakistan are unsafe, and every person receives an average of 4.1 therapeutic injections per year in Pakistan (19). Extrapolating from this frequency and safety data, approximately 1 in 3 persons might receive an unsafe injection every year in Pakistan (19). Furthermore, cross-sectional studies of persons with thalassemia in Pakistan have shown a high prevalence of bloodborne infections, including HIV, hepatitis B, and hepatitis C, suggestive of infection from blood transfusions (20,21). Nosocomial or iatrogenic transmission including unsafe blood transfusions and reuse of medical equipment has contributed to several HIV outbreaks in other countries, including ≈10,000 children in orphanages in Romania (22), >400 children in Libya with frequent co-infection with hepatitis B and C (23), and 242 adults and children in Cambodia (24).

Several factors might play a role in the propagation of unsafe injection practices in low-income countries. These factors include sociocultural factors such as healthcare providers' belief that compliance is better with injections than with oral medication and patients might seek healthcare elsewhere if not provided injections; financial incentives on the part of both patient and provider through fee-for-injection practices and contingent on provider ability to purchase and maintain a supply of injecting equipment; corruption, when money allocated for healthcare, such as disposable injecting equipment, is used elsewhere, leading to reuse of equipment; lack of policies and procedures around safe injection practices, such that policies forbidding the reuse of injecting equipment are not implemented nor enforced in low-income countries as they are in high-income countries; ready access to injectable medications without a prescription; and lack of awareness of risks associated with unsafe injection practices (25). Given these factors, developing a multi-strategy approach that might be adapted and tailored as necessary might help prevent future outbreaks of HIV and other bloodborne pathogens. These strategies include community and healthcare provider education to address excessive and unnecessary use

of therapeutic injections, implementation and monitoring of policies around single-use injecting equipment, and addressing gaps in infection prevention and control.

Injection drug use was reported as the primary or contributing cause of HIV transmission in 3 of the 7 outbreaks (Larkana [2003], Sargodha [2007], and Faisalabad [2019]). Periodic HIV surveillance data are available for key populations in specific cities from the National AIDS Control Programme Integrated Biologic and Behavioral Surveillance surveys, but they are not designed to measure prevalence for the general population or key populations in rural areas (4–8). The HIV prevalence among PWID documented by each survey increased from 10.8% to 38.4%; however, because the survey was expanded to new cities across the different reporting periods, direct comparison of the change in prevalence is not possible. Whether any change in prevalence might be attributable to sporadic outbreaks or a steady increase in HIV prevalence in this subpopulation is unknown. None of the literature describing outbreaks with injection drug use as the primary or contributing source of transmission reported a phylogenetic analysis, leaving timelines of infections in these outbreaks unclear.

Although the Integrated Biologic and Behavioral Surveillance surveys offer insight into HIV prevalence among key populations, the absence of routine HIV surveillance in the general population prevents understanding of the actual burden of the HIV epidemic in Pakistan. Considering the high prevalence of HIV in PWID, men who have sex with men, and female sex workers, as well as unsafe injection practices as we have described, spillover to the general population is only a matter of time. Widespread surveillance of HIV might be challenging and might yield little information given the low general population prevalence of 0.1% (9). However, adding surveillance of targeted populations at higher risk, such as pregnant women, patients at infectious disease or tuberculosis clinics, and persons requiring frequent transfusions, might provide early warning signs to changes in HIV prevalence. Likewise, systematic monitoring of the blood supply might represent an efficient, less costly approach to surveillance. Currently, routine surveillance is not conducted in any of these settings. Although phylogenetic analyses, which assist in understanding circulating strains and subtypes, might contribute to our understanding of a rise in cases, only 1 publication identified in this review reported a phylogenetic analysis; it showed that, despite preliminary data suggestive of a new outbreak, transmission

occurred over a decade (16). Without comprehensive surveillance and phylogenetic data, ascertaining whether new HIV diagnoses or a sudden increase in diagnoses in an area represent an outbreak or simply missed HIV diagnoses with endemic transmission over time is difficult.

Outbreaks are underrepresented in the literature; those that are published have limited ability to characterize the full epidemiologic and phylogenetic footprint of an outbreak. Nonsystematic tracking of media reports identified at least 2 other potential outbreaks known to national or provincial AIDS control programs but not described by our systematic review (26,27). Given the frequency of media reports of HIV outbreaks, albeit without full epidemiologic data, and well-documented data on the widespread prevalence of unsafe injections across Pakistan, the paucity of systematic outbreak investigations is striking. Of the reports included in our systematic review, only 5 (20%) were peer-reviewed; the remaining were published as letters to the editor, editorials, general correspondence, abstracts, nongovernment organization publications, and government reports, without clear description of methods, study design, and data collection. Given the limited outbreak investigations and robust data reporting in peer-reviewed and gray literature, our systematic review likely underestimates the frequency of the problem and its associated burden of disease.

The main strength of our review is that we searched multiple bibliographic databases, with the addition of Google Scholar and the Virtual Health Library, nongovernmental organization and government websites, and conference abstracts to ensure all relevant publications were captured. However, we note several limitations. First, we recognize that the definition of an outbreak is challenging in the setting of limited phylogenetic and surveillance data. A study by Ansari et al. (16) determined that the observed increase in cases was likely a progression of endemic disease only after the results of phylogenetic analysis. As such, other outbreaks reported in this review might, if the same analyses were available, have been determined not to be outbreaks. Second, our literature review was limited to English-language publications. Although a potential exists for missing articles written in Urdu and other local languages, English is one of the official languages in the country and is the predominant language for scientific and medical research dissemination in Pakistan (28,29). Finally, although unlikely, a small chance exists that a unique outbreak might have been men-

tioned in a publication focusing on surveillance or other data and thus been missed by our tiered review approach. We also recognize that outbreak reports written by government entities might be for internal review only or might be posted online for a limited time, resulting in a possible bias towards availability of more recent outbreaks.

In summary, reported outbreaks in Pakistan suggest that the spread of HIV might continue if adequate prevention strategies are not adopted. Education campaigns to improve knowledge in the general public about unsafe injection practices, both therapeutic and recreational, might limit HIV transmission and occurrence of outbreaks. Assessing patient and provider misconceptions about the benefits of therapeutic injections could guide public health messaging and reduce demand for unnecessary medical interventions. Reviewing injection safety and infection prevention and control practices could inform healthcare reform efforts to limit iatrogenic exposures and the potential for HIV outbreaks. Last, developing and putting into place comprehensive HIV surveillance systems could assist in outbreak identification, prompting investigations that explore risk factors and underlying transmission sources. Reporting of outbreaks in peer-reviewed literature, including epidemiologic studies and phylogenetic analyses, might shed additional light on the etiologies of outbreaks and effective prevention strategies. Across the spectrum of reports identified by our systematic review, all reports had the consistent message of sounding an alarm and highlighting a potentially rapidly growing problem in Pakistan.

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EID Podcast: Unusual Outbreak of Rift Valley Fever in Sudan

Rift Valley Fever is a devastating disease that can cause bleeding from the eyes and gums, blindness, and death. In 2019, an outbreak of this vectorborne disease erupted among people and animals in a politically volatile region of Sudan. This outbreak broke traditional patterns of Rift Valley Fever, sending scientists scrambling to figure out what was going on and how they could stop it.

In this EID podcast, Dr. Ayman Ahmed, a scientist at the University of Texas Medical Branch and a lecturer at the Institute of Endemic Diseases in Sudan, discusses the intersection of political unrest and public health.

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Appendix

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Appendix Table 1. PRISMA 2009 checklist

Appendix Table 2. Literature Search Strategy

Appendix Table 3. HIV Outbreaks in Pakistan, January 2000–December 2019

Appendix Table 1. PRISMA 2009 checklist*

| Article section | Item no. | Checklist item | Reported on page no. |
|------------------------------------|----------|---|---------------------------------------|
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | p. 1 |
| Abstract | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | Summary, p. 2 |
| Introduction | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | Introduction, pp. 2-3 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | Introduction, p. 3 |
| Methods | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | N/A |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | Methods, p. 3 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | Methods, pp. 3-4 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Methods, p. 3, Appendix Table 1, |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | Methods, p. 4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | Methods, pp. 3-4 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | Methods, p. 4 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | N/A |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | N/A |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis. | N/A |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | Methods, p. 4 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A |
| Results | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | Results, p. 5, Figure |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | Results, pp. 5-6, Appendix Table 3 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Results, pp. 5-6 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | N/A |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | N/A |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | Results, pp. 5-6 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |
| Discussion | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | Discussion, pp. 6-10 |

| Article section | Item no. | Checklist item | Reported on page no. |
|-----------------|----------|---|----------------------|
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | Discussion, pp. 9-10 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | Discussion, pp. 7-10 |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | p. 10 |

*Adapted from Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. PLoS Med 6:e1000097 (<https://doi.org/10.1371/journal.pmed.1000097>). Additional information available at <https://www.prisma-statement.org>.

Appendix Table 2. Literature Search Strategy

| Database or entity | Search Strategy* |
|---|--|
| Search request #1: HIV/AIDS outbreaks in Pakistan. Searches for literature on the subject. Limits: English, 2000–2019. Original search run date: 09/20/2019. Updated search run date: 12/11/20. | |
| Medline (Ovid) 1946–present | <pre> ((hiv OR human immunodeficiency virus* OR acquired immune deficiency syndrome* OR acquired immunodeficiency syndrome*) AND (case OR cases)).ti. OR ((hiv OR human immunodeficiency virus* OR acquired immune deficiency syndrome* OR acquired immunodeficiency syndrome*).mp. OR exp HIV/ OR exp Acquired Immunodeficiency Syndrome/ AND (outbreak* OR epidemic* OR pandemic* OR cluster*).mp. OR exp Disease Outbreaks/)) AND (Pakistan* OR azad Kashmir OR baolchistan OR Bahawalpur OR dera ghazi khan OR Faisalabad OR Gilgit OR Gujranwala OR Gujrat OR Islamabad* OR Jhelum OR karachi OR Khyber Pakhtunkhwa OR kot imrana OR Lahore OR Larkana OR mardan OR multan OR Muzaffarabad OR Nowshera OR Peshawar OR Punjab OR quetta OR Rahim yar khan OR Rawalpindi OR Sargodha OR Sheikhupura OR Sialkot OR Sindh OR sukkur).mp. OR exp Pakistan/ </pre> |
| Embase (Ovid) 1947–present | <pre> ((hiv OR human immunodeficiency virus* OR acquired immune deficiency syndrome* OR acquired immunodeficiency syndrome*) AND (case OR cases)).ti. OR ((hiv OR human immunodeficiency virus* OR acquired immune deficiency syndrome* OR acquired immunodeficiency syndrome*).mp. OR exp Human immunodeficiency virus/ OR exp acquired immune deficiency syndrome/ AND (outbreak* OR epidemic* OR pandemic* OR cluster*).mp. OR exp epidemic/)) AND (Pakistan* OR azad Kashmir OR baolchistan OR Bahawalpur OR dera ghazi khan OR Faisalabad OR Gilgit OR Gujranwala OR Gujrat OR Islamabad* OR Jhelum OR karachi OR Khyber Pakhtunkhwa OR kot imrana OR Lahore OR Larkana OR mardan OR multan OR Muzaffarabad OR Nowshera OR Peshawar OR Punjab OR quetta OR Rahim yar khan OR Rawalpindi OR Sargodha OR Sheikhupura OR Sialkot OR Sindh OR sukkur).mp. OR exp Pakistan/ </pre> |
| CAB Abstracts (Ovid) 1910–present | <pre> ((hiv OR human immunodeficiency virus* OR acquired immune deficiency syndrome* OR acquired immunodeficiency syndrome*) AND (case OR cases)).ti. OR ((hiv OR human immunodeficiency virus* OR acquired immune deficiency syndrome* OR acquired immunodeficiency syndrome*).mp. OR exp human immunodeficiency viruses/ OR exp acquired immune deficiency syndrome/ AND (outbreak* OR epidemic* OR pandemic* OR cluster*).mp. OR exp epidemics/ OR exp outbreaks/)) AND (Pakistan* OR azad Kashmir OR baolchistan OR Bahawalpur OR dera ghazi khan OR Faisalabad OR Gilgit OR Gujranwala OR Gujrat OR Islamabad* OR Jhelum OR karachi OR Khyber Pakhtunkhwa OR kot imrana OR Lahore OR Larkana OR mardan OR multan OR Muzaffarabad OR Nowshera OR Peshawar OR Punjab OR quetta OR Rahim yar khan OR Rawalpindi OR Sargodha OR Sheikhupura OR Sialkot OR Sindh OR sukkur).mp. OR exp pakistan/ </pre> |
| Global Health (Ovid) 1910–present | <pre> ((hiv OR human immunodeficiency virus* OR acquired immune deficiency syndrome* OR acquired immunodeficiency syndrome*) AND (case OR cases)).ti. OR </pre> |

| Database or entity | Search Strategy* |
|------------------------------|---|
| PsycInfo (Ovid) 1806–present | <pre> ((hiv OR human immunodeficiency virus* OR acquired immune deficiency syndrome* OR acquired immunodeficiency syndrome*).mp. OR exp human immunodeficiency viruses/ OR exp acquired immune deficiency syndrome/ AND (outbreak* OR epidemic* OR pandemic* OR cluster*).mp. OR exp epidemics/ OR exp outbreaks/)) AND (Pakistan* OR azad Kashmir OR baolchistan OR Bahawalpur OR dera ghazi khan OR Faisalabad OR Gilgit OR Gujranwala OR Gujrat OR Islamabad* OR Jhelum OR karachi OR Khyber Pakhtunkhwa OR kot imrana OR Lahore OR Larkana OR mardan OR multan OR Muzaffarabad OR Nowshera OR Peshawar OR Punjab OR quetta OR Rahim yar khan OR Rawalpindi OR Sargodha OR Sheikhpura OR Sialkot OR Sindh OR sukkur).mp. OR exp pakistan/) ((hiv OR human immunodeficiency virus* OR acquired immune deficiency syndrome* OR acquired immunodeficiency syndrome*) AND (case OR cases)).ti. OR ((hiv OR human immunodeficiency virus* OR acquired immune deficiency syndrome* OR acquired immunodeficiency syndrome*).mp. OR exp HIV/ OR exp AIDS/ AND (outbreak* OR epidemic* OR pandemic* OR cluster*).mp. OR exp Epidemics/)) AND (Pakistan* OR azad Kashmir OR baolchistan OR Bahawalpur OR dera ghazi khan OR Faisalabad OR Gilgit OR Gujranwala OR Gujrat OR Islamabad* OR Jhelum OR karachi OR Khyber Pakhtunkhwa OR kot imrana OR Lahore OR Larkana OR mardan OR multan OR Muzaffarabad OR Nowshera OR Peshawar OR Punjab OR quetta OR Rahim yar khan OR Rawalpindi OR Sargodha OR Sheikhpura OR Sialkot OR Sindh OR sukkur).mp. #1(hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome"):ti AND (case OR cases):ti Limits 110 #2(hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome"):ti,ab,kw Limits 25455 #3MeSH descriptor: [HIV] explode all treesMeSH 2972 #4MeSH descriptor: [Acquired Immunodeficiency Syndrome] explode all trees MeSH 1732 #5#2 OR #3 OR #4Limits 25455 #6(Pakistan* OR "azad Kashmir" OR baolchistan OR Bahawalpur OR "dera ghazi khan" OR Faisalabad OR Gilgit OR Gujranwala OR Gujrat OR Islamabad* OR Jhelum OR karachi OR "Khyber Pakhtunkhwa" OR "kot imrana" OR Lahore OR Larkana OR mardan OR multan OR Muzaffarabad OR Nowshera OR Peshawar OR Punjab OR quetta OR "Rahim yar khan" OR Rawalpindi OR Sargodha OR Sheikhpura OR Sialkot OR Sindh OR sukkur):ti,ab,kwLimits 2578 #7MeSH descriptor: [Pakistan] explode all treesMeSH 413 #8#6 OR #7Limits 2578 #9(outbreak* OR epidemic* OR pandemic* OR cluster*):ti,ab,kwLimits 25990 #10MeSH descriptor: [Disease Outbreaks] explode all treesMeSH 270 #11#9 OR #10Limits 25990 #12#5 AND #11Limits 1560 #13#1 OR #12Limits 1659 #14#13 AND #8Limits 6 </pre> |
| Cochrane Library | <pre> (Pakistan* OR azad Kashmir OR baolchistan OR Bahawalpur OR dera ghazi khan OR Faisalabad OR Gilgit OR Gujranwala OR Gujrat OR Islamabad* OR Jhelum OR karachi OR Khyber Pakhtunkhwa OR kot imrana OR Lahore OR Larkana OR mardan OR multan OR Muzaffarabad OR Nowshera OR Peshawar OR Punjab OR quetta OR Rahim yar khan OR Rawalpindi OR Sargodha OR Sheikhpura OR Sialkot OR Sindh OR sukkur).mp. #1(hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome"):ti AND (case OR cases):ti Limits 110 #2(hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome"):ti,ab,kw Limits 25455 #3MeSH descriptor: [HIV] explode all treesMeSH 2972 #4MeSH descriptor: [Acquired Immunodeficiency Syndrome] explode all trees MeSH 1732 #5#2 OR #3 OR #4Limits 25455 #6(Pakistan* OR "azad Kashmir" OR baolchistan OR Bahawalpur OR "dera ghazi khan" OR Faisalabad OR Gilgit OR Gujranwala OR Gujrat OR Islamabad* OR Jhelum OR karachi OR "Khyber Pakhtunkhwa" OR "kot imrana" OR Lahore OR Larkana OR mardan OR multan OR Muzaffarabad OR Nowshera OR Peshawar OR Punjab OR quetta OR "Rahim yar khan" OR Rawalpindi OR Sargodha OR Sheikhpura OR Sialkot OR Sindh OR sukkur):ti,ab,kwLimits 2578 #7MeSH descriptor: [Pakistan] explode all treesMeSH 413 #8#6 OR #7Limits 2578 #9(outbreak* OR epidemic* OR pandemic* OR cluster*):ti,ab,kwLimits 25990 #10MeSH descriptor: [Disease Outbreaks] explode all treesMeSH 270 #11#9 OR #10Limits 25990 #12#5 AND #11Limits 1560 #13#1 OR #12Limits 1659 #14#13 AND #8Limits 6 </pre> |
| Scopus 1960–present | <pre> ((TITLE (hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome") AND TITLE (case OR cases)) OR ((TITLE-ABS-KEY (hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome")) AND (TITLE-ABS-KEY (outbreak* OR epidemic* OR pandemic* OR cluster*)))) AND (TITLE-ABS-KEY (pakistan* OR "azad Kashmir" OR baolchistan OR bahawalpur OR "dera ghazi khan" OR faisalabad OR gilgit OR gujranwala OR gujrat OR islamabad* OR jhelum OR karachi OR "Khyber Pakhtunkhwa" OR "kot imrana" OR lahore OR larkana OR mardan OR multan OR muzaffarabad OR nowshera OR peshawar OR punjab OR quetta OR "Rahim yar khan" OR rawalpindi OR sargodha OR sheikhpura OR sialkot OR sindh OR sukkur)) AND (LIMIT-TO (PUBYEAR, 2019) OR LIMIT- TO (PUBYEAR, 2018) OR LIMIT-TO (PUBYEAR, 2017) OR LIMIT-TO (PUBYEAR, 2016) OR LIMIT-TO (PUBYEAR, 2015) OR LIMIT-TO (PUBYEAR, </pre> |

| Database or entity | Search Strategy* |
|--|--|
| Academic Search Complete (Ebsco) | <p>2014) OR LIMIT-TO (PUBYEAR, 2013) OR LIMIT-TO (PUBYEAR, 2012) OR LIMIT-TO (PUBYEAR, 2011) OR LIMIT-TO (PUBYEAR, 2010) OR LIMIT-TO (PUBYEAR, 2009) OR LIMIT-TO (PUBYEAR, 2008) OR LIMIT-TO (PUBYEAR, 2007) OR LIMIT-TO (PUBYEAR, 2006) OR LIMIT-TO (PUBYEAR, 2005) OR LIMIT-TO (PUBYEAR, 2004) OR LIMIT-TO (PUBYEAR, 2003) OR LIMIT-TO (PUBYEAR, 2002) OR LIMIT-TO (PUBYEAR, 2001) OR LIMIT-TO (PUBYEAR, 2000)) AND (LIMIT-TO (LANGUAGE, "English"))</p> <p>(</p> <p>TI((hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome") AND (case OR cases))</p> <p>OR</p> <p>(</p> <p>TI,AB,KW,SU (hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome")</p> <p>AND</p> <p>TI,AB,KW,SU (outbreak* OR epidemic* OR pandemic* OR cluster*)</p> <p>))</p> <p>AND</p> <p>TI,AB,KW,SU (pakistan* OR "azad Kashmir" OR baolchistan OR bahawalpur OR "dera ghazi khan" OR faisalabad OR gilgit OR gujranwala OR gujrat OR islamabad* OR jhelum OR karachi OR "Khyber Pakhtunkhwa" OR "kot imrana" OR lahore OR larkana OR mardan OR multan OR muzaffarabad OR nowshera OR peshawar OR punjab OR quetta OR "Rahim yar khan" OR rawalpindi OR sargodha OR sheikhupura OR sialkot OR sindh OR sukkur)</p> <p>Limits: peer-reviewed</p> |
| CINAHL (Ebsco) | <p>(</p> <p>TI((hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome") AND (case OR cases))</p> <p>OR</p> <p>(</p> <p>TI,AB,SU (hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome") OR (MH "Human Immunodeficiency Virus+") OR (MH "Acquired Immunodeficiency Syndrome")</p> <p>AND</p> <p>TI,AB,SU (outbreak* OR epidemic* OR pandemic* OR cluster*) OR (MH "Disease Outbreaks")</p> <p>))</p> <p>AND</p> <p>TI,AB,SU (pakistan* OR "azad Kashmir" OR baolchistan OR bahawalpur OR "dera ghazi khan" OR faisalabad OR gilgit OR gujranwala OR gujrat OR islamabad* OR jhelum OR karachi OR "Khyber Pakhtunkhwa" OR "kot imrana" OR lahore OR larkana OR mardan OR multan OR muzaffarabad OR nowshera OR peshawar OR punjab OR quetta OR "Rahim yar khan" OR rawalpindi OR sargodha OR sheikhupura OR sialkot OR sindh OR sukkur) OR (MH "Pakistan")</p> <p>Limits: peer-reviewed</p> |
| ProQuest Central (Proquest) 1952–present | <p>(</p> <p>TI((hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome") AND (case OR cases))</p> <p>OR</p> <p>(</p> <p>TI,AB,SU (hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome")</p> <p>AND</p> <p>TI,AB,SU (outbreak* OR epidemic* OR pandemic* OR cluster*)</p> <p>))</p> <p>AND</p> <p>TI,AB,SU (pakistan* OR "azad Kashmir" OR baolchistan OR bahawalpur OR "dera ghazi khan" OR faisalabad OR gilgit OR gujranwala OR gujrat OR islamabad* OR jhelum OR karachi OR "Khyber Pakhtunkhwa" OR "kot imrana" OR lahore OR larkana OR mardan OR multan OR muzaffarabad OR nowshera OR peshawar OR punjab OR quetta OR "Rahim yar khan" OR rawalpindi OR sargodha OR sheikhupura OR sialkot OR sindh OR sukkur)</p> <p>Limits: peer-reviewed</p> |

| Database or entity | Search Strategy* |
|--|--|
| PubMed Central (NLM) | <p>(((((((((hiv [Title] OR "human immunodeficiency virus" [Title] OR "acquired immune deficiency syndrome" [Title] OR "acquired immunodeficiency syndrome"[Title])) OR (hiv [Abstract] OR "human immunodeficiency virus" [Abstract] OR "acquired immune deficiency syndrome" [Abstract] OR "acquired immunodeficiency syndrome"[Abstract])) OR "hiv"[MeSH Terms] OR "acquired immunodeficiency syndrome"[MeSH Terms])) AND (((outbreak[Title] OR outbreaks[Title] OR epidemic[Title] OR epidemics[Title] OR pandemic[Title] OR pandemics[Title] OR cluster[Title] OR clusters[Title])) OR (outbreak[Abstract] OR outbreaks[Abstract] OR epidemic[Abstract] OR epidemics[Abstract] OR pandemic[Abstract] OR pandemics[Abstract] OR cluster[Abstract] OR clusters[Abstract])) OR "disease outbreaks"[MeSH Terms])) OR (((hiv [Title] OR "human immunodeficiency virus" [Title] OR "acquired immune deficiency syndrome" [Title] OR "acquired immunodeficiency syndrome"[Title]) OR "acquired immunodeficiency syndrome"[Title]) AND (case[Title] OR cases[Title])) AND (((pakistan* [Title] OR "azad Kashmir" [Title] OR baolchistan [Title] OR bahawalpur [Title] OR "dera ghazi khan" [Title] OR faisalabad [Title] OR gilgit [Title] OR gujranwala [Title] OR gujrat [Title] OR islamabad [Title] OR jhelum [Title] OR karachi [Title] OR "Khyber Pakhtunkhwa" [Title] OR "kot imrana" [Title] OR lahore [Title] OR larkana [Title] OR mardan [Title] OR multan [Title] OR muzaffarabad [Title] OR nowshera [Title] OR peshawar [Title] OR punjab [Title] OR quetta [Title] OR "Rahim yar khan" [Title] OR rawalpindi [Title] OR sargodha [Title] OR sheikhupura [Title] OR sialkot [Title] OR sindh [Title] OR sukkur[Title])) OR (pakistan* [Abstract] OR "azad Kashmir" [Abstract] OR baolchistan [Abstract] OR bahawalpur [Abstract] OR "dera ghazi khan" [Abstract] OR faisalabad [Abstract] OR gilgit [Abstract] OR gujranwala [Abstract] OR gujrat [Abstract] OR islamabad [Abstract] OR jhelum [Abstract] OR karachi [Abstract] OR "Khyber Pakhtunkhwa" [Abstract] OR "kot imrana" [Abstract] OR lahore [Abstract] OR larkana [Abstract] OR mardan [Abstract] OR multan [Abstract] OR muzaffarabad [Abstract] OR nowshera [Abstract] OR peshawar [Abstract] OR punjab [Abstract] OR quetta [Abstract] OR "Rahim yar khan" [Abstract] OR rawalpindi [Abstract] OR sargodha [Abstract] OR sheikhupura [Abstract] OR sialkot [Abstract] OR sindh [Abstract] OR sukkur[Abstract])) OR "pakistan"[MeSH Terms])</p> |
| Virtual Health Library (WHO) | <p>(tw:(hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome")) AND (tw:(pakistan* OR "azad Kashmir" OR baolchistan OR bahawalpur OR "dera ghazi khan" OR faisalabad OR gilgit OR gujranwala OR gujrat OR islamabad* OR jhelum OR karachi OR "Khyber Pakhtunkhwa" OR "kot imrana" OR lahore OR larkana OR mardan OR multan OR muzaffarabad OR nowshera OR peshawar OR punjab OR quetta OR "Rahim yar khan" OR rawalpindi OR sargodha OR sheikhupura OR sialkot OR sindh OR sukkur)) AND (tw:(outbreak* OR epidemic* OR pandemic* OR cluster*))</p> <p>OR</p> <p>(ti:(hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome")) AND (ti:(case OR cases)) AND (tw:(pakistan* OR "azad Kashmir" OR baolchistan OR bahawalpur OR "dera ghazi khan" OR faisalabad OR gilgit OR gujranwala OR gujrat OR islamabad* OR jhelum OR karachi OR "Khyber Pakhtunkhwa" OR "kot imrana" OR lahore OR larkana OR mardan OR multan OR muzaffarabad OR nowshera OR peshawar OR punjab OR quetta OR "Rahim yar khan" OR rawalpindi OR sargodha OR sheikhupura OR sialkot OR sindh OR sukkur))</p> |
| Google Scholar (narrow search using Harzing's Publish or Perish) | <p>(Outbreak OR cluster) AND Allintitle: Pakistan hiv (Outbreak OR cluster) AND Allintitle: Pakistan "human immunodeficiency virus" (Outbreak OR cluster) AND Allintitle: Pakistan AIDS (Outbreak OR cluster) AND Allintitle: Pakistan "acquired immune deficiency syndrome" (Outbreak OR cluster) AND Allintitle: Pakistan "acquired immunodeficiency syndrome" Allintitle: Pakistan hiv epidemic Allintitle: Pakistan hiv cases Allintitle: Pakistan aids cases</p> |
| Search request #2: HIV/AIDS outbreaks in Pakistan. Additional searches for gray literature on the subject. Limits: English, 2000–2019. Search date: 11/25/2020 | |
| UNAIDS | Pakistan AND outbreak |
| WHO | <p>(tw:(Pakistan* OR "azad Kashmir" OR baolchistan OR Bahawalpur OR "dera ghazi khan" OR Faisalabad OR Gilgit OR Gujranwala OR Gujrat OR Islamabad* OR Jhelum OR karachi OR "Khyber Pakhtunkhwa" OR "kot imrana" OR Lahore OR Larkana OR mardan OR multan OR Muzaffarabad OR Nowshera OR Peshawar OR Punjab OR quetta OR "Rahim yar khan" OR Rawalpindi OR Sargodha OR Sheikhupura OR Sialkot OR Sindh OR sukkur)) AND (tw:(hiv OR "human immunodeficiency virus" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome" OR AIDS)) AND (tw:(outbreak* OR epidemic* OR pandemic* OR cluster*))</p> |
| IAS Conference | <p>(Pakistan OR lahore) AND outbreak http://programme.ias2019.org/Search/Search?search=pakistan https://programme.aids2018.org/ https://www.ias2017.org/ https://www.aids2016.org/ http://www.abstract-archive.org/ About 384 abstracts on Pakistan</p> |

| Database or entity | Search Strategy* |
|---|---|
| Search request #3: HIV/AIDS outbreaks in Pakistan. Additional hand searches of government Web sites for reports on the subject. Limits: English, 2000–2019. Search date: 12/11/2020 | |
| Government of Balochistan Province | (HIV OR AIDS) AND (outbreak OR epidemic OR pandemic OR cluster) http://balochistan.gov.pk |
| Health Department, Government of Punjab Province | (HIV OR AIDS) AND (outbreak OR epidemic OR pandemic OR cluster) https://health.punjab.gov.pk/Index.aspx |
| Health Department, Government of Sindh | (HIV OR AIDS) AND (outbreak OR epidemic OR pandemic OR cluster) https://www.sindhhealth.gov.pk/ |
| Government of Northwest Frontier Province | (HIV OR AIDS) AND (outbreak OR epidemic OR pandemic OR cluster) [no website found] |
| National AIDS Control Programme | (HIV OR AIDS) AND (outbreak OR epidemic OR pandemic OR cluster) https://nacp.gov.pk/ |
| National Institute of Health-Islamic Republic of Pakistan | (HIV OR AIDS) AND (outbreak OR epidemic OR pandemic OR cluster) https://www.nih.org.pk/ |

*To identify duplicates, we used the EndNote automated "find duplicates" function with preference set to match title, author, and year.

Appendix Table 3. HIV outbreaks in Pakistan, January 2000– December 2019

| Publication | Initial investigating agency | No. positive of no. tested (case positivity rate) | Primary population | Outbreak identification, transmission routes, and reported risk factors | Notes |
|--|---|---|--|---|--|
| Larkana, Larkana District, Sindh Province, 2003 (1–3) Shah et al, 2004*; Rehman et al, 2007†; Altaf et al, 2016* | SACP | 17 positive among 175–183 tested (9.3%–9.7%) | PWID | Testing was initiated in PWID after identification of an index patient through routine surveillance. Rehman et al: In a case control study (7 cases and 14 controls), injection drug use in groups, syringe reuse, sex with commercial sex workers, >3 casual sexual partners, and early initiation of sex were identified as risk factors. | Shah et al: Authors reported that an epidemiologic study is forthcoming, but no report was identified in this literature review.‡ Rehman et al: It is unclear if the cases in the case control study belong to the original population of the 2003 outbreak, as the timing of the investigation relative to the outbreak was not reported. |
| Sargodha, Sargodha District, Punjab Province, 2007 (4) Emmanuel et al, 2009† | NIH-Pakistan | 205 positive among 400 tested (51.3%) | PWID, all men | Testing was conducted as part of routine surveillance of PWID, with a multi-stage cluster sampling design (205 HIV-positive and 195 HIV-negative). Authors identified injecting in groups, sharing paraphernalia, and living in northern areas of the city as risk factors. | |
| Jalalpur Jattan, Gujrat District, Punjab Province, 2008 (5–7) Ansari et al, 2013†; Qadar et al, 2019*; Davlidova et al, 2019† | FELTP-NIH Pakistan performed the investigation after New Light AIDS Control Society conducted screening camps | 88 positive among 246 tested in 2008 (35.8%) | General population, including women and children | Ansari et al: Community testing was initiated after an increase in diagnoses of HIV. Among 53 cases interviewed during the investigation, authors identified a high prevalence (96%) of therapeutic injections. Ear and nose piercings (women), surgical and dental procedures, and barber shop visits (men) were also common. | Ansari et al: 74 of 88 (84%) found positive on RDT were also positive on ELISA. Phylogenetic analysis indicated that infections were likely acquired over a decade and did not reflect an outbreak. Davlidova et al: Authors noted that an additional 750 people were diagnosed with HIV in 2018, potentially indicative of endemic transmission. |
| Larkana, Larkana District, Sindh Province, 2016 (3) Altaf et al, 2016* | NACP | 56 positive among 205 tested (27.3%) | Patients with end-stage renal disease | Testing initiated at a dialysis center after identification of an index patient. Authors cited poor infection control practices and procedures and use of blood products from unregulated laboratories and blood banks as risk factors. | Positive cases were diagnosed by RDT; of a sample of 20 cases, 19 (95%) were later confirmed positive on laboratory testing. |
| Kot Imrana, Sargodha District, Punjab Province, 2018 (6–12) Zaid et al, 2018*§; Wahid, 2019*; Qadar et al, 2019*; Masood, 2019*; Lancet Infectious Diseases Editorial Team, 2019*; Davlidova et al, 2019†; Zahra et al, 2019* | District health department and PACP in Sargodha | 35–204 positive among 2,717 town residents (1.3%–7.5% town prevalence); unknown number tested | General population, with higher prevalence in women and children | Community testing was initiated after several individuals received an HIV diagnosis in June 2018. Multiple authors reported that infected patients had received unsafe injections from one specific quack.¶ Zaid et al: Authors hypothesized that lack of HIV education, quacks,¶ use of contaminated syringes, re-use of razors at barber shops, unsafe sexual practices, including with sex workers, same-sex relations, and injection drug use were risk factors. | Wahid: Additional testing through 2019 revealed 669 positive among 5,000 tested (13.4%). |
| Ratodero, Larkana District, Sindh Province, 2019 (7,10–24) | | | | | |

| Publication | Initial investigating agency | No. positive of no. tested (case positivity rate) | Primary population | Outbreak identification, transmission routes, and reported risk factors | Notes |
|--|--|--|---|--|---|
| Arif, 2019*; Ahmed et al, 2019*§; Green, 2019*; Lancet Infectious Diseases Editorial Team, 2019*; Masood, 2019* Davlidova et al, 2019†; Zaid et al, 2019*§; Zahra et al, 2019*§; Dyer, 2019* Shaikh et al, 2019#; Mir, 2019#; WHO, 2019#; NIH Islamabad, 2019#; WHO, 2019#; UNAIDS, 2019#; UNAIDS, 2019#; NIH Islamabad, 2019# | SACP, with support from a WHO-led investigation, in partnership with SACP, Aga Khan University, Dow University, FELTP, UN agencies, and local partners | 157–1,112 positive among 4,100–36,000 tested (3.1%–3.8%) | Approximately 80% of cases were children | Shaikh et al: 12 children with persistent fever received an HIV diagnosis in April 2019. Among 5 children with confirmatory testing at SACP Referral Lab, none had parents with HIV, prompting initiation of community testing. UNAIDS: Preliminary findings from the joint investigation concluded that poor infection control practices, including a lack of sterilization and the reuse of syringes and intravenous drips, were the most notable risk factors. Other reports also included unsafe practices at blood banks, improper hospital waste management, association with a specific physician, male circumcision with unhygienic blades, and ear and nose piercing with unsafe needles as potential risk factors. | Mir: Case control study of 406 pediatric cases and 406 controls is forthcoming. |
| Faisalabad, Faisalabad District, Punjab Province, 2019 (12) Zahra et al, 2019*§ | PACP | 2,863 positive among unknown number tested | PWID, located in the cities of Chiniot, Sahiwal, Jhang, and Nankana Sahib | First identification of positive patients was not reported. Authors reported that most individuals acquired HIV through reused syringes and needles, medical services from quacks,¶ and dental surgeries. | |

PLHIV, People Living With HIV; SACP, Sindh AIDS Control Program; PWID, People Who Inject Drugs; NIH, National Institute of Health; FELTP, Field Epidemiology Laboratory Training Program; NACP, National AIDS Control Programme; WHO, World Health Organization; RDT, Rapid Diagnostic Test; PACP, Punjab AIDS Control Programme

*Letter to the editor, correspondence, editorial, or other non-peer-reviewed publication.

†Peer-reviewed publication.

‡Per correspondence with Rehman et al, the data from their 2007 report does not represent the forthcoming epidemiologic investigation of the Larkana, Larkana District, 2003 outbreak described by the Shah, 2004 report.

§Media report cited as primary reference.

¶A quack is an unqualified healthcare provider.

#Grey literature or government report.

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