A pediatric HIV outbreak in Pakistan

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Abstract

Background: Following reports of an outbreak of HIV infection among children in Larkana District, Pakistan, an international team investigated the extent and cause of the outbreak between April and June 2019.

Aims: To investigate the incidence of HIV among children in Larkana District, Pakistan and describe the distribution of cases by time, place and person.

Methods: Self-referred persons were tested for HIV using the national testing protocol. Local epidemiology of HIV was reviewed to generate hypotheses. An infection prevention and control (IPC) team conducted site visits and reviewed IPC practices.

Results: Between 25 April and 27 June 2019, a total of 30 191 persons were tested for HIV in Larkana District, and 876 of them tested positive. Of those who tested positive, 719 (82%) were children aged <15 years. Traditional skin piercing procedures and transmission from high-risk populations to children were ruled out during the investigation. Informative interviews with parents or guardians of a convenience sample of 211 children aged <15 years showed that 99% of children had an injection or infusion for medical treatment within the past 12 months. Our investigation identified lack of HIV prevalence data for the general population including tuberculosis patients and those who attended antenatal care services.

Conclusions: Investigations indicate that unsafe healthcare practices in formal and informal healthcare settings as the most likely cause of the 2019 outbreak of HIV infection in Larkana, Pakistan. Measures should be taken to improve IPC practices at the facility level, especially in pediatric and antenatal care clinics.

Keywords: HIV, pediatric, outbreak, Pakistan, unsafe practices, iatrogenic, exposure, IPC

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Introduction

In 2020, the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated that there were 200 000 persons living with HIV in Pakistan (1), a country with a population of 207 million (2). The epidemic is concentrated among key populations, i.e. injecting drug users, men who have sex with men, and transgender people. At the end of 2018, the number of children aged <15 years registered in HIV treatment centres in Pakistan was 614 (3).

Pakistan has faced challenges in infection prevention and control (IPC), particularly with unsafe injections. Since the late 1990s, several studies reported that overuse (4) and unsafe use (5–8) of injections were a major drivers of a large epidemic of hepatitis C and hepatitis B infections. Unlike in most other countries, injection use indicators have not improved in recent years in Pakistan (9).

Several outbreaks of HIV infection have previously been reported in Pakistan (10). A recent systematic review by Rabold et al. identified 7 outbreaks between 2002–2019 (11) among injecting drug users, the general population due to unsafe injections administered in healthcare settings and in the community, and hemodialysis patients. These outbreaks reflected major challenges in basic infection control practices. While these outbreaks caused substantial concern at the time, they were not followed by systematic IPC interventions that could have led to improved national IPC practices in Pakistan.

In April 2019, the media reported that several children without known risk factors were diagnosed with HIV in the Ratodero Taluka Subdistrict in Larkana District (12). The Sindh Provincial Department of Health, in coordination with the District Commissioner in Larkana and the Sindh AIDS Control Programme (SACP), began a major campaign to test people for HIV at the Taluka Headquarters Hospital in Ratodero, including the testing of hundreds of children (13). After identifying more pediatric HIV infections, SACP established 5 additional provisional testing facilities at various primary healthcare sites in the district. Initial data collected by SACP from HIV treatment centres showed that 94% of mothers of HIV-positive children were HIV negative, suggesting that the primary mode of transmission was not perinatal. On 23 May 2020, the Pakistan Federal Minister of
Health requested support from WHO to conduct an outbreak investigation to identify the source of infection and propose interventions for control. This paper summarizes the findings of the investigation as well as recommendations to the Ministry of National Health Services Regulations and Coordination, government officials, and other key stakeholders.

Methods
WHO sent a multi-disciplinary rapid response team (RRT) to Larkana that included epidemiologists; clinicians specialized in pediatric HIV and IPC; laboratory scientists; and blood safety specialists from SACP, the Field Epidemiology and Laboratory Training Programme (FELTP) Pakistan, Aga Khan University (AKU), UNAIDS, UNICEF, United States Centers for Diseases Control and Prevention (US CDC), and WHO. The RRT’s first aim was to identify potential causes of the outbreak, including mother-to-child transmission, transmission from cultural practices, transmission from key populations through sexual or intravenous drug use practices, or iatrogenic exposure through healthcare exposures.

HIV testing procedures
In the SACP-led testing facilities established because of the rise in HIV cases in Larkana District, all persons who presented were eligible for testing. Testing was conducted using a 3-serial-testing strategy which followed the national HIV testing algorithm, consisting of 3 serial tests. The first test (A1) was conducted using Alere Combo®, the second (A2) using Unigold®, and the third (A3) using SD Bioline® (14). A1 and A2 were conducted at the testing facility and A3 was conducted at the treatment centre. To follow this testing algorithm, SACP staff physically relocated to Larkana District to train healthcare workers on implementation; provided the test kits; monitored stocks; and supervised storage, handling, and testing procedures. A3 was reserved for treatment centres so that it could be conducted by experienced laboratory personnel as part of quality assurance. The RRT observed the testing procedures and the quality of the test kits at all the testing sites.

A case was defined as any child aged 18 months or older or any adult with 3 positive serial tests (A1+A2+A3). For children < 18 months of age with 3 serial positive antibody tests, specimens were collected for nucleic acid testing (NAT) to confirm the HIV status, although molecular testing was not immediately available. Children < 18 months of age with a positive antibody born to women with a negative HIV status were considered as cases for analysis. Children < 18 months of age with a positive antibody test and whose mothers were HIV-positive were considered to have maternal exposure, given prophylactic treatment, followed up until confirmation, and not included in this analysis.

Descriptive epidemiology
We used Microsoft Excel for compiling and analyzing all collected data. Using daily totals from testing facilities as compiled by the Ministry of National Health Services, we generated epidemic curves showing the number of persons tested, the number who tested positive, and a 7-day simple moving average of test positivity. We reviewed patient registers at the treatment centres and extracted information regarding age, sex, residence [district and subdistrict (Taluka)], final HIV status, and CD4 count. Using 2017 census data (15), we calculated age- and sex-specific attack rates for confirmed cases registered at the treatment centre who resided in Larkana District. We mapped the distribution of pediatric (aged < 15 years) cases by geographic area, and determined the clinical stage of confirmed cases using the CD4 count (when available) according to WHO guidelines (16). The FELTP team approached parents and guardians of child-HIV cases registered at treatment centres in Taluka Hospital Ratodero to obtain their consent to participate in informative interviews using a structured close-ended questionnaire. Demographic information, household-level information, clinical histories, presenting symptoms, and exposure histories (including vertical, cultural, and medical) were obtained from participants.

IPC investigations
Experts in IPC visited 5 public and private acute care hospitals, 10 private clinics, 1 dispensary, 1 pharmacy, and 1 barber shop in Ratodero and Larkana City, and the local office of the Expanded Programme of Immunization (EPI) to observe basic IPC measures to identify gaps and breaches. Cleanliness, disinfection and injection practices, handling of sharp and used injection material, and medical waste disposal were assessed through observations and interviews using checklists for IPC and waste management, and photos taken without identifiable staff or patients.

The IPC group also conducted site visits at 10 blood banks (public and private), the thalassemia care centre, the regional blood centre with its satellite hospital blood bank, private clinics, and hospitals. Checklists for blood transfusions, IPC, and waste management were used during observations and interviews. Data on blood collection, testing, processing, and utilisation at the bedside were collected from the Sindh Blood Transfusion Authority, Larkana District Blood Transfusion Authority, and individual blood banks.

To understand the background of HIV epidemiology in the region and investigate potential horizontal and vertical modes of transmission of HIV infection, we reviewed available surveillance data from tuberculosis clinics and antenatal clinics. We also reviewed national and Larkana-specific surveillance data on key populations (17) (e.g. men who have sex with men, female sex workers, transgender people, and injecting drug users) and met with service providers to identify possible interactions between key populations and the general population, including children.
Protection of human subjects

Protection of human subjects was observed in alignment with WHO guidelines on ethical issues in public health surveillance (2017). It was also reviewed by the US CDC and was conducted in compliance with applicable federal laws and US CDC policies (see e.g. 45 C.F.R. part 46; 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.). Adult guardians (parents, grandparents, or uncles/aunts) of children diagnosed with HIV provided verbal consent to testing and participation in an interview.

Results

Descriptive epidemiology

Between 25 April and 27 June 2019, a total of 30191 persons were tested for HIV in Larkana District (Figure 1A), and 876 persons tested positive (Figure 1B). The 7-day test percentage positivity ranged between 1.5% and 5.5%. Of those who tested positive, 719 (82%) were children aged < 15 years and 157 (18%) were adults aged ≥ 15 years. Among the 300 pregnant women tested, 19 (6.3%) tested positive.

Final HIV case status could not be determined for the 54 (12%) children aged < 18 months because NAT was not immediately available. Of the 719 children who tested positive at the testing facilities, 580 (81%) were registered at the treatment centre and were confirmed as cases, with 345 (60%) initiating antiretroviral treatment (ART) for HIV. Of the 157 adults who tested positive for HIV at the testing facilities, 118 (75%) were registered at the treatment centre and were confirmed as cases, with 111 (94%) initiating ART.

Additional demographic and clinical information were available for 494 (71%) of the 698 confirmed cases. Among these cases, with an age range of 1 month to 65 years, 444 (92%) were children and 63% were male. Of these, 216 (43%) cases were aged between 3 and 6 years. The overall age-specific attack rate for children was 4.9 per 10 000 (Figure 2). The attack rate was higher among males than females for all ages < 10 years. Males aged 3 years had the highest attack rate at 18.0 per 10 000; the highest attack rate for females was 8.7 per 10 000 (aged 2 years). Among the 50 adult cases, 21 (57%) were females. Adults aged 30 to 34 years had the highest

Figure 1 Trends at testing sites for the number of persons tested (A), the number of persons testing positive (B), and test positivity—Sindh Province, 25 April–27 June 2019

![Figure 1](image-url)
HIV-positive children were identified across 7 districts, but 71% (n=325) were from Taluka Ratodero. The baseline CD4 count was available for 68 (15%) children aged < 15 years. Of these children, 60% (n=41) were at clinical stage 2 or 3 (16) upon presentation to the treatment centre. For the 28 (76%) adults with baseline CD4 counts; 13 (46%) had > 500 cells/µl, 11 had 200-49 cells/µl, and 4 (14%) had < 200 cells/µl.

**Informative interviews at the treatment centre**

The informative interviews with parents or guardians conducted by FELTP resulted in data on 211 children aged < 15 years with a confirmed HIV diagnosis residing in Larkana District. Parents of 99% of these children reported that their children had received an injection or infusion for medical treatment within the past 12 months. Other medical percutaneous exposures included a blood transfusion (17%), a cut with a sharp instrument by a doctor (8%), surgery (1%), or stitches (1%). Non-medical percutaneous exposures included ear piercing (23%), predominantly for females, and male circumcision (20%). A few children (≤ 2%) had their hair cut with a razor or had cuts associated with a religious practice, *Zanjeer Zani* (≤ 2%).

**Infection prevention and control**

Observations of IPC practices during the site visits identified gaps in the basic implementation of IPC measures, including a high risk of exposure to sharp equipment (direct and indirect reuse of syringes and drip sets) and the unsafe disposal of healthcare waste, such as used syringes and needles. These gaps were observed in facilities in close proximity to where children played in the street. At the barber shop, the IPC experts noted that razor blades were reused for several clients and there was an overall lack of hygiene protocol. At EPI sites, all the vaccinations observed by the IPC experts were administered with single-use syringes (1 ml auto-disable syringe with integrated needles) and with appropriate sharp disposal and waste management.

**Background HIV data**

Quality assurance procedures and HIV positivity of screened blood products varied across the reviewed blood banks, blood centres, and health facilities. Two blood centres used WHO pre-qualified test kits with daily quality control; they reported between 0.24% and 0.3% HIV positivity among screened donor blood. In contrast, at both public and private blood banks, donor blood was screened with test kits that were not on the WHO list of prequalified in vitro diagnostic products and were used without quality control. The reported HIV positivity of screened blood from blood banks was 0.04%. Unauthorised blood banks operating in the community were also identified.

Systematic testing for co-infection with HIV was not conducted at all the sites providing care for tuberculosis. No routine data was available for HIV prevalence in ANC or other services. In the few centres where routine HIV testing was offered to pregnant women, positive results were very rare. However, the rapid HIV test kits used in these sites were not prequalified by WHO. Epidemiological data from key populations in Larkana District revealed an HIV prevalence of 18% among transgender people, 16% among injecting drug users, 5% among male sex workers, 4% among female sex workers, and 4% among men who have sex with men (17). Key informants from non-governmental organizations (NGOs) working with these populations could not identify any links between them and the Ratodero children affected by the outbreak.

**Discussion**

We report an unprecedented HIV outbreak in Larkana District involving a large number of children. From April to June 2019, 876 persons were reported as HIV infected; 82% of which were children aged < 15 years. Our investigations indicated unsafe health care services at health facilities as the most likely cause of the outbreak.
This conclusion is supported by findings from the interviews with the parents or guardians of children diagnosed with HIV, of whom 99% had received a therapeutic injection within the past 12 months. Findings from site visits to health centres and private clinics illustrate breaches in IPC measures. Practices at some blood banks raised concerns of unsafe blood transfusions. Other hypotheses regarding possible causes were not consistent with the epidemiological findings.

First, only 10% of patients’ mothers were infected with HIV (13), which is not consistent with vertical transmission as the primary cause of the outbreak. Infants would also be expected to have a higher prevalence of HIV than older age bands due to HIV-associated mortality, which was not observed among the children, with highest age-adjusted attack rates being in the 2 to 4-year age band.

Second, the frequency of traditional skin piercing and circumcision procedures was low for the children evaluated in the informative interviews, with far more children reporting therapeutic medical interventions.

Third, there were no identified interactions (e.g. sexual abuse, drug use) between the infected children and the high-risk key population. The young age of most of the children also points away from the initiation of high-risk behaviours; data from integrated HIV biobehavioural surveillance (IBBS) in Larkana District suggest that the average age for initiating injecting drugs and selling sex by transgender, female, or male sex workers was 23, 15, 17, and 16 years, respectively (17). The collective findings pointed to unsafe medical practices and exposures as the primary cause of the outbreak.

Our findings regarding unsafe healthcare practices are supported by the results of a subsequent case-control investigation conducted by FELTP, which included 100 children newly identified as HIV-positive living in Ratodero and matched to 200 control children (18). This investigation revealed a strong association with intravenous infusions, often given through reused drip sets in the clinics of private practitioners. Intramuscular injections were not associated with being a case. Though still associated with infection, reused syringes were far less common than reused intravenous infusions and had a weaker association. Another case-control investigation conducted by Aga Khan University identified parenteral routes due to unsafe injection and blood safety practices as the predominant mode of HIV transmission, while also noting a high prevalence of hepatitis B (18%) and C (6%) among cases (13).

Unsafe injection practices have been reported as leading causes of hepatitis B, hepatitis C, and HIV outbreaks in Pakistan (11). The use of shared glass or disposable syringes in medical practice, when not properly disinfected, contributes to the global burden of blood-borne infections (19) and was cited as the leading cause of several HIV, hepatitis B, and hepatitis C outbreaks in Cambodia (20), India (21), China (22), and Pakistan (23).

In 2009, up to 38% of physicians and unqualified healthcare providers in Pakistan reused their injection equipment, while overprescribing injections for their clients (23). The general population in Pakistan believes that injections are more effective than oral medications (24). The financial incentives for healthcare workers also perpetuate excessive injection practices; patients in rural communities presenting to general practitioners and unqualified providers usually expect treatment that includes injected medicines. Determinants of unsafe injection practices include a lack of awareness regarding the risks (25) and the limited availability of safe injection devices.

The repeated outbreaks of HIV infection in Pakistan also have several social determinants, including widespread poverty, power imbalances between men and women, labour migration, and a lack of awareness about HIV transmission modes among the general population (26). Concurrently, malpractice by health practitioners and widespread quackery have often been cited as the direct cause of blood-borne virus outbreaks (27, 28). Unnecessary and unsafe use of injections, unsafe healthcare, and the resulting repeated HIV outbreaks reflect the structural weaknesses of the health system.

The HIV outbreak in Larkana District has proved to be a catalyst for change. In response to the outbreak, the Health Department of Sindh established a family-centred HIV testing and ART clinic at Taluka Hospital Ratodero for children, their parents, guardians, and other adults. Based on the results of the investigation, the Health Department started a province-wide IPC programme. An immediate policy for safe injection procedures at hospital level was developed and implemented, and a supply chain of adequate infection control and safe injection material in government hospitals was initiated. The Sindh Health Department then released an IPC policy assigning a provincial IPC group to manage and coordinate IPC activities, and assigned fulltime IPC teams at hospitals. WHO also developed an IPC training package that was endorsed by the provincial team. A cadre of provincial IPC master trainers were trained to provide further IPC step-down trainings to hospital teams.

Immediate expansion of the work is now required to reach private practitioners and NGOs providing healthcare at the community level. A public-private collaboration with the Sindh Health Care Commission (SHCC) is needed to strengthen the auditing of IPC practices within private clinics and facilities and unlicensed healthcare providers. This health system strengthening approach to reinforcing IPC in Sindh Province is imperative to ending this HIV outbreak among children in Larkana District and should establish a strong foundation for the prevention of other outbreaks in the future.

**Limitations**

Our investigation had 2 limitations. First, testing was limited to self-referrals. Some infected individuals may still not have been tested and diagnosed. Because of this limitation, the spatial distribution should be interpreted...
with care as it probably reflects HIV-testing-seeking behaviour more than the actual distribution of cases. Second, we were not able to determine the timing of acquisition of infection, so the diagnoses probably represented prevalent cases. The epidemic curve likely reflects the timing of the testing efforts rather than incidence. To compensate for this limitation, we assessed other clinical syndromic criteria to determine the clinical stage for affected children and estimate the duration of the infection.

**Conclusion and recommendations**

Data from 2021 indicate that the outbreak in Larkana District is still ongoing, with 1492 cases diagnosed as of February 2021. Sustained actions are needed to prevent future outbreaks. First, it is important to strengthen HIV case-based surveillance to enable the detection of changes in the epidemic among low-risk groups in Pakistan. This could be done through improved case notification and sentinel surveillance among pregnant women and implementation of mechanisms to respond rapidly to unusual signals, such as the detection of cases of HIV infection among children. The Ministry of National Health Services Regulations and Coordination in Pakistan announced on World Hepatitis Day 2019 that it has started a country-wide policy to improve IPC and blood and injection safety (28). This new initiative addresses IPC, injection safety, testing and treatment for blood-borne pathogens, and strengthened surveillance (29). Improving community awareness and engagement is also necessary to reduce the demand for and administration of unnecessary and unsafe injections. Implementing these activities will hopefully ensure that the Larkana District outbreak is the last occurrence of this series of healthcare-associated HIV outbreaks in Pakistan. As Pakistan currently develops its investment case for Universal Health Coverage, strengthening health systems based on a primary healthcare approach is the way forward (30). The COVID-19 pandemic—in addition to highlighting the importance of advancing IPC measures in Pakistan—has provided many lessons on essential public health functions (31). The outbreak in Larkana District shows that safety in healthcare and equity in delivering essential health services are the only paths towards achieving the health-related Sustainable Development Goal (SDG-3).

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**Flambée épidémique de VIH chez les enfants au Pakistan**

**Résumé**

**Contexte :** Suite à des rapports signalant une flambée épidémique d’infection à VIH chez des enfants dans le district de Larkana (Pakistan), une équipe internationale a enquêté sur l’ampleur et la cause de la flambée entre avril et juin 2019.

**Objectif :** Étudier l’incidence du VIH chez les enfants dans le district de Larkana et décrire la répartition des cas en fonction du temps, du lieu et des individus.

**Méthodes :** Les patients se présentant volontairement ont été soumis à un test de dépistage du VIH selon le protocole national de dépistage. L’épidémiologie locale du VIH a été examinée afin de formuler des hypothèses. Une équipe pour la prévention et le contrôle des infections a réalisé des visites sur sites et a examiné les pratiques en la matière.

**Résultats :** Entre le 25 avril et le 27 juin 2019, un total de 30 191 personnes ont fait l’objet d’un test de dépistage du VIH dans le district de Larkana, et 876 d’entre elles ont reçu un résultat positif. Parmi les personnes testées positives, 719 (82 %) étaient des enfants de moins de 15 ans. Les techniques traditionnelles de perçage de la peau et la transmission du virus aux enfants par des populations à haut risque ont été exclues au cours de l’enquête. Des entretiens informatifs réalisés auprès des parents ou tuteurs de 211 enfants âgés de moins de 15 ans issus d’un échantillon de commodité ont révélé que 99 % d’entre eux avaient subi une injection ou une perfusion dans le cadre d’un traitement médical au cours des 12 derniers mois. Notre enquête a mis en évidence un manque de données concernant la prévalence du VIH dans la population générale, y compris chez les patients atteints de tuberculose et chez ceux ayant consulté des services de soins prénatals.

**Conclusion :** L’enquête a démontré que des pratiques de soins de santé non sécurisées dans les établissements de santé formels et informels sont les causes les plus probables de la flambée épidémique de VIH survenue en 2019 dans le district de Larkana (Pakistan). Il est nécessaire de prendre des mesures dans le but d’améliorer les pratiques de prévention et de contrôle des infections au niveau des établissements de santé, en particulier dans les cliniques de soins pédiatriques et prénatals.
References


