Review Article

Novel and Rare Diseases in Sindh, Pakistan: A Narrative Review of Inherited Disorders, Emerging Infections, Diagnostic Gaps and a Framework for Action

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Abstract

Rare diseases affect an estimated 3.5–5.9% of people worldwide, and Pakistan combines the main drivers of inherited disease with a fast-changing infectious disease landscape. Sindh, its second most populous province, carries both burdens, yet evidence is scattered across single-centre reports.

Aim of this review is to synthesise recent evidence on inherited rare disorders and novel or emerging diseases in Sindh, identify system gaps, and propose a framework for action. Narrative review of literature retrieved through SciSpace, Consensus and web searches, covering 1998 to November 2026. Sindh-specific studies were prioritised; Pakistan-wide and other-province studies served as labelled comparators. Consanguineous marriage, reported in about 60% of Pakistani unions, drives autozygosity and recessive disease. Cohorts report parental consanguinity in 66.5% of inherited metabolic disorder cases nationally and 86.8% of thalassaemia families in Hyderabad. In upper Sindh, 86% of thalassaemia patients had iron overload while 4% received chelation. Novel threats include extensively drug-resistant typhoid emerging in Hyderabad in 2016, a paediatric HIV outbreak in Larkana in 2019, primary amoebic meningoencephalitis in Karachi, Crimean-Congo haemorrhagic fever, cutaneous leishmaniasis and chikungunya. Common gaps are the lack of a rare-disease registry for Sindh, limited confirmatory and genomic diagnostics, absent universal newborn screening, weakly enforced premarital screening, and fragmented surveillance. Sindh needs a linked registry and surveillance platform, early-detection programmes, regional genomic and microbiological laboratories, defined care pathways, and population-based research. We propose a five-step framework to sequence these investments.

Keywords: Rare diseases; Sindh; Pakistan; consanguinity; inborn errors of metabolism; thalassaemia; emerging infections; newborn screening; genomic medicine

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Introduction

Rare diseases are individually uncommon but collectively common. An analysis of the Orphanet database estimated that 3.5–5.9% of the global population, or 263–446 million people, live with a rare disease; about 72% of the 6,172 catalogued disorders are genetic and about 70% have exclusively paediatric onset.[1] The burden is greatest where genetic risk is concentrated and diagnostic services are thin. Pakistan fits that description. Consanguineous marriage has been strongly preferred for generations: national and Karachi data from the early 1990s showed that about 60% of marriages were consanguineous, over 80% of these between first cousins, with no decline across three to four decades.[2] Recessive alleles that stay hidden in outbred populations are therefore expressed in the homozygous state, producing a heavy load of inherited metabolic, haematological, neurological, ocular and skeletal disorders.

Sindh, Pakistan's southern province, adds a second layer. Over the past decade it has been the site of several "firsts": the first known large outbreak of extensively drug-resistant (XDR) typhoid,[3] a large paediatric HIV outbreak in Larkana,[4] repeated cases of primary amoebic meningoencephalitis (PAM) in Karachi,[5] a rise in Crimean-Congo haemorrhagic fever (CCHF),[6] and epidemics of cutaneous leishmaniasis[7] and chikungunya.[8] These diseases are "novel" not because they are unknown to medicine but because they are new, newly resistant or newly intense in this setting.

The evidence on both groups is fragmented. It is spread over single-centre series from Karachi, Hyderabad and Jamshoro, and over national registries that include Sindh only in part. Institutional momentum is growing: the Society for Novel and Rare Diseases (SNARE) and allied bodies now advocate for diagnosis, research and policy,[9] and clinicians have called for stronger genetics services.[10] A single synthesis that places inherited and emerging diseases side by side, and asks what health-system capacity they share, has not been available. This review therefore has three aims: (i) to summarise what is known about inherited rare disorders and novel or emerging diseases in Sindh; (ii) to identify the diagnostic, surveillance and care gaps common to both; and (iii) to propose a framework and research agenda for the province.

Methodology

We conducted a narrative review with a structured, documented search. Because Sindh-specific evidence is sparse and heterogeneous, a formal systematic review with meta-analysis was neither feasible nor appropriate; the review follows the reporting principles of the SANRA scale for narrative reviews, and Table 1 sets out the search design.

Literature was retrieved through the SciSpace and Consensus scholarly search connectors and supplemented by targeted web searches for official reports and recent outbreak news, with the final search on 8 November 2026. Sindh-specific studies were prioritised. Pakistan-wide studies, or studies from other provinces such as Punjab, were used only as comparators and are labelled as such in the text and tables. One reviewer screened titles and abstracts, extracted key findings (design, setting, sample size, main results), and checked each reference against its DOI record. No formal risk-of-bias scoring was applied; study design and setting are reported so readers can judge weight.

Consanguinity and the inherited disease burden

A population-level driver

Marriage within the extended family continues to be reported at high rates in recent clinical cohorts (Figure 1, Figure 2A). In a Hyderabad survey of 311 families with thalassaemic children, 86.8% of marriages were consanguineous, and in 31.5% the mother was the daughter of the father's sister.[11] In the national registry of inherited metabolic disorders (IMDs) built at the Aga Khan University Hospital, 66.5% of 3,880 cases had consanguineous parents.[12] A systematic review of inherited retinal dystrophies in Pakistan found parental consanguinity in about 70% of cases, homozygous variants in about 89% of variants, and recessive inheritance in over 95% of cases.[13] A registry from Punjab, a comparator province, reported consanguinity in 89% of 167 families with 72 distinct rare genetic diseases.[14]

Table 1: *Search design and selection criteria.*

Item	Detail
Review type	Narrative review with structured search
Sources	SciSpace, Consensus, targeted web search (for official reports and recent news)
Period covered	1998 to 8 November 2026
Language	English
Search concepts	Sindh; Karachi; Hyderabad; Pakistan; rare disease; consanguinity; inborn errors of metabolism; thalassaemia; lysosomal storage; newborn screening; genetic services; XDR typhoid; HIV outbreak; Larkana; *Naegleria fowleri* ; Crimean-Congo haemorrhagic fever; leishmaniasis; chikungunya; floods
Inclusion	Original studies, outbreak investigations, registries and reviews reporting data from Sindh, or from Pakistan with direct relevance to Sindh; peer-reviewed with verifiable DOI
Exclusion	Records without DOI or complete metadata; duplicate repository records; non-human or purely laboratory studies without clinical relevance
Synthesis	Narrative; Sindh data presented first, comparators labelled

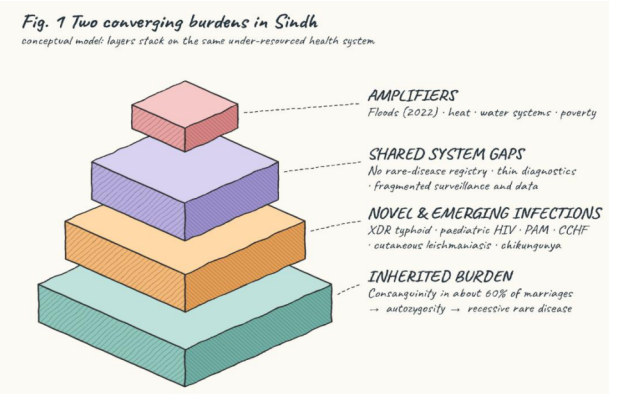


Figure 1: *Conceptual model of two converging burdens in Sindh. Inherited disease driven by*

consanguinity and emerging infections stack on the same under-resourced health system, with shared gaps in registries, diagnostics and surveillance, and amplifiers such as the 2022 floods, heat, water systems and poverty. Hand-sketched schematic prepared for this review.

Why consanguinity matters for diagnosis

Consanguinity also shapes how rare diseases should be investigated. In Pakistani families, genome-wide mapping combined with exome sequencing found homozygous variants explaining Sandhoff disease and MBOAT7-related neurodevelopmental disease.[15] A collaborative genomic programme in Lahore tested 1,019 individuals from 349 families, reached a genetic diagnosis in 61.3% of index patients, and changed management in about half of those diagnosed, mostly by starting the appropriate treatment.[16] These data come from Punjab, but they show what a regional diagnostic service could achieve for Sindhi families who currently lack access.

Spectrum of rare genetic disorders in Sindh

Table 2 lists the main Sindh-linked studies. They fall into five clusters, described below.

Haemoglobinopathies

Beta-thalassaemia is the most visible rare genetic disease. Nationally, the carrier frequency is 5–7%, there are over 10 million carriers, and about 5,000 children are born with thalassaemia major each year.[18] Premarital screening has been legislated in Sindh, Khyber Pakhtunkhwa and Balochistan, but implementation remains the problem.[18] In upper Sindh, a study of 360 patients found iron overload in 86% but chelation in only 4%, with 152 thalassaemia-related deaths reported across 94 families.[17] In Hyderabad, 98.7% of 311 parents had not consulted a doctor before marriage and 72.3% had never been tested.[11] These data show that the gap lies in programme delivery rather than knowledge of the disease.

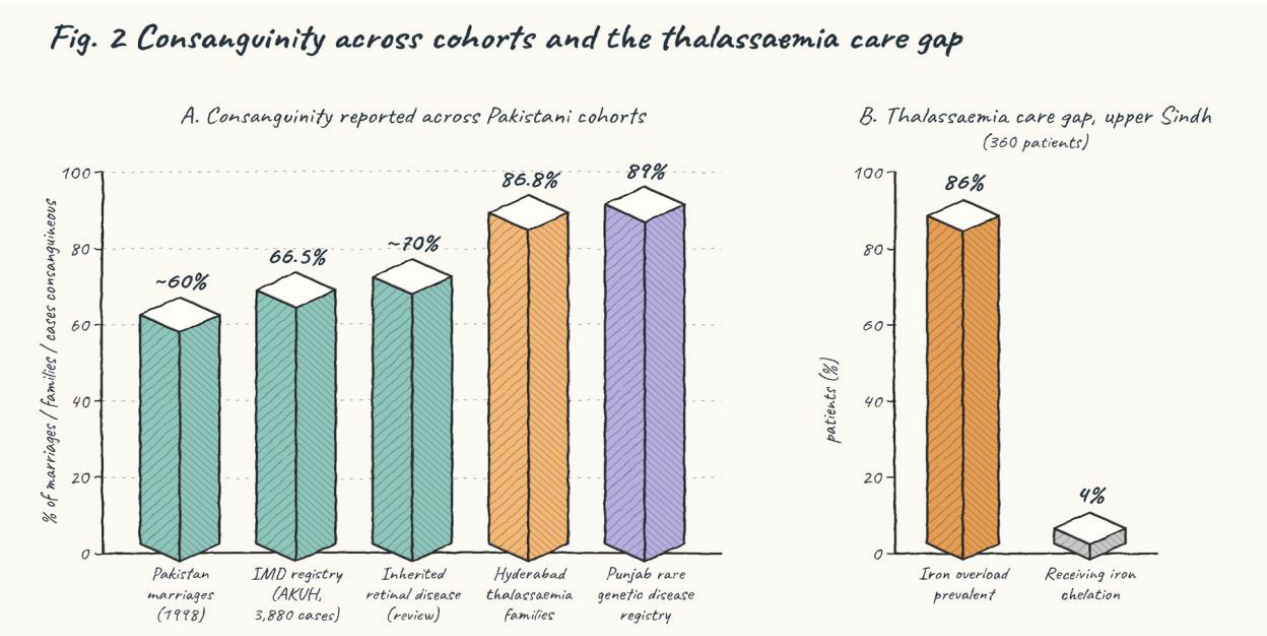


Figure 2: *Panel A: reported prevalence of parental consanguinity across Pakistani cohorts (Pakistan 1990/91 national and Karachi data;[2] IMD registry;[12] inherited retinal disease review;[13] Hyderabad thalassaemia families;[11] Punjab registry, comparator[14]. Panel B: care gap among 360 thalassaemia patients in upper Sindh[17]. Values of about 60% and about 70% are approximate figures as reported by the sources. Hand-sketched chart.*

Novel and emerging diseases in Sindh

Table 3 summarises the main emerging threats. Most were first recognised in Sindh or reached unusual intensity there.

Extensively drug-resistant typhoid

In November 2016 an outbreak of ceftriaxone-resistant *Salmonella* Typhi began in Hyderabad. By

Table 2: *Selected studies of rare genetic disorders from Sindh and relevant comparators..*

Condition / theme	Setting	Key findings	Ref.
Beta-thalassaemia	Upper Sindh (n=360)	Iron overload 86%; chelation 4%; 152 related deaths in 94 families	17
Thalassaemia and consanguinity	Hyderabad (311 families)	86.8% consanguineous; 98.7% no premarital medical consultation; 72.3% never tested	11
Thalassaemia, national picture	Pakistan	Carrier frequency 5–7%; about 5,000 major births a year; premarital screening legislated in Sindh	18
Metabolic storage disorders	Karachi (public hospital)	40/140 suspected children confirmed; 65% lysosomal, 35% glycogen storage	19
Selective IMD screening	Karachi (tertiary hospital)	178 children screened; many disorders unconfirmable for lack of local tests	20
IMD registry	Karachi laboratory; all provinces	3,880 cases, 59 distinct IMDs; consanguinity 66.5%	12
Oculocutaneous albinism	Sindhi inbred families	44 patients, 8 families; homozygous OCA1 p.Gly419Arg; OCA2 splice variant	22
MPS III and IV	Pakistani families (comparator)	WGS in 14 families, 58 individuals	21
Neurological disease	Pakistani families (comparator)	HEXB (Sandhoff) and MBOAT7 homozygous variants	15
Inherited retinal disease	Pakistan (review)	277 variants in 87 genes; about 70% consanguineous	13
Congenital anomalies	Karachi (3 public hospitals)	18,728 screened; major anomalies 1.8%, minor 18.1%	23
Genomic diagnosis	Lahore (comparator)	1,019 individuals, 349 families; diagnosis in 61.3% of index patients	16

early 2017 the investigation had identified 101 confirmed cases in four months, restricted to two subdistricts.[24] More than 300 XDR cases had emerged in Sindh since November 2016 at the time of the first genomic report; whole-genome sequencing showed a clonal H58 lineage with chromosomal resistance genes and an IncY plasmid carrying blaCTX-M-15 and qnrS, resistant to chloramphenicol, ampicillin, trimethoprim-sulfamethoxazole, fluoroquinolones and third-generation cephalosporins.[3] The clone spread across the country: at a Lahore-based laboratory network the share of ceftriaxone-resistant isolates rose from none in 2017 to 30% in 2018 and 50% in 2019, and a survey of 321 frontline clinicians suggested inappropriate diagnostics and antibiotic practices.[25] Sequencing of 58 isolates later showed multiple variants with new chromosomal integrations of the resistance gene.[26] A review reported 5,274 XDR cases among 8,188 typhoid cases notified in Pakistan, and warned that azithromycin was the last reliable oral option.[27] In Karachi, eating meals outside the home more than once a month was associated with culture-confirmed typhoid (odds ratio 4.11).[28] A typhoid conjugate vaccine campaign vaccinated about 207,000 children aged 6 months to 10 years in Hyderabad in 2018, and its effectiveness has since been evaluated in a cohort study.[29]

Paediatric HIV outbreak in Larkana

In April 2019, a screening camp was set up in Larkana after clinicians noticed an unusual number of paediatric HIV diagnoses. Between 24 April and 15 July 2019, 31,239 people were tested and 930 (3%) were positive; 763 (82%) of those were under 16 years and 604 of them were aged 5 years or less.[4] An international investigation recorded 876 positives among 30,191 people tested between 25 April and 27 June 2019, again 82% in children (719 cases), and reviewed infection prevention and control practices.[30] Sequencing of 344 samples from children showed CRF02_AG and subtype A1 as the commonest viruses, which is relevant to treatment-naive drug resistance and to tracing the source.[31] The outbreak

Table 3: *Novel and emerging diseases in Sindh: key evidence.*

Disease	First recognised / peak	Key findings	Ref.
XDR typhoid	Hyderabad, Nov 2016	H58 clone with IncY plasmid (blaCTX-M-15, qnrS); over 300 cases by 2018; national spread; TCV campaign in 2018	3,24–26,29
XDR typhoid risk factors	Karachi, 2019	Eating out >1 time a month: OR 4.11	28
Paediatric HIV	Larkana, April 2019	930 of 31,239 tested positive (3%); 82% children; CRF02_AG and A1 predominant	4,30,31
PAM (*N. fowleri*)	Karachi, 2008 onward	39 patients 2010–2021; ablution with tap water implicated; PCR improves detection	5,32–34
CCHF	Sindh, 2015–2016 rise	Cases 0 (2008) to 16 (2015–2016); seroprevalence 2.7% humans, 36.2% livestock (national)	6,36,37
Cutaneous leishmaniasis	Interior Sindh, 2022	About 4,400 cases; 100–150 new cases daily at peak	7
Chikungunya	Sindh, Dec 2016	Spread to three provinces by mid-2017	8
Post-flood outbreaks	Pakistan, 2022	Cholera, typhoid, malaria, dengue, skin and eye disease	38

XDR, extensively drug-resistant; TCV, typhoid conjugate vaccine; PAM, primary amoebic meningoencephalitis; CCHF, Crimean-Congo haemorrhagic fever; OR, odds ratio.

exposed weaknesses in injection safety and infection control rather than a single point-source failure.

Primary amoebic meningoencephalitis

Naegleria fowleri causes PAM, which is almost always fatal. Karachi reports a growing series, including cases without any recreational water exposure that are thought to follow ablution with tap water.[5] Of 116 suspected cases tested at one Karachi laboratory, 19 were PCR-positive, and wet-preparation microscopy was positive in only 7 of 15 PCR-positive samples for which it was available.[32] A single-centre study of 39 patients treated in Karachi between 2010 and 2021 found a male predominance (84.6%), CSF findings mimicking bacterial meningitis, and positive wet preparations in 69.2% of those tested.[33] A 2025 report highlights persistence of the organism in saline municipal water and describes a February 2025 fatality in a woman whose only water exposure was domestic ablution.[34] Treatment remains poor, though survival has been documented after miltefosine-containing regimens.[35]

Crimean-Congo haemorrhagic fever

Laboratory-confirmed CCHF in Sindh rose from zero in 2008 to 16 in 2015–2016, prompting structured surveillance [6. In a four-province survey in 2017–2018, seroprevalence was 2.7% in humans and 36.2% in livestock, highest in rural areas with animal contact.[36] During 2019, 28 of 280 suspected patients (10%) tested PCR-positive across all four provinces, mostly in August–September, and all sequenced strains belonged to the Asia-1 genotype.[37] The seasonal peak coincides with livestock movement before festivals, which makes pre-festival veterinary and community measures a logical target.

Vector-borne and flood-related disease

Cutaneous leishmaniasis ("desert boil") affected about 4,400 people in interior Sindh in 2022 during a health emergency, with 100–150 new cases daily at the peak.[7] Chikungunya was first detected in Pakistan in December 2016 in Sindh and the federal capital and had spread to three provinces by mid-2017.[8] The catastrophic floods of June 2022 were followed by cholera, diarrhoeal disease, typhoid, malaria, dengue and skin and eye infections, which shows how climate shocks amplify existing risks.[38]

Diagnostic, surveillance and system gaps

Reading the inherited and emerging disease evidence together shows the same gaps.

No registry for Sindh: Existing registries are laboratory- or hospital-based and capture only patients who reach a few centres. The Aga Khan registry is a major advance, but it consolidates cases from one laboratory.[12]

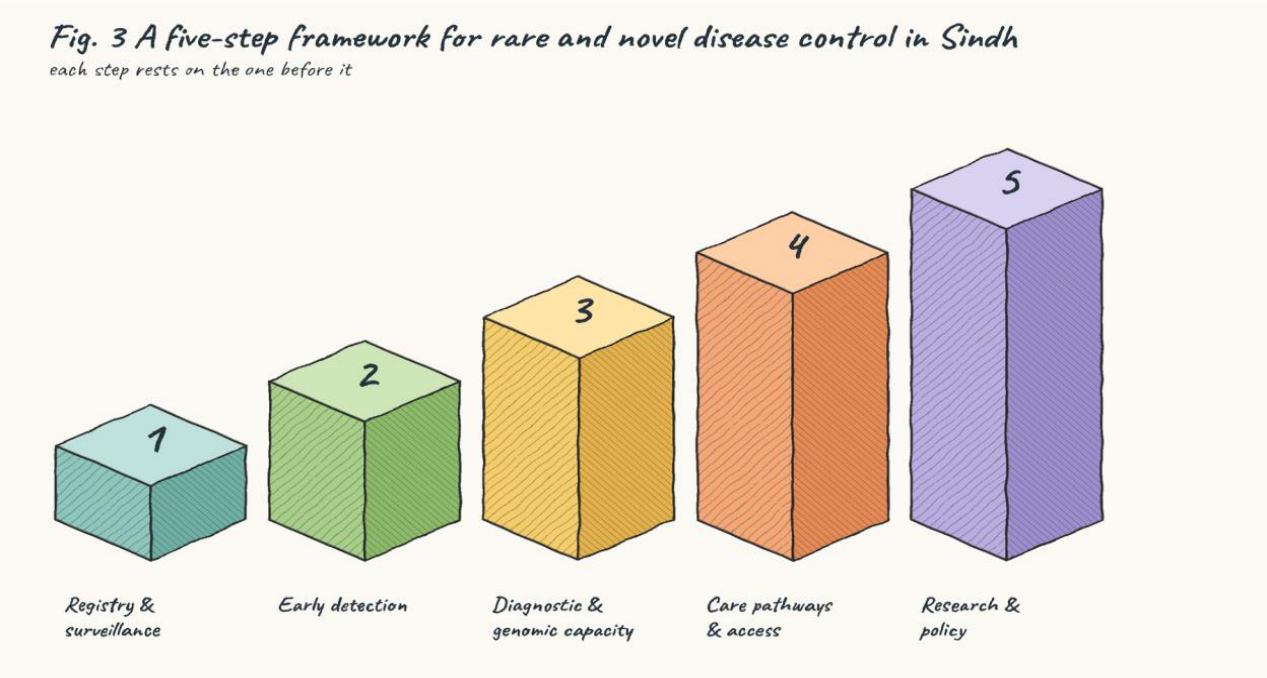


Figure 3: *Proposed five-step framework for controlling rare and novel diseases in Sindh. Hand-sketched schematic prepared for this review.*

***Limited confirmatory and genomic testing*:** Clinicians in Karachi could screen for IMDs but could not confirm several categories locally.[20] Genetic services in Pakistan remain limited and costly for most families.[10] Where genomic testing was provided, as in Lahore, diagnostic yield was high and often changed treatment.[16]

No universal newborn screening: Pakistani experts have recommended starting nationally with congenital hypothyroidism as a prototype and expanding the panel.[39] The Karachi anomaly programme shows that systematic examination of newborns is achievable in public hospitals.[23]

Weak enforcement of prevention laws: Premarital screening is law in Sindh, yet most families of thalassaemic children had neither been tested nor consulted a doctor before marriage.[11,18]

Slow microbiological confirmation: Wet-preparation microscopy misses many PAM cases,[32] survey data suggest inappropriate typhoid diagnostics[25], and CCHF needs laboratory-based surveillance to guide response.[37]

Infection prevention weaknesses: The Larkana outbreak pointed to injection practices and infection control,[30] and typhoid risk is linked to food hygiene and water access.[28]

A framework for action

We propose five steps in sequence (Figure 3, Table 4). Each rests on the one before: a registry and surveillance platform reveals the burden; early detection finds cases; diagnostic capacity confirms them; care pathways treat them; and research and policy sustain the system. The framework is a proposal derived from the evidence reviewed here, not an evaluated model, and suggested leads are indicative.

Research priorities

Priority questions follow from the gaps above:

1. What is the population prevalence and spectrum of rare genetic disease in Sindh, estimated from a registry rather than clinic series?
2. What are the founder variants and allele frequencies in Sindhi communities, and which could support low-cost carrier screening?
3. Would a newborn screening pilot in Sindh be cost-effective, and which conditions should the first panel include?
4. Why does premarital screening legislation fail to

translate into testing, and which delivery models work?

5. How are XDR typhoid, HIV, PAM and CCHF changing genomically and geographically, and how effective are vaccination and water-quality interventions?
6. How do floods, heat and water infrastructure change the risk of emerging infections?

Limitations

This is a narrative review and does not provide a comprehensive, reproducible census of all studies. Searching used a limited set of platforms and one reviewer, so relevant reports in regional journals may be missed. Most Sindh studies are single-centre, hospital-based and descriptive, so prevalence cannot be inferred. Several sources are Pakistan-wide or from Punjab and were used only as comparators. Some figures, such as consanguinity rates, are approximate or come from older surveys. Recent outbreak figures change quickly, and values quoted here are those in the cited publications. The framework is a reasoned proposal rather than a tested intervention.

Conclusions

Sindh faces two burdens at once: inherited rare diseases sustained by high consanguinity, and novel or emerging infections that have appeared or intensified there since 2016. Both depend on the same missing foundations: registries, confirmatory laboratories, early detection and coordinated care. A staged investment in a registry and surveillance platform, newborn and premarital screening, regional genomic and microbiological laboratories, defined care pathways and population-based research would improve both groups at once. SNARE and academic centres such as those of the authors are well placed to lead this agenda.

Conflict of Interest None

Funding Source None

Table 4: *Proposed framework: components, evidence basis and actions.*

Component	Evidence basis	Proposed actions	Suggested lead
1. Registry and surveillance	Registry gaps [12]; fragmented outbreak detection [4,37]	Provincial rare-disease and IMD registry linked to hospital laboratories; integrated outbreak alert system for XDR typhoid, HIV, PAM and CCHF	Provincial health department with academic partners
2. Early detection	Newborn screening evidence [23,39]; premarital screening gaps [11,18]	Pilot newborn screening starting with congenital hypothyroidism; enforce premarital thalassaemia testing with counselling	Health department; paediatric and obstetric societies
3. Diagnostic and genomic capacity	Unconfirmable IMD categories [20]; genomic yield [16]	Regional hub laboratory with tandem MS and exome/genome sequencing; molecular PCR for PAM; sequencing of pathogens	University hospitals with national reference laboratories
4. Care pathways and access	Iron overload vs chelation [17]; limited services [10]	Defined referral networks; secure chelation and transfusion supply; genetic counselling; infection control training	Hospitals, thalassaemia centres, donors
5. Research and policy	Evidence from single centres only; Sindh genomic data scarce	Population-based Sindhi cohorts; provincial rare-disease policy; partnership with SNARE [9	Universities, SNARE, government

MS, mass spectrometry. Suggested leads are indicative.

Authors' Contribution

BRD: Conception.

MLM: Design of the work.

BRD, MLM: Data acquisition, analysis, or interpretation.

MLM: Draft the work.

BRD: Review critically for important intellectual content.

All authors approve the version to be published.

All authors agree to be accountable for all aspects of the work

References

1. Nguengang Wakap S, Lambert DM, Olry A, Rodwell C, Gueydan C, Lanneau V, et al. Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. Eur J Hum Genet. 2020;doi:10.1038/s41431-019-0508-0
2. Hussain R, Bittles AH. The prevalence and demographic characteristics of consanguineous marriages in Pakistan. J Biosoc Sci. 1998;doi:10.1017/S0021932098002612
3. Klemm EJ, Shakoor S, Page AJ, Qamar FN, Judge K, Saeed DK, et al. Emergence of an extensively drug-resistant Salmonella enterica serovar Typhi clone harboring a promiscuous plasmid encoding resistance to fluoroquinolones and third-generation cephalosporins. mBio. 2018;doi:10.1128/-mBio.00105-18
4. Mir F, Mahmood F, Siddiqui AR, Baqi S, Abidi SH, Kazi AM, et al. HIV infection predominantly affecting children in Sindh, Pakistan, 2019: a cross-sectional study of an outbreak. Lancet Infect Dis. 2020;doi:10.1016/-S1473-3099(19)30743-1
5. Ghanchi NK, Khan E, Khan A, Muhammad W, Malik F, Zafar A. Naegleria fowleri meningoencephalitis associated with public water supply, Pakistan, 2014. Emerg Infect Dis. 2016;doi:10.3201/eid2210.151236
6. Syed MA, Ahmed Z, et al. Risk factors of Crimean-Congo hemorrhagic fever in Sindh Province,Pakistan. Int J Infect Dis. 2024; doi:10.1016/j.ijid.2024.107141
7. Yasir M, Herekar F. Desert boil strikes hard: an outbreak of cutaneous leishmaniasis in Sindh, Pakistan. Trop Doct. 2022;doi:10.1177/-00494755221093469
8. Badar N, Salman M, Ansari J, Ikram A, Qazi J, Alam MM. Epidemiological trend of chikungunya outbreak in Pakistan: 2016-2018. PLoS Negl Trop Dis. 2019;doi:10.1371/-journal.pntd.0007118
9. Akram J. The Society for Novel and Rare Diseases (SNARE). J Pak Soc Intern Med. 2025;6(1):1-2.
10. Ashfaq M, Ahmed SA, Aziz-Rizvi R, Hasan Z, Kirmani S, Munim S, et al. Identifying the current status and future needs of clinical, educational, and laboratory genetics services in Pakistan: a web-based panel discussion. J Community Genet. 2022;doi:10.1007/s12687-022-00615-x
11. Memon AM, Laghari ZA, Warsi J, Ijaz F, Sadiq N, Aftab RK. Parental awareness of thalassemia transmission and the impact of consanguineous marriages: a cross-sectional survey. J Univ Coll Med Dent. 2024;doi:10.51846/jucmd.v4i1.3274
12. Jafri L, Majid H, Ahmed S, Jamil A, Mateen S, Shah A, et al. Developing a rare disease registry for inherited metabolic disorders in Pakistan. Orphanet J Rare Dis. 2026;doi:10.1186/s13023-026-04510-3
13. Munir A, Afsar S, Rehman AU. A systematic review of inherited retinal dystrophies in Pakistan: updates from 1999 to April 2023. BMC Ophthalmol. 2024;doi:10.1186/s12886-024-03319-7
14. Tabassum I, Shafique M, Akhtar MS. Uncovering the molecular signatures of rare genetic diseases in the Punjabi population. Int J Mol Sci. 2025;doi:10.3390/ijms27010206
15. Khan S, Rawlins LE, Harlalka GV, Umair M, Ullah A, Shahzad S, et al. Homozygous variants in the HEXB and MBOAT7 genes underlie neurological diseases in consanguineous families. BMC Med Genet. 2019; doi:10.1186/s12881-019-0907-7
16. Cheema HA, Bertoli-Avella AM, Skrahina V, Anjum MN, Waheed NK, Saeed A, et al. Genomic testing in 1019 individuals from 349 Pakistani families results in high diagnostic yield and clinical utility. NPJ Genom Med. 2020;doi:10.1038/s41525-020-00150-z
17. Ahmed A, Khan RH, Naz S, Chaudhry M, Malik S. Descriptive epidemiology and clinical attributes of beta-thalassemia in upper Sindh region of Pakistan. J Rawalpindi Med Coll. 2025;doi:10.37939/jrmc.v29i1.2774

18. Khaliq S. Thalassemia in Pakistan. Hemoglobin. 2022;doi:10.1080/03630269.2022.2059670
19. Nasir S, Mehnaz A, Jamal A, Rafique M, Yahya Y, Kamran A. Metabolic storage disorders at a tertiary care hospital, Pakistan. J Liaquat Univ Med Health Sci.2023;doi:10.22442/-jlumhs.2023.01016
20. Kanani F, Shahid S, Sameer D, Maqsood S. Selective screening for inherited metabolic disorders in a tertiary care hospital of Karachi: a retrospective chart review. Pak J Med Sci. 2023;doi:10.12669/pjms.40.2(ICON).8985
21. Gul R, Firasat S, Schubert M, Ullah A, Peña E, Thuesen ACB, et al. Identification of genetic variants associated with a wide spectrum of phenotypes clinically diagnosed as Sanfilippo and Morquio syndromes using whole genome sequencing. Front Genet. 2023; doi:10.3389/fgene.2023.1254909
22. Bai JJ, Shaikh H, Sohu GM, Narsani AK, Waryah AM. Molecular analysis of OCA1 and OCA2 genes in Sindhi inbred families. Pak J Ophthalmol.2024; doi:10.36351/pjo.v40i3.-1813
23. Samad L, Junejo S, Muhammad AA, Sherwani M, Fatima M, Nawab M, et al. Newborn screening for external congenital anomalies at three public hospitals in Karachi, Pakistan. BMJ Paediatr Open. 2026;doi:10.1136/bmjpo-2025-004015
24. Yousafzai MT, Qamar FN, Shakoor S, Saleem K, Lohana H, Karim S, et al. Ceftriaxone-resistant Salmonella Typhi outbreak in Hyderabad city of Sindh, Pakistan: high time for the introduction of typhoid conjugate vaccine. Clin Infect Dis. 2019;doi:10.1093/cid/ciy877
25. Nizamuddin S, Ching C, Kamal R, Zaman MH, Sultan F. Continued outbreak of ceftriaxone-resistant Salmonella enterica serotype Typhi across Pakistan and assessment of knowledge and practices among healthcare workers. Am J Trop Med Hyg. 2021;doi:10.4269/ajtmh.20-0783
26. Kamal R, Ching C, Zaman MH, Sultan F, Abbas S, Khan E, et al. Identification of multiple variant extensively drug-resistant typhoid infections across Pakistan. Am J Trop Med Hyg. 2023;doi:10.4269/ajtmh.22-0071
27. Akram J, Khan AS, Khan HA, Gilani SA, Akram SJ, Ahmad FJ, et al. Extensively drug-resistant (XDR) typhoid: evolution, prevention, and its management. Biomed Res Int. 2020; doi:10.1155/2020/6432580
28. Batool R, Qureshi S, Yousafzai MT, Kazi M, Ali M, Qamar FN. Risk factors associated with extensively drug-resistant typhoid in an outbreak setting of Lyari Town Karachi, Pakistan. Am J Trop Med Hyg. 2022;doi:10.4269/ajtmh.21-1323
29. Yousafzai MT, Karim SMM, Luangasanatip N, Kazi M, Memon H, Junejo A, et al. Effectiveness of typhoid conjugate vaccine against culture-confirmed Salmonella enterica serotype Typhi in an extensively drug-resistant outbreak setting of Hyderabad, Pakistan: a cohort study. 2024;doi:10.60692/r1nq0-3as49
30. Hermez J, Ismail M, Morgan O, Pasha MS, Schenkel K, Doherty M, et al. A pediatric HIV outbreak in Pakistan. East Mediterr Health J. 2024;doi:10.26719/emhj.24.002
31. Abidi SH, Nduva GM, Siddiqui D, Rafaqat W, Mahmood SF, Siddiqui AR, et al. Phylogenetic and drug-resistance analysis of HIV-1 sequences from an extensive paediatric HIV-1 outbreak in Larkana, Pakistan. Front Microbiol. 2021;doi:10.3389/fmicb.2021.658186
32. Ghanchi NK, Jamil B, Khan E, Ansar Z, Samreen A, Zafar A, et al. Case series of Naegleria fowleri primary ameobic meningoencephalitis from Karachi, Pakistan. Am J Trop Med Hyg. 2017;doi:10.4269/ajtmh.17-0110
33. Rehman SU, Farooq S, Tariq MB, Nasir N, Wasay M, Masood S, et al. Clinical manifestations and outcome of patients with primary amoebic meningoencephalitis in Pakistan: a single-center experience. PLoS One. 2023;doi:10.1371/journal.pone.0290394
34. Kumar N, Kumari S, Sultana S, Khan MS, Mahmoud A. Naegleria fowleri in saline waters: emerging threat of primary amebic meningoencephalitis in Karachi. Ann Med Surg (Lond).2025; doi:10.1097/MS9.00000000000-03772
35. Cope JR, Conrad DA, Cohen N, Cotilla M, Da-Silva AJ, Jackson J, et al. Use of the novel therapeutic agent miltefosine for the treatment of primary amebic meningoencephalitis: report of 1 fatal and 1 surviving case. Clin Infect Dis. 2016;doi:10.1093/cid/civ1021

36. Zohaib A, Saqib M, Athar MA, Hussain MH, Sial AUR, Tayyab M, et al. Crimean-Congo hemorrhagic fever virus in humans and livestock, Pakistan, 2015-2017. Emerg Infect Dis. 2020;doi:10.3201/eid2604.191154

37. Umair M, Khurshid A, Alam MM, Akhtar R, Salman M, Ikram A. Genetic diversity and phylogenetic analysis of Crimean-Congo hemorrhagic fever viruses circulating in Pakistan during 2019. PLoS Negl Trop Dis. 2020;doi:10.1371/journal.pntd.0008238.

38. Alied M, Salam A, Sediqi SM, Kwaah P, Tran L, Huy NT. Disaster after disaster: the outbreak of infectious diseases in Pakistan in the wake of 2022 floods. Ann Med Surg (Lond). 2023;doi:10.1097/MS9.0000000000001597