

26th
April 2025

Rethinking Hospitalization for Possible Serious Bacterial Infections in Young Infants

Evidence from Pakistan to
inform National Guidelines

Participating Hospitals



Organized by:
Department of Paediatrics & Child Health,
Aga Khan University

PSBI Dissemination Seminar

Optimizing place of treatment &
antibiotic regimens for young infants
presenting with signs of possible serious
bacterial infection (PSBI)

26TH
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11am – 1pm

Objectives

- ✦ To present the findings of PSBI Trials 1 and 2, evaluating outpatient treatment and early switch antibiotic therapy as strategies to simplify antibiotic regimens for managing PSBI in young infants aged 0–59 days.
- ✦ To discuss the clinical, programmatic, and policy implications of adopting simplified PSBI treatment strategies within national and regional guidelines for newborn infection management.

Participating Hospital

Context

Neonatal infections remain a major cause of preventable deaths in Pakistan. PSBI (Possible Serious Bacterial Infection) refers to a public health initiative and a guideline for managing young infants (0–59 days) with signs of severe infection when referral to a higher-level hospital is not feasible. This approach was developed by the WHO and later adapted by the Department of Health, Government of Pakistan, for wide implementation in the IMNCI (Integrated Management of Newborn & Childhood Illness). The aim is to improve outcomes for infants with PSBI by providing simplified antibiotic treatment in primary health facilities.

The WHO, together with partners, has further studied the classification of PSBI based on severity and tested new treatment algorithms. These continue to uphold the core principle of outpatient management, but with added layers of safety—an approach that healthcare providers, including physicians, may be more comfortable with.

Two large multicountry randomized controlled trials (RCTs) coordinated by WHO and conducted across Africa and Asia evaluated the safety and efficacy of outpatient antibiotic regimens for young infants presenting with:

- ✦ A single low-mortality-risk sign (fever, fast breathing in infants <7 days, or severe chest indrawing) – RCT₁
 - ✦ One moderate-risk or multiple low-risk signs – RCT₂
- NOTE: Infants with critical illness were not eligible and hence results will not apply to the critically ill babies.

Together, these trials included over 12,000 infants and offer strong, pragmatic evidence to support a revision of PSBI management guidelines, particularly for outpatient care.

Pakistan Participation in the Trials

Pakistan was a key site in the trials. The trials were conducted in Karachi at four hospitals, including Sindh Government Children Hospital (SGCH), National Institute of Child Health (NICH), The Aga Khan Hospital for Women and Children, Kharadar (AKU-KH) and Sindh Institute of Child Health and Neonatology (SICHN). The trials enrolled over 2,000 Pakistani infants, contributing significantly to the global sample of 12,000+.

Trial Designs & Interventions

RCT 1 – Outpatient vs Inpatient Treatment for Single Low-Mortality-Risk PSBI Signs

- ✦ **Eligibility:** Infants with one low risk sign only (fever $\geq 38^{\circ}\text{C}$, fast breathing < 7 days old, or chest indrawing)
- ✦ **Intervention:**
 - **Outpatient arm:** Injectable gentamicin (2 days) + oral amoxicillin (7 days)
 - **Inpatient arm:** Injectable gentamicin + ampicillin for 7 days
- ✦ **Setting:** Randomized at first contact, no CRP testing
- ✦ **Goal:** Evaluate whether direct outpatient care is as safe as inpatient care

RCT 2 – CRP-Guided Antibiotic Switch for Moderate-Risk or Multiple Low-Risk Signs

- ✦ **Eligibility:** Infants with moderate-risk (not feeding well, low temp $< 35.5^{\circ}\text{C}$, movement only on stimulation) or multiple low-risk signs
- ✦ **Intervention:** All infants started on inpatient care with ampicillin + gentamicin. At 48 hours, those clinically stable + CRP negative were randomized to:
 - **Outpatient switch group** Discharged on oral amoxicillin (5 more days)
 - **Continued inpatient group:** Full 7-day injectable treatment
- ✦ **Goal:** Test early step-down to outpatient care based on CRP results and clinical reassessment

Key Results Relevant to Pakistan

RCT 1 – Single Low-Risk Sign
(fever, fast breathing in
<7 days, or chest indrawing)

Pakistan sample contributed to
1,125 of the 7,001 infants enrolled
globally.

- ✦ Total deaths (Pakistan):
8 infants
- ✦ Treatment failure events
(including deaths): 79
- ✦ Outpatient deaths: 2
- ✦ Hospital deaths: 6

Conclusion:

Deaths were rare and comparable
between inpatient and outpatient
groups. Outpatient treatment is
non-inferior to inpatient care

**RCT 2 – Moderate-Risk or
Multiple Low-Risk Signs)**

Pakistan sample contributed to
799 of the 5,253 infants enrolled
globally.

- ✦ Total deaths (Pakistan):
2 infants
- ✦ Treatment failure events
(including deaths): 29
- ✦ Outpatient deaths: 0
- ✦ Hospital deaths: 2

Conclusion:

No deaths in outpatient group in
RCT2

Additional Insights from Pakistan Sites

- ✦ High adherence to treatment protocols
- ✦ 95% received complete outpatient regimens (gentamicin +
amoxicillin)
- ✦ Low rates of severe adverse events
- ✦ Comparable or lower mortality in outpatient arms
- ✦ Strong follow-up infrastructure implemented with CHWs

Why This Matters for Pakistan

- ✦ **Referral acceptance is low:** Many families in Pakistan decline hospital referral due to cost, distance, or gender/social barriers.
- ✦ **Hospital overcrowding:** Tertiary hospitals are overwhelmed and not always equipped for infection prevention.
- ✦ **Primary care is underused:** The Lady Health Worker (LHW) program and secondary hospitals could offer decentralized outpatient PSBI care.
- ✦ **Cost Reduction:** In both RCT1 & RCT2 there was a significant reduction in cost of treatment

Policy Recommendations for Pakistan

Discuss update of national and provincial PSBI treatment guidelines to allow outpatient care for:

- ✦ Infants with a single low-mortality-risk sign
- ✦ Infants with moderate-risk or multiple low-risk signs

Enable outpatient antibiotic protocols at secondary hospitals, urban health centers, and BHUs

Leverage LHWs and frontline providers to support referral, follow-up, and family counseling

Train primary care physicians and nurses on the outpatient PSBI regimen

Ensure availability of dispersible amoxicillin and gentamicin injection in the MNCH supply chain

Institutionalize follow-up systems using community-based and mHealth-supported approaches

What's Next for Implementation in Pakistan?

- ✦ Use AKU and government trial learnings to pilot outpatient PSBI management in provinces
- ✦ Integrate updated protocols into IMNCI training
- ✦ Disseminate evidence through PMDC-accredited CME sessions, the Pakistan Paediatric Association, and District Health Office (DHO) networks
- ✦ Advocate for PC-1 inclusions to support training, drugs, and follow-up capacity

Conclusion

Pakistan now has local evidence that outpatient care for select PSBI cases is safe, effective, and feasible. With careful implementation, this approach can significantly expand access to life-saving treatment, reduce newborn mortality, and strengthen primary care-based newborn services.



For media inquiries, please get in touch with
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