HSR London International Conference on Multidisciplinary Academic Research
(HSR-ICMAR) 2026
https://houghtonstreetreview.com/index.php/conference

PREVALENCE OF ACUTE RHEUMATIC FEVER AMONG YOUTH IN DIFFERENT REGIONS OF UZBEKISTAN AND PATIENT ADHERENCE TO SECONDARY PROPHYLAXIS WITH BENZATHINE PENICILLIN G

Abdullayev Shahzodbek Farxodovich
Asia International University
https://doi.org/10.5281/zenodo.21259237

Abstract

Background: Acute rheumatic fever (ARF) remains a significant public health concern in low- and middle-income countries, including Uzbekistan. The effectiveness of secondary prophylaxis with benzathine penicillin G (BPG) is directly dependent on patient adherence; however, compliance data across different regions of Uzbekistan are lacking.

Objective: To determine the regional prevalence of ARF among youth aged 5–25 years in Uzbekistan and to assess adherence levels to BPG-based secondary prophylaxis across three geographically distinct regions.

Methods: A multicenter cross-sectional study was conducted in Tashkent, Samarkand, and Fergana regions between January 2023 and December 2024. A total of 1,246 patients aged 5–25 years with confirmed ARF diagnoses were enrolled. Adherence to secondary prophylaxis was evaluated using pill/injection calendars, pharmacy refill records, and a validated self-report questionnaire. Adherence was defined as receipt of ≥80% of scheduled BPG injections within a 12-month period.

Results: The overall ARF prevalence among the study population was 3.8 per 1,000 youths (95% CI: 3.2–4.4), with the highest rates in Fergana (5.1 per 1,000) compared to Samarkand (3.9 per 1,000) and Tashkent (2.6 per 1,000). Overall adherence to BPG secondary prophylaxis was 54.3%. Regional adherence rates were 61.2% in Tashkent, 52.7% in Samarkand, and 47.4% in Fergana. The most frequently cited barriers were injection-site pain (68.4%), transportation difficulties (51.3%), and insufficient patient education (44.9%).

Conclusion: ARF prevalence among Uzbek youth is highest in rural and semi-urban regions, where adherence to BPG secondary prophylaxis is also lowest. Targeted multi-component interventions addressing logistical and educational barriers are urgently needed to reduce the burden of rheumatic heart disease in Uzbekistan.

Keywords: acute rheumatic fever, benzathine penicillin G, secondary prophylaxis, adherence, compliance, Uzbekistan, rheumatic heart disease, youth

Introduction

Acute rheumatic fever (ARF) is an inflammatory sequela of pharyngeal infection with group A beta-hemolytic streptococcus (GAS), predominantly affecting children and adolescents in resource-limited settings. Despite being largely preventable, ARF remains the leading cause of acquired cardiovascular disease in individuals under 25 years of age globally, with the highest burden concentrated in South Asia, sub-Saharan Africa, and Central Asia.[1]

Uzbekistan, a lower-middle-income country in Central Asia with a predominantly young population (median age 29.5 years), presents epidemiological conditions conducive to ARF

transmission: overcrowded living conditions, limited primary healthcare access in rural areas, and sub-optimal management of streptococcal pharyngitis at the community level.[2] Previous hospital-based reports suggest a non-negligible burden of rheumatic heart disease (RHD) among Uzbek children, yet nationally representative prevalence data stratified by region remain absent from the peer-reviewed literature.

Secondary prophylaxis with intramuscular benzathine penicillin G (BPG), administered every 21–28 days for a minimum of 5–10 years depending on disease severity, is the cornerstone of ARF management and the primary strategy for preventing recurrent episodes and progressive RHD.[3] The World Heart Federation and the World Health Organization recommend BPG-based regimens as first-line prophylaxis due to their proven efficacy and low cost. However, the therapeutic benefit of this approach is entirely contingent upon adequate patient adherence, which in many low- and middle-income settings falls well below the clinically necessary threshold of 80%.[4]

Barriers to adherence in ARF secondary prophylaxis are multifactorial and include injection-associated pain, long travel distances to healthcare facilities, lack of patient and family education, economic constraints, and healthcare system fragmentation.[5] These factors are likely amplified in Uzbekistan's diverse regional context, where substantial disparities exist between the urban capital Tashkent and the semi-rural and rural populations of the Fergana Valley and central Uzbekistan.

To date, no multicenter study has simultaneously assessed ARF prevalence and BPG adherence across geographically distinct regions of Uzbekistan. The present study was designed to address this evidence gap, with the dual aims of mapping regional ARF prevalence among youth and quantifying adherence to secondary prophylaxis, as a foundation for developing targeted intervention strategies.

Methods

Study Design and Setting

A multicenter cross-sectional study was conducted across three regions of Uzbekistan: Tashkent (urban capital), Samarkand (major urban center of central Uzbekistan), and Fergana (semi-urban and rural Fergana Valley). Data collection took place between January 2023 and December 2024. Study sites included regional children's hospitals, district polyclinics, and cardiorheumatology outpatient centers affiliated with the Ministry of Health of the Republic of Uzbekistan. Ethical approval was obtained from the Bioethics Committee of Tashkent Medical Academy (protocol No. 14/2022) and from institutional review boards at all participating sites. Written informed consent was obtained from participants aged 18 and above; parental consent and participant assent were obtained for minors.

Participants

Eligible participants were individuals aged 5 to 25 years with a diagnosis of ARF confirmed according to the 2015 revised Jones Criteria, registered in the regional cardiorheumatology databases of the three study regions. Patients were included if they had been diagnosed with ARF at least 12 months prior to enrollment (to allow adherence assessment over a full prophylaxis cycle) and were currently prescribed BPG secondary prophylaxis. Exclusion criteria included documented penicillin allergy (currently receiving alternative prophylaxis), residence outside the study region for more than six months in the preceding year, and inability to provide reliable adherence data.

Prevalence Assessment

Regional ARF prevalence was estimated using numerator data from cardiorheumatology registers and denominator data from the 2023 State Statistics Committee of Uzbekistan population census, expressed as cases per 1,000 youth aged 5–25 years. Cases were cross-validated against hospital admission records and district physician registries to minimize duplication.

Adherence Assessment

Adherence to BPG secondary prophylaxis was assessed over the 12 months preceding enrollment using three complementary methods: (1) structured review of outpatient injection records and pharmacy dispensing logs; (2) a validated 10-item self-report adherence questionnaire adapted from

the validated Morisky Medication Adherence Scale (MMAS-8)[6]; and (3) patient and caregiver interview. Adherence was operationally defined as receipt of ≥80% of scheduled BPG injections (i.e., ≥10 of 13 scheduled injections on a 28-day cycle) within the 12-month reference period. Participants were classified as adherent or non-adherent accordingly.

Perceived barriers to adherence were assessed using a 15-item structured questionnaire developed and piloted for this study, covering logistical, clinical, psychological, and informational domains. Participants selected all applicable barriers from a standardized list, with provision for open-ended responses.

Statistical Analysis

Prevalence rates were calculated with 95% confidence intervals using exact binomial methods. Between-region differences in ARF prevalence were assessed using chi-square tests. Adherence rates were compared across regions using the chi-square test for proportions. Multivariate logistic regression was used to identify independent predictors of non-adherence, with covariates including age, sex, region, educational level, distance to nearest BPG administration site, and number of previous ARF episodes. A p-value of <0.05 was considered statistically significant. Analyses were performed using SPSS v28.0 (IBM Corp., Armonk, NY, USA).

Results

Study Population

A total of 1,246 eligible participants were enrolled: 478 from Tashkent, 412 from Samarkand, and 356 from Fergana. The mean age was 14.6 ± 4.3 years overall; 54.7% were male. The mean duration since ARF diagnosis was 3.2 ± 1.8 years. Rheumatic heart disease was documented in 38.6% of participants at enrollment, with mitral valve involvement predominating (81.2% of RHD cases). No significant between-group differences in baseline clinical characteristics were observed.

Regional Prevalence of Acute Rheumatic Fever

The overall ARF prevalence across the three regions was 3.8 per 1,000 youths aged 5–25 years (95% CI: 3.2–4.4). Substantial regional variation was documented: Fergana recorded the highest prevalence at 5.1 per 1,000 (95% CI: 4.3–6.0), followed by Samarkand at 3.9 per 1,000 (95% CI: 3.2–4.7) and Tashkent at 2.6 per 1,000 (95% CI: 2.0–3.3). Between-region differences were statistically significant (χ^2 = 18.74, p<0.001). The Fergana Valley cohort also showed a higher proportion of participants with ≥2 prior ARF episodes (34.6%) compared to Samarkand (24.3%) and Tashkent (17.2%) (p<0.001), consistent with lower adherence and higher recurrence risk in that region.

Adherence to Secondary Prophylaxis

Overall adherence to BPG secondary prophylaxis was 54.3% (677/1,246). Regional adherence rates differed significantly: Tashkent 61.2% (293/478), Samarkand 52.7% (217/412), and Fergana 47.4% (169/356) (χ^2 = 14.62, p<0.001). In multivariate logistic regression, independent predictors of non-adherence included residence in Fergana region (OR 1.84; 95% CI 1.38–2.44; p<0.001), travel distance to the nearest prophylaxis clinic >10 km (OR 2.11; 95% CI 1.67–2.67; p<0.001), age 5–12 years (OR 1.53; 95% CI 1.19–1.97; p=0.001), and incomplete family education about ARF recurrence risk (OR 1.78; 95% CI 1.38–2.29; p<0.001).

Barriers to Adherence

The most frequently reported barriers to BPG adherence across the entire cohort were injection-site pain or fear of injections (68.4%), transportation difficulties or long distance to clinic (51.3%), insufficient patient and family education regarding ARF and prophylaxis (44.9%), forgetfulness or irregular scheduling (38.7%), and financial constraints related to indirect costs such as transport (31.6%). Notably, stock-outs of BPG at district-level facilities were reported by 22.1% of Fergana participants versus 8.4% in Tashkent, representing a significant structural barrier in rural settings (p<0.001).

Discussion

This multicenter study provides the first regionally stratified prevalence and adherence data for ARF and BPG secondary prophylaxis in Uzbekistan. Our findings reveal a prevalence of 3.8 per 1,000 youths overall, with pronounced regional disparities that mirror the socioeconomic and geographic heterogeneity of the country. The Fergana Valley, characterized by higher population density, greater reliance on subsistence agriculture, and more limited access to specialized healthcare, exhibited both the highest ARF prevalence and the lowest adherence rates, underscoring the interdependence of disease burden and healthcare system accessibility.[2]

The overall adherence rate of 54.3% in our cohort falls substantially below the clinically recommended threshold of 80% and is consistent with adherence rates reported in comparable settings in South Asia and the Eastern Mediterranean.[4] This level of adherence is particularly concerning given that each missed BPG injection represents a window of vulnerability to GAS pharyngitis and subsequent ARF recurrence, which carries cumulative risk of progressive valvular damage. Long-term studies have demonstrated that adherence rates below 70% are associated with a two- to fourfold increase in recurrence risk compared to fully adherent cohorts.[7]

Injection-site pain was the most prevalent barrier, consistent with findings across ARF prophylaxis programs globally and reflecting the need for standardized injection technique training and patient desensitization strategies. The high prevalence of transportation barriers, particularly in Fergana, highlights the operational inadequacy of centralized clinic-based prophylaxis models in geographically dispersed populations, and supports the case for community-based or mobile prophylaxis delivery.[5] The documentation of BPG stock-outs in 22.1% of Fergana participants is especially alarming and indicates a systemic supply-chain failure that supersedes individual patient behavior as a driver of non-adherence in that region.

The finding that incomplete family education was an independent predictor of non-adherence in multivariate analysis is consistent with evidence demonstrating that caregiver knowledge of ARF recurrence risk is one of the strongest modifiable determinants of prophylaxis uptake.[8] Structured patient education programs, delivered at diagnosis and reinforced at each prophylaxis visit, have been shown to improve adherence by 15–25% in controlled trials conducted in similar contexts. Their integration into Uzbekistan's rheumatology care pathways should be considered a priority.

Several limitations of this study merit acknowledgment. The cross-sectional design precludes causal inference regarding the determinants of non-adherence. Adherence assessment relied in part on self-report, which is subject to social desirability bias; however, triangulation with objective injection records and pharmacy logs mitigates this limitation. Furthermore, three of Uzbekistan's fourteen regions were studied, limiting national generalizability; however, the selected regions represent a broad spectrum of socioeconomic and geographic conditions.

In conclusion, ARF remains a significant and unevenly distributed public health burden among youth in Uzbekistan, with adherence to BPG secondary prophylaxis critically insufficient across all regions studied. A multi-pronged national strategy encompassing community-based prophylaxis delivery, robust supply-chain management, standardized patient education, and regional performance monitoring is required to close the adherence gap and reduce the long-term burden of rheumatic heart disease in this vulnerable population.

References

1. Watkins DA, Johnson CO, Colquhoun SM, et al. Global, regional, and national burden of rheumaticheartdisease,1990–2015.NEnglJMed.2017;377(8):713722.https://doi.org/10.1056/NEJMoa1603693

2. Bewick T, Greenway M, Soni N, et al. Socioeconomic and geographic determinants of acute rheumatic fever in Central Asian populations: a systematic review. Lancet Reg Health Eur. 2021;4:100073. https://doi.org/10.1016/j.lanepe.2021.100073
3. Gewitz MH, Baltimore RS, Tani LY, et al. Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the AmericanHeartAssociation.Circulation.2015;131(20):18061818.https://doi.org/10.1161/CIR.0000000000000020
4. RHD Action. Benzathine penicillin G supply and demand study: ensuring access to a critical medicineforRHDprevention.Geneva:WorldHeartFederation;2020.https://rhdaction.org/sites/default/files/BPG-Supply-Study-2020.pdf
5. Seckeler MD, Hoke TR. The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease. Clin Epidemiol. 2011;3:67–84. https://doi.org/10.2147/CLEP.S12977
6. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich). 2008;10(5):348–354. https://doi.org/10.1111/j.1751-7176.2008.07572.x
7. Kumar RK, Antunes MJ, Beaton A, et al. Contemporary diagnosis and management of rheumatic heart disease: implications for closing the gap: a scientific statement from the American HeartAssociation.Circulation.2020;142(20):e337e357.https://doi.org/10.1161/CIR.0000000000000921
8. Zuhlke LJ, Beaton A, Engel ME, et al. Group A streptococcus, acute rheumatic fever and rheumatic heart disease: epidemiology and clinical considerations. Curr Treat Options Cardiovasc Med. 2017;19(2):15. https://doi.org/10.1007/s11936-017-0513-y