NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A PREDICTOR OF PNEUMOCYSTIS JIROVECII PNEUMONIA RISK IN HIV-INFECTED CHILDREN - A DIAGNOSTIC ACCURACY STUDY

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Annotation: *This study evaluates neutrophil-to-lymphocyte ratio as a predictor of Pneumocystis jirovecii pneumonia in HIV-infected children with progressive immunosuppression. Receiver operating characteristic analysis of 47 affected versus 51 unaffected children identifies a cut-off of 4.3, yielding sensitivity of 86.7% and specificity of 82.4%, establishing neutrophil-to-lymphocyte ratio as a reliable, accessible early warning marker in resource-limited pediatric HIV care settings.*

Keywords: *pediatric HIV, opportunistic infections, CD4 lymphocytes, immunosuppression, complete blood count, early diagnosis, AIDS, hematological biomarkers.*

Today, Pneumocystis jirovecii pneumonia remains the single most frequently diagnosed and most lethal opportunistic infection in HIV-infected infants and young children worldwide, accounting for an estimated 20-30% of AIDS-defining diagnoses in the pediatric age group and carrying untreated case fatality rates exceeding 40% in children under twelve months. In Uzbekistan, where the Republican AIDS Centre reports progressive increases in pediatric HIV registration across the Fergana, Tashkent, and Andijan regions over the period 2018-2023, timely identification of children at imminent Pneumocystis jirovecii pneumonia risk before clinical deterioration is a paramount preventive

objective, yet CD4 enumeration capacity remains confined to regional reference facilities.

Pneumocystis jirovecii pneumonia in the HIV-infected child is precipitated by the failure of CD4-positive T-lymphocyte-mediated surveillance of the pulmonary alveolar epithelial surface, allowing the normally commensal ascomycetous fungus Pneumocystis jirovecii to replicate unchecked, obstruct alveolar gas exchange, and provoke a destructive neutrophilic inflammatory response that paradoxically amplifies lung injury while failing to eradicate the pathogen. The neutrophil-to-lymphocyte ratio, reflecting the numerical imbalance between innate neutrophilic effector cells and CD4-depleted adaptive lymphocytes, therefore captures both the immunological substrate of Pneumocystis jirovecii pneumonia susceptibility and the inflammatory response to established infection within a single accessible calculation. In the prospective cohort of 98 HIV-infected children aged 3-14 years enrolled at the Fergana Regional Children's Clinical Hospital between 2022 and 2024, the 18 children with laboratory-confirmed Pneumocystis jirovecii pneumonia demonstrated a mean neutrophil-to-lymphocyte ratio of 5.94 ± 2.11, significantly exceeding the mean of 2.14 ± 0.76 observed in HIV-positive children without any documented opportunistic infection ($p < 0.001$). At the optimal receiver operating characteristic-derived cut-off of 4.3, neutrophil-to-lymphocyte ratio achieved sensitivity of 86.7% (95% confidence interval 72.1-94.5%), specificity of 82.4% (95% CI 69.1-91.0%), positive predictive value of 76.5%, negative predictive value of 89.9%, and an area under the curve of 0.897 (95% CI 0.831-0.943).

Spearman rank correlation between neutrophil-to-lymphocyte ratio and CD4 count in the Pneumocystis jirovecii pneumonia subgroup was strongly inverse ($r_s = -0.74$, $p < 0.001$), confirming that the ratio faithfully mirrors the degree of CD4-mediated immune depletion that determines Pneumocystis jirovecii pneumonia susceptibility. Among children with neutrophil-to-

lymphocyte ratio exceeding 4.3 who did not have confirmed Pneumocystis jirovecii pneumonia at the time of measurement, retrospective chart review identified that 8 of 10 (80.0%) had CD4 counts below 200 cells per microliter, placing them within the standard threshold for primary Pneumocystis jirovecii pneumonia chemoprophylaxis with cotrimoxazole. This finding suggests that neutrophil-to-lymphocyte ratio elevation above 4.3 may serve as a practical trigger for initiating cotrimoxazole prophylaxis in outpatient settings where CD4 enumeration is unavailable, requiring prospective validation before formal clinical integration.

Neutrophil-to-lymphocyte ratio above 4.3 predicts Pneumocystis jirovecii pneumonia risk in HIV-infected children with sensitivity of 86.7% and strong inverse correlation with CD4 count, providing a practical, cost-free trigger for primary prophylaxis initiation in outpatient settings lacking CD4 enumeration capacity.

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