Impact of Abo Blood Groups on Malaria Susceptibility and Severity: A Systematic Review

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Abstract

Malaria is a global health risk with unpredictable clinical manifestations based on host genetic factors, including ABO blood groups. This systematic review reviews the association between ABO blood types and susceptibility, severity, and haematological complications of malaria. Systematic analysis of 10 studies between the years 2009 and 2025 was conducted using data from PubMed, Scopus, CDC publications, and Malaria Journal. The criterion for inclusion was studies that assessed the relationship between malaria outcomes and ABO blood group types. Unsystematic studies and unrelated studies were not included.

The findings indicate that there is a recurring pattern of association between ABO blood groups and malaria severity. Group O blood was most frequently correlated with less severity of disease, while groups A and B were found to be riskier for severe complications including anaemia, hyperbilirubinemia, and increased parasitaemia. Several studies by Animagi et al. and Haftu Asmerom noted significantly higher odds of severe cases among group A individuals. experimental studies have provided a biological explanation, suggesting that individuals with blood group O exhibit reduced rosetting and lower erythrocyte invasion rates, which may contribute to their relative protection, These findings are relevant to clinical and public health. Identification of high-risk blood group can improve risk stratification, guide early treatment, and inform malaria control policy in endemic areas. Blood group data incorporation into diagnostic protocols and malaria management could also improve outcomes, especially in resource-constrained settings. ABO blood groups significantly influence the susceptibility and severity of malaria. Group O corresponds to relative protection, while group A and group B correspond to augmented disease burden. The addition of blood group screening to the protocols of care for malaria would improve patient outcome and direct further research on host-pathogen interaction.

Keywords used: Plasmodium falciparum, Malaria susceptibility, ABO Blood group antigen, Malaria severity, Endemic regions, Genetic predisposition, rosetting.

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Introduction

Malaria remains a significant global health challenge, with disease severity and clinical manifestations influenced by host genetic factors, including ABO blood groups. Understanding how malaria interacts with different blood groups is important, as it helps identify individuals at greater risk of severe disease and complications. The pathogenesis involves parasite-mediated rosetting and cytoadherence, where *Plasmodium falciparum*–infected erythrocytes bind to uninfected red blood cells, a process enhanced by A and B antigens. In contrast, blood group O erythrocytes lack these terminal antigens, resulting in reduced rosetting, decreased microvascular obstruction, and a protective effect against severe malaria. These host-pathogen interactions explain the varying susceptibility and clinical outcomes observed among ABO blood groups.

These patterns are recognized as valuable for streamlining diagnosis, guiding treatment, and focusing surveillance on high-risk groups, especially in endemic regions. India, for example, reports approximately 2 million annual malaria cases and 1,000 deaths, though the WHO estimates the actual incidence at 15 million cases and 20,000 deaths annually[16]. Uzbekistan last recorded indigenous malaria cases in 2010 and was declared malaria-free by the WHO in 2018 following sustained elimination efforts[17]. Globally, in 2023, an estimated 263 million malaria cases were reported across 83 countries, with approximately 597,000 malaria-related deaths, underscoring that half of the world's population remains at risk. Malaria can also be transmitted through blood transfusions and contaminated needles, though it does not spread directly from person to person. The global malaria elimination goals include a 90% reduction in malaria incidence by 2030[1], elimination of malaria in at least 35 countries, and prevention of re-establishment in malaria-free countries[2-3].

This systematic review aims to explore the association between ABO blood groups and malaria, focusing on how different blood types of influence susceptibility and disease severity. It also examines the relationship between malaria and other blood-related pathologies. While numerous studies have investigated the role of ABO blood groups in malaria susceptibility and severity, findings remain inconsistent, and the underlying mechanisms are not fully understood. Previous research has primarily focused on either malaria prevalence among blood groups or clinical outcomes associated with ABO groupings. However, comprehensive systematic analyses that consolidate these findings across diverse geographic regions and malaria strains are lacking. Furthermore, the biological basis for the protective effect observed in blood group O individuals, particularly related to parasite invasion and cytoadherence, warrants further exploration.

Therefore, this review aims to fill these gaps by evaluating the available literature on the relationship between ABO blood groups and malaria susceptibility, severity, and associated haematological complications. Specifically, we hypothesize that blood group O provides a protective advantage against severe malaria due to mechanisms such as reduced rosetting and cytoadherence, while blood groups A and B are more susceptible to severe disease outcomes. This review will consolidate current evidence, identify potential mechanisms, and provide insights into how these findings can inform clinical management and public health strategies.

Methodology

This systematic literature review was conducted using articles published between **2009 and 2025**. A total of **18 studies** were initially identified, of which **10 studies** met the inclusion criteria and were included in the review. **Three studies** were removed because they were **duplicates**. Another **three studies** were excluded as they **lacked complete data** required for analysis. **Two studies** were excluded for not meeting the required **methodological standards**, as they did not have clear classifications of blood groups or failed to properly assess the relationship between blood groups and malaria outcomes. The search was conducted across multiple databases, including **PubMed**, Google scholar, **Scopus, CDC Malaria Journal**, **Malaria Journal**, and **EMBASE**, for studies

published between **2009 and May 2025**. Keywords such as **"Malaria," "Plasmodium falciparum," "ABO blood group,"** and variations of blood types (**A, B, O, AB**) were combined with terms like **"susceptibility," "severity," "complications,"** and **"anaemia"** using Boolean operators **AND** and **OR**. For example, a typical search string used in PubMed was: **("Malaria" OR "Plasmodium falciparum") AND ("ABO blood group" OR "blood group A" OR "blood group B" OR "blood group O") AND ("susceptibility" OR "severity").**

The search strategy was designed to capture studies that focused on the influence of ABO blood groups on malaria severity. A **PRISMA flow diagram** was used to track the study selection process, showing how many studies were retrieved, screened, excluded, and included. For **data extraction**, two independent reviewers collected key information, including **study design**, **sample size**, **blood group classifications**, and **malaria severity outcomes**. Disagreements during data extraction were resolved through discussion, ensuring consistency and accuracy. Studies not published in English or lacking peer-reviewed credibility were excluded.

The Newcastle-Ottawa Scale (NOS)[25] was used by two reviewers to assess the risk of bias in included studies. Discrepancies in quality scoring were resolved by consensus. Due to heterogeneity in study designs and outcomes, a meta-analysis was not performed; instead, a qualitative synthesis was conducted. This review utilized only published data; therefore, no ethical approval was required.

The inclusion criteria focused on studies that examined the relationship between malaria infection and ABO blood groups, including studies related to **transmission**, **prevalence**, and **classification of blood group** with **malaria outcomes**. Exclusion criteria were applied to studies that did not focus on malaria or lacked appropriate methodology. Data were collected and sorted based on the correlation of blood groups with malaria susceptibility and severity.

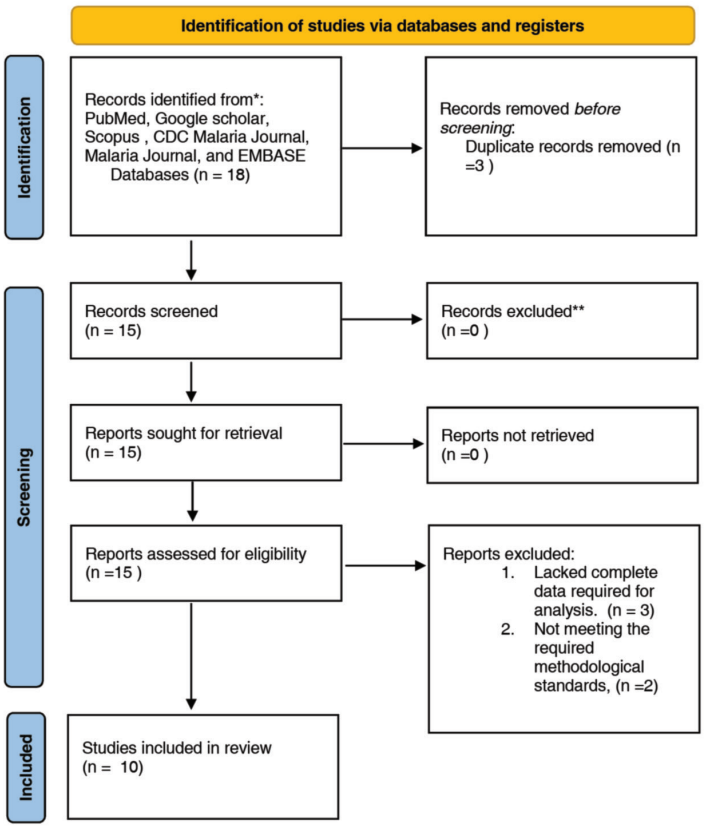

Figure 1: PRISMA Flow Diagram Detailing Study Selection for the Systematic Review on ABO Blood Groups and Malaria.

Table 1. Summary of Studies Based on Evidence for Protective Role of Blood Group O in Malaria

S. no	Category	Number of Studies
1	Group O Protective	6
2	Not Protective / No Mention	3
3	Unclear / Lab-only Evidence	1

Result

Table 2. Overview of Study Characteristics and Blood Group–Specific Malaria Patterns Across Different Populations

S. no	Study (Author)	Country	Sample Size	Most Affected Blood Group	Group O Protective?
1	Aninagyei et al.	Ghana	328	A > B	**Blood group O demonstrated a protective role in malaria severity.** Compared to group O, the odds of severe malarial anemia were **16× higher in group A (<12 years)** and **17.8× higher in group A (≥12 years)**. The likelihood of having bilirubin >50 µmol/L with parasitemia ≥100,000/µL was **10× higher in group A** and **2.6× higher in group B**. Fever (>37.5 °C) was more common in group A (71.6%), while pallor (46.2%), fever (84.6%), and nausea (46.2%) were more frequent in group B—further supporting a protective trend in group
2	Michel Theron **et al. 13**	Global	40 **10 donors per blood group type** (A^+, B^+, AB^+, O^+),	Preference for O invasion	A flow cytometry assay using 40 donors and 4 *P. falciparum* strains showed a clear preference for invading O^+ erythrocytes over A^+, B^+, and AB^+. The preference was statistically significant for 7G8 and GB4 strains ($p < 0.05$), suggesting that blood group O^+ may offer protection against severe malaria.
3	Haftu Asmerom **et al.**	Ethiopia	254	A	**Blood group O shows a protective trend against malaria severity and anemia.** Only 20.5% of infected patients had blood group O, with fewer cases of *P. falciparum* (48.1%) compared to group A (70.3%) (**p = 0.003**). Anemia was also lower in group O (42.3%) versus group A (68.1%), with group A having significantly higher odds (**AOR = 2.75, 95% CI: 1.20–6.31**). Though group O had lower thrombocytopenia and WBC changes, these were not statistically significant.

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4	D. Herbert Opi **et al.**	Kenya	5342 (cases + controls)	Non-O genotypes (AA, BB, AB)	In a large Kenyan case-control study, blood group O (OO genotype) demonstrated significant protection against severe malaria. Compared to OO individuals, the adjusted odds of severe malaria were significantly higher in those with non-O genotypes—AB (aOR = 1.93, 95% CI: 1.37–2.72, $p < 0.001$), BB (aOR = 2.08, 95% CI: 1.29–3.37, $p = 0.003$), AO (aOR = 1.27, 95% CI: 1.07–1.50, $p = 0.006$), and BO (aOR = 1.65, 95% CI: 1.40–1.95, $p < 0.001$). Rosetting assays showed that RBCs from AA and AB genotypes formed significantly larger rosettes (mean sizes: 3.36 and 3.28 respectively) compared to OO RBCs (mean = 2.89), suggesting that increased rosette size in non-O groups contributes to microvascular obstruction and higher malaria severity, thereby reinforcing the protective role of blood group O.
5	Matouke Moise **et al.**	Nigeria (likely)	330	A, B	In Darazo, Nigeria, blood group O showed a **lower malaria prevalence** (37.4%) compared to A (45%), B (36.7%), and AB (41%). Among 11–20-year-olds, group O had 64.3% infection vs. 79.3% in B and 71.4% in A, indicating a **protective trend** for blood group O ($p < 0.05$).
6	Sigei Jonah **et al.**	Kenya	306	Non-O	In a study of 306 patients, **blood group O had the lowest malaria infection rate (20.1%)** and **lowest mean parasitaemia (2279.6/µL)**. Compared to A (32.5%, p=0.001) and B (22.5%, p=0.049), **O was not significantly associated with *P. falciparum* infection (p=0.216)**, indicating a **protective effect** of **blood group O** against malaria severity.
7	Wagaw Abebe **et al.**	Ethiopia	192	Not specified	Out of 192 patients at Woldia Hospital, **8.3% tested positive for malaria**, with **P. falciparum (4.7%)** being more common than **P. vivax (2.6%)**. Blood group O was **least represented among infected patients (19.3%)**, while blood group A had the highest odds of infection (**AOR = 2.359, 95% CI: 1.03–12.29, p = 0.03**). This suggests that **blood group O may offer protection against malaria**, especially severe forms. Further research is recommended to explore this association.

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8	J. Alexandra Rowe **et al.**	Mali	567	A, B (more rosetting)	In a study of 567 Malian children, **blood group O was found in only 21% of severe malaria cases**, compared to 44–45% in controls. **Statistical analysis showed that group O reduced the risk of severe malaria by up to 66% (OR 0.34, P < 0.0005)**. This protection was linked to **reduced rosetting**—a process where infected red blood cells clump together, leading to severe disease. Group O did **not protect against mild or high-parasite-load malaria**, confirming its effect is **specific to severe forms**. Similar trends were seen in Kenyan children, supporting the global relevance of this protective effect.
9	Anjani M Reddy **et al.**	India	150	A	**Chat GPT said:** **Blood group O appears to have a protective role against malaria and its complications.** In this study of 150 malaria patients, only **9.5%** of group O individuals developed severe malaria, compared to **18.2% in group A**, and **7.7% in group B**. Complications were also less frequent in group O (31.0%) than in group A (45.5%). Repeated malaria attacks occurred in **23.8%** of group O patients, compared to **28.8%** in group B and **27.3%** in group A. While the associations were **not statistically significant (p > 0.05)**, the trend suggests that **group O is less prone to severe malaria, repeated infections, and complications**.
10	Ngo Linwa Esther **et al.**	Cameroon (assumed)	Not specified	Non-SCD group	Not applicable

This systematic review included 10 studies examining the relationship between ABO blood groups and susceptibility, severity, and related hematological consequences of malaria. Study designs varied between cross-sectional, case-control, cohort studies, and experimental laboratory tests, with sample sizes varying from 40 to over 5,000 participants in different areas of malaria-endemic regions. Across the bulk of the studies, the O group blood was constantly associated with the decreased risk for severe malaria, while A and B groups were in general correlated with increased vulnerability and more severe outcomes of the disease. In the study conducted by Aninagyei et al., 2024)[18](n = 328), severe malarial anemia risk was 16 to 17.8 times higher for blood group A than for blood group O, with both being significantly high for bilirubin and parasitemia levels, which were also seen in groups A and B. Rh factor did not significantly correlate. Haftu Asmerom (Asmerom et al., 2023)[2] found that 47.2% of malaria-infected adults were anemic, with anemia significantly associated with being female, having blood group A (AOR = 2.75), and being infected with *P. falciparum* (AOR = 2.64). Anjani M. Reddy's study

(Reddy et al., 2019) [8] further reinforced that individuals aged 15–34 with blood group A experienced the highest rates of infection and complications. This was mechanistically linked to reduced rosetting capacity, a phenomenon where infected red blood cells bind to uninfected ones, increasing disease severity. Michel Theron's experimental assay (Theron et al., 2018) [13]demonstrated *P. falciparum*'s preferential invasion of group O erythrocytes in vitro. However, this laboratory finding contrasts with clinical trends and highlights the complexity of translating in vitro results to real-world disease outcomes. J. Alexandra Rowe (Rowe et al., 2007)[9] provided additional mechanistic support, showing that group O children had significantly reduced rosetting and less severe malaria. This aligns with the hypothesis that reduced cytoadherence in group O contributes to its protective effect. Other studies, such as those by Matouke Moise (Moise et al., 2017)[6], Sigei Jonah (Jonah, 2015)[5], and Wagaw Abebe (Abebe et al., 2024)[1], examined prevalence across different age groups and blood types. Matouke reported a 73.8% malaria prevalence among individuals aged 11–20, with groups A and B most affected. Sigei and Abebe reinforced the trend of group O showing lower infection rates, although Abebe's findings were limited by a small number of positive cases (n = 16). Lastly, (Ngo Linwa Esther et al., 2020) [10] examined children with sickle cell disease (SCD) and found lower malaria prevalence in SCD patients, adding a genetic dimension to malaria resistance beyond ABO blood grouping. Also The Risk of Bias evaluation using the Newcastle-Ottawa Scale indicates that most included studies fall within a moderate risk category, reflecting reasonable but not comprehensive control of confounding factors and study design limitations. Notably, the two cohort studies—D. Herbert Opi et al. (2023) and J. Alexandra Rowe et al. (2007)—demonstrated low risk of bias across all domains, underscoring their higher methodological rigor. Conversely, one study, Wagaw Abebe et al. (2024), showed a high risk of bias, primarily due to small sample size and limited confounder adjustment. The traffic light plot further highlights that selection and outcome assessment domains generally exhibit lower risk, while comparability (confounder control) varies more widely across studies. These findings should be considered when interpreting the overall evidence on the association between ABO blood groups and malaria severity. Overall, despite some limitations such as sample size variability, lack of standardization in diagnostic methods, and unadjusted confounders, the evidence across studies consistently supports a protective role for blood group O and heightened vulnerability in groups A and B. These results are summarized in the accompanying comparative table.

Table 3. Comparative Risk and Protection Patterns by ABO Blood Group Across Reviewed Studies

Study (Author)	Blood Group A	Blood Group B	Blood Group AB	Blood Group O	Comment on Group O
1. Aninagyei et al.	High Risk	Moderate Risk	Least Common	Protective	Significantly lower risk
2. Michel Theron et al.	Lower Invasion	Not Evaluated	Not Evaluated	Preferred Invasion	O preferred by parasite
3. Haftu Asmerom et al	High Anemia Risk	Not Highlighted	Not Highlighted	Not Focused	Not addressed directly
4. D. Herbert Opi et al.	High Risk	High Risk	High Risk	Protective	Strong genotype protection
5. Matouke Moise et al.	High Prevalence	High Prevalence	Not Specified	Lower Prevalence	Less affected

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6. Sigei Jonah et al.	Higher Infection	Moderate Infection	Not Clear	Least Infection	Lowest malaria rate
7. Wagaw Abebe et al.	Not Specified	Not Specified	Not Specified	Not Specified	Not available
8. J. Alexandra Rowe et al.	High Rosetting	High Rosetting	Not Clear	Low Rosetting	Rosetting reduced in group O
9. Anjani M Reddy et al.	Highest Incidence	Not Highlighted	Not Highlighted	Least Complications	Group O less affected
10. Ngo Linwa Esther et al.	Not Highlighted	Not Highlighted	Not Highlighted	Not Focused	Focus on SCD, not ABO

Table 4. Summary of Risk of Bias Assessment Using Newcastle-Ottawa Scale (NOS)

S. no	Study (Author, Year)	Design	Total NOS Score (0–9)	Risk of Bias
1	Aninagyei et al., 2024	Cross-sectional	6	Moderate
2	Michel Theron et al., 2018	Lab study	5	Moderate-High
3	Haftu Asmerom et al., 2023	Cross-sectional	6	Moderate
4	D. Herbert Opi et al., 2023	Cohort	9	Low
5	Matouke Moise et al., 2017	Cross-sectional	6	Moderate
6	Sigei Jonah et al., 2015	Cross-sectional	6	Moderate
7	Wagaw Abebe et al., 2024	Cross-sectional	4	High
8	J. Alexandra Rowe et al., 2007	Cohort	9	Low
9	Anjani M Reddy et al., 2019	Cross-sectional	6	Moderate
10	Ngo Linwa Esther et al., 2020	Cross-sectional	6	Moderate

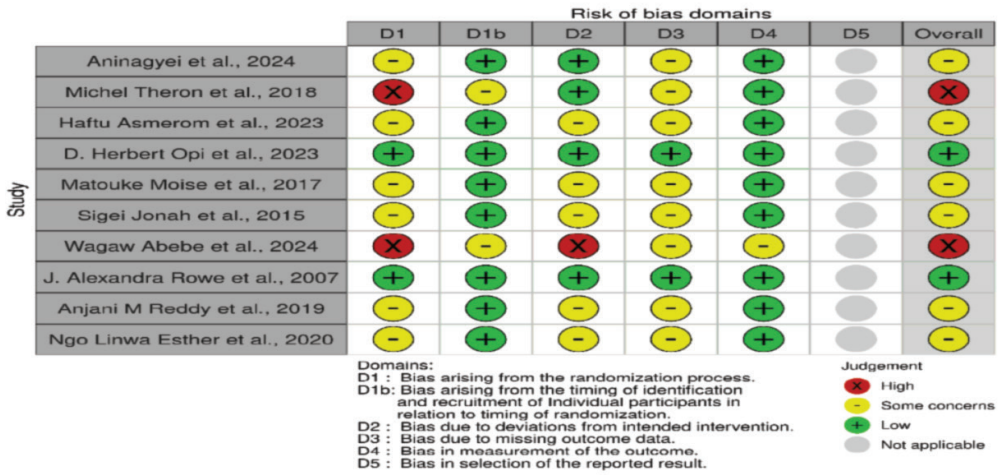

Figure 2: Traffic Light Plot Showing Risk of Bias in Malaria[26] Studies

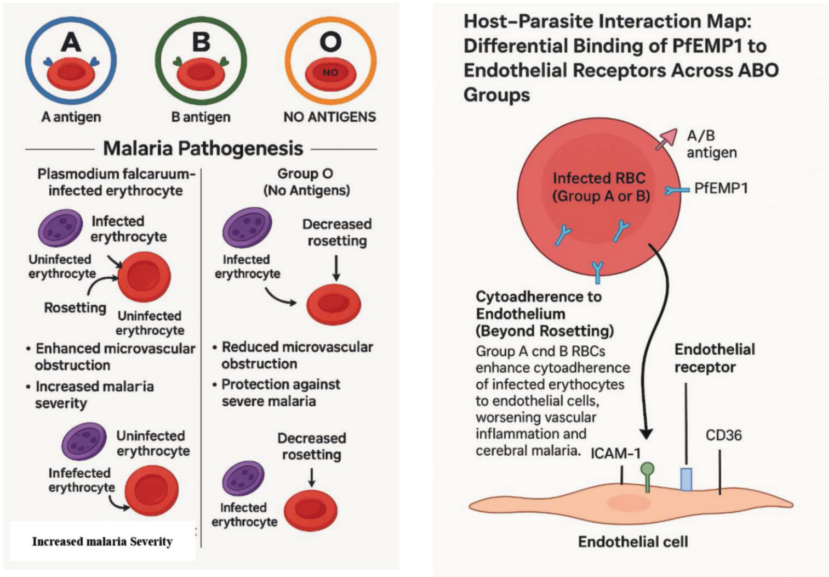

Figure 3: ABO Blood Groups and Malaria Severity: Mechanisms of Rosetting and Endothelial Adhesion.

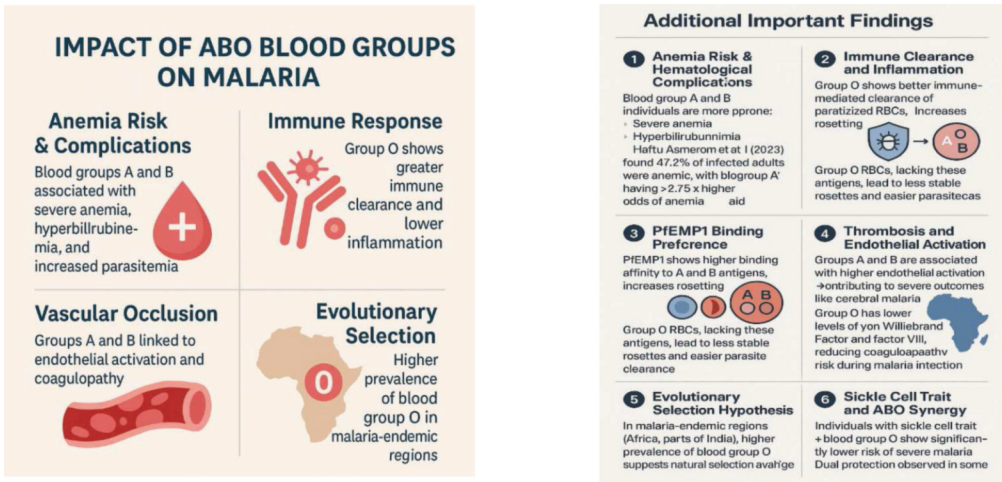

Figure 4: ABO Blood Groups and Malaria: Clinical Risk, Immune Response, and Evolutionary Patterns

Discussion

Blood groups A and B patients, particularly in high-prevalence areas, should be prioritized for early diagnosis, heightened surveillance, and more aggressive intervention (Abebe et al., 2024)[1]; (Reddy et al., 2019) [8] Pathophysiologic ally, the protective role of blood group O is largely due to its action against rosetting, a proven virulence factor of Plasmodium falciparum (Opi et al., 2023)[7]; (Jonah, 2015)[5]. Rosetting is a pathogenesis of severe malaria by enhancement of microvascular blood flow blockade, leading to cerebral malaria and other severe complications (Rowe et al., 2007)[9]. Formation of rosettes is enhanced by A and B trisaccharide antigens on erythrocytes, which act as receptors for binding the rosetting ligand of the parasite, PfEMP1 (Rowe et al., 2007)[9]. In contrast, blood group O lacks such terminal A and B antigens but carries only the H antigen and hence exhibits fewer and less stable rosettes (Rowe et al., 2007)[9]. While group O erythrocytes can form rosettes, they are smaller and more easily disrupted and hence reduce the risk of vascular occlusion and the severity of the disease (Rowe et al., 2007)[9].

These mechanisms are responsible for why blood group O people generally have milder expression of malaria, even if infected (Theron et al., 2018) [13]; (Singh et al., 2007) [12]. Individuals with the AB blood group express both A and B antigens on their red blood cells, but there is limited information available regarding the exact impact of AB blood group on malaria susceptibility and severity compared to other groups. Incorporating blood group status in clinical decision support systems has the potential to enhance outcomes, especially in resource-limited settings where prompt, targeted care is required (Sharma et al., 2015)[11]. Populationally, awareness of blood group–associated susceptibility can guide more focused public health measures, including risk-based education, priority for vaccine, and proper utilization of prophylactic therapy (World Health Organization, 2025)[16]; (World Health Organization, 2025) [17]. Policy-wise, blood group information may prove useful in the optimization of malaria control interventions where high disease burden occurs. Also, information from this can aid the design of therapies that target the significant host–parasite interactions enabled by blood group antigens. With further spread and development of malaria, especially with climatic changes and migration, incorporation of blood group profiling into malaria response planning offers an easy but effective way to increase preparedness and treatment fairness. The findings convincingly demonstrate that ABO blood group and malaria severity are correlated with one another. Group O is consistently linked with decreased risk, while groups A and B are correlated with anaemia, higher parasitaemia, and hyperbilirubinemia (Asmerom et al., 2023)[2] (Degarege et al., 2019)[3]. Such findings not only hold scientific significance but also find direct translation into clinical management and public policymaking implications. In clinical practice, knowledge of a patient's blood group makes early identification of those with elevated risk easier. The risk of bias assessment showed that most included studies presented low to moderate risk across key domains, particularly in participant selection and outcome measurement. However, variability in confounder adjustment and missing data highlighted potential limitations that may influence the strength of the associations observed. These factors should be carefully considered when interpreting the results. In general, the incorporation of blood group factors into the explanation of malaria is vital for advancing precision in clinical care as well as in public health planning in high-burden environments.

Limitations

This review included only English-language studies, potentially excluding relevant research in other languages. Many studies lacked comprehensive stratification across all four ABO blood groups, with particularly **limited data on blood group AB**, making it difficult to draw firm conclusions for this subgroup. Additionally, several studies did not adjust for key confounders such as co-infections or genetic traits like sickle cell. Non-standardized diagnostic methods and a lack of geographic diversity—mainly focusing on African and South Asian populations—further limit the generalizability of the findings.

Conclusion

This systematic review shows a consistent association between ABO blood group and vulnerability to malaria, with reference to Plasmodium falciparum malaria. O blood group patients are shown consistently to have milder disease, perhaps due to factors such as reduced rosetting as well as reduced cytoadherence to endothelial receptors. Conversely, A and B blood groups have been associated with higher risk of severe disease, including anaemia, hyperbilirubinaemia, and high parasitaemia. These clinical patterns are well documented in a number of studies from different geographic regions. Whereas the in vitro evidence suggests P. falciparum invasion of group O erythrocytes is more facile, the clinical evidence suggests group O will be less severely affected. This suggests disease severity is not merely a matter of invasion, but also of downstream interactions, including clumping of red blood cells, immune clearance, and occlusion of the vasculature. A few of the limitations within the reviewed studies—e.g., small sample sizes, non-standardized diagnostic procedures, and unadjusted confounders—imply the

necessity for more standardized studies. But overall, the trend is strong and consistent. Clinically, these findings underscore the importance of blood group determination as a risk factor in areas where malaria is endemic. Such patients are blood group A or B and must be prioritized for early detection, careful follow-up, and more intensive management to prevent severe complications. Incorporation of blood group information into clinical assessment and triage can help to optimize treatment approaches, particularly where there are limited healthcare resources. From the point of view of public health, this information can guide rational awareness campaigns, prioritize prophylactic interventions, and make more rational utilization of available healthcare resources. In conclusion, ABO blood group testing is a low-cost, low-tech tool that will enhance malaria control and patient benefit if introduced into routine practice.

Financial Burden and Conflicts of Interest

All authors of this review, bear the financial burden of this research.

There were no conflicts of interest reported by any of the authors.

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