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Relevance of C-Reactive Protein (CRP) as an alert marker in imported malaria in Morocco

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Introduction

Malaria, a major parasitic disease, persists in Morocco exclusively in its imported form. In this non-endemic context, C-Reactive Protein (CRP), a rapid and easily accessible inflammatory marker, is systematically measured in the evaluation of febrile patients. However, its specific predictive value for imported malaria remains poorly defined and understudied in North African settings.

This study therefore aims to assess the usefulness of CRP as an early warning tool to guide clinicians toward parasitological testing.

Methods and materials

This retrospective study was conducted from January 2017 to December 2024 at the Parasitology-Mycology Department of Mohammed V Military Teaching Hospital in Rabat.

It included 816 patients suspected of imported malaria, defined by the presence of fever (>38°C) and a history of travel to a malaria-endemic area within the preceding month.

Blood samples were examined using thin smears and thick films (reference methods) for parasite detection and parasitemia quantification.

Serum CRP levels were measured by chemiluminescence (positivity threshold >5 mg/L).

Data were analyzed using Excel and R software (version 4.3.1).

Mean CRP values were compared using Student's t-test or the Mann-Whitney test, depending on data distribution. A p-value <0.05 was considered statistically significant.

Results

Demographic characteristics

The study included 816 suspected cases over seven years. The population was predominantly male, with 757 men (92.77%) and 59 women (7.23%), giving a sex ratio (M/F) of 12.8.

The mean age was 34.2±12.5 years (range: 18-65 years).

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Prevalence and parasitology

Microscopic examination confirmed malaria infection in 326 patients (40%).

The distribution of *Plasmodium species* showed a distinct pattern:

- Plasmodium falciparum: 40.8% (n=133)
- Plasmodium ovale: 36.81% (n=120)
- Plasmodium vivax: 15.03% (n=49)
- Plasmodium malariae: 7.06% (n=23)
- Mixed infections: 0.3%

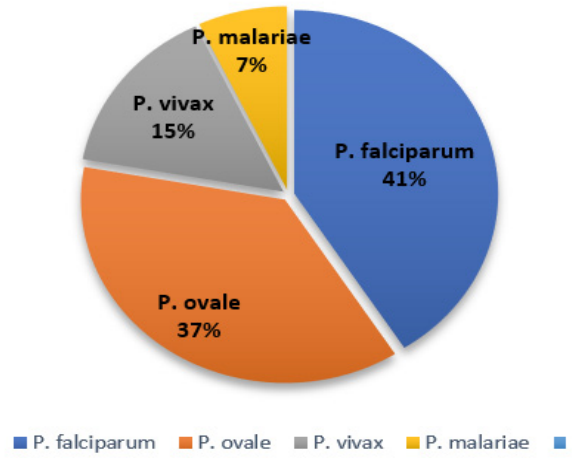

Figure 1: Distribution of plasmodium species among positive patients (n=326).
P. falciparum (40.8%), P. ovale (36.81%), P. vivax (15.03%), P. malariae (7.06%), and mixed infections (0.3%)

C-Reactive Protein (CRP) profile

Analysis of CRP levels revealed marked differences between patient groups:

- Among 269 malaria-positive patients with available CRP data, 85.39% (n=230) had CRP levels >5 mg/L.
- Distribution by range:
  - o 5-20 mg/L: 12.61%
  - o 20-50 mg/L: 23.48%
  - o 50-100 mg/L: 34.78%
  - o 100-200 mg/L: 21.30%
  - o 200 mg/L: 7.83%
- The mean CRP among malaria cases was 85.39±42.7 mg/L. Over half (56.08%, n=183) had CRP>50 mg/L, indicating severe inflammation.
- In contrast, non-malarial patients (n=490) had a significantly lower mean CRP of 56.79 mg/L (p<0.001).

Correlation with *Plasmodium* species and parasitemia

A detailed analysis showed significant relationships between CRP and infection parameters:

- **Variation by species**

P. falciparum infections had the highest CRP levels (98.2 mg/L), while P. ovale infections had lower values (71.5 mg/L, p<0.01).

- **Correlation with parasitemia**

A moderate but significant positive correlation was found between parasite density and CRP level (Pearson's r=0.45, p<0.001), suggesting that inflammatory intensity is proportional to parasite burden.

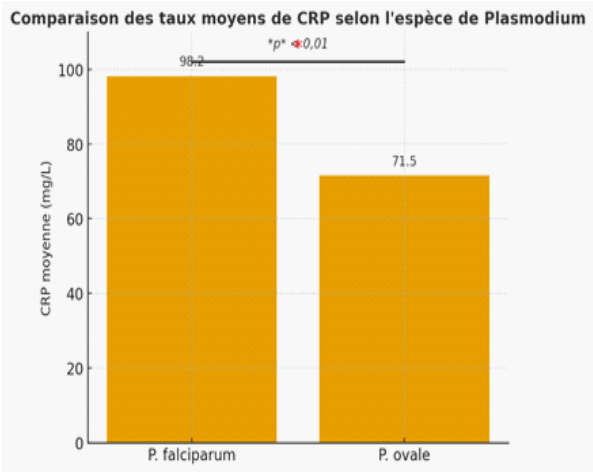

Figure 2: Comparison of mean CRP levels between patient groups.

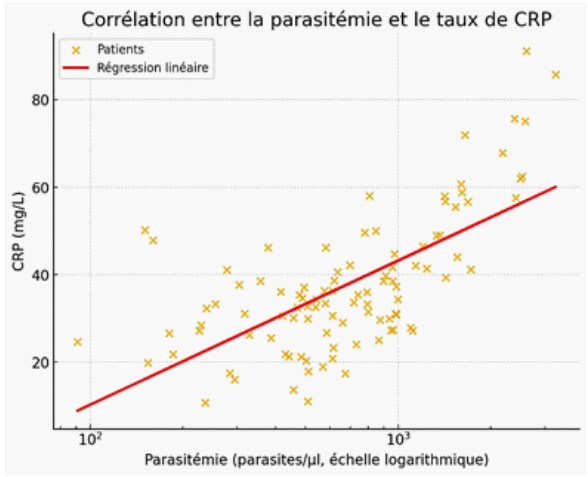

Figure 3: Correlation between parasitemia and CRP Level:

Discussion

This study confirms that imported malaria remains a frequent cause of fever in Morocco, with a 40% confirmation rate among suspected cases.

The predominance of P. falciparum and P. ovale reflects the travel patterns of patients, mainly from sub-Saharan Africa.

Our results clearly demonstrate that CRP elevation is highly frequent during malaria episodes, affecting 85.39% of confirmed cases. This aligns with pathophysiological data showing that CRP synthesis is triggered by pro-inflammatory cytokines (TNF, IL-1, IL-6) in response to Plasmodium antigens.

Table 1: Biological characteristics by malaria status.

Parameter	Malaria-positive (n=326)	Malaria-negative (n=490)	p-value
Mean CRP (mg/L) ± SD	85.39±42.7	56.79±38.9	<0.001
CRP>5 mg/L, n (%)	230/269 (85.39%)	280(57.14%)	<0.001
CRP>50 mg/L, n (%)	183(56.08%)	115(23.47%)	<0.001
Mean Parasitemia (parasites/µL)	12,450±18,500	—	—

Beyond being an inflammation marker, CRP acts as an opsonin, binding to parasitized erythrocytes and promoting their clearance via phagocytosis or complement activation.

Its kinetics, paralleling clinical evolution with a possible 24-hour delay, also makes it a valuable tool for monitoring therapeutic response.

The significantly higher mean CRP in malaria patients (85.39 mg/L vs. 56.79 mg/L; p<0.001) supports its use as a non-specific early warning marker.

Over half of malaria patients had CRP>50 mg/L, and nearly one-third exceeded 100 mg/L — consistent with the SPILF (French Infectious Diseases Society) guidelines reporting CRP >100 mg/L in most malaria cases.

Very high values (>200 mg/L), observed in 7.83% of cases, may indicate severe or complicated forms, as suggested by Kamgaing et al. and others.

We also demonstrated that CRP elevation correlates with both parasite species and parasitemia level, echoing findings from Monde AA et al. who proposed CRP as a potential severity indicator in malaria.

Our results are broadly consistent with global data, including Ndiaye et al. who reported CRP elevation in 96.5% of cases.

Nevertheless, CRP's major limitation is its lack of specificity.

Elevated CRP is seen in many bacterial and viral infections that represent differential diagnoses of imported malaria.

Thus, while CRP has an excellent negative predictive value, it cannot be used as a standalone diagnostic test.

Conclusion ET perspectives

In summary, this study conducted in a non-endemic Moroccan setting confirms the relevance of CRP as an early and sensitive alert marker in the management of imported malaria.

Its frequent elevation, and correlation with parasite species and density, should prompt clinicians to urgently perform parasitological testing in any febrile patient returning from endemic regions.

CRP measurement thus represents a valuable and accessible diagnostic tool, guiding clinicians toward microscopic confirmation.

Nevertheless, definitive diagnosis relies on microscopy (thin/thick smears) or rapid diagnostic tests, which identify the *Plasmodium* species and quantify parasitemia.

Future work should include

- Determining the optimal CRP threshold for imported malaria using ROC curve analysis.
- Assessing correlations between CRP and clinical severity markers (organ failure, complicated malaria).
- Integrating CRP into prospective decision algorithms combining clinical and biological parameters to optimize and accelerate malaria diagnosis.

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