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Dynamics of ACT parasite clearance in falciparum malaria among a cohort of inhabitants in a malaria hyper-endemic focus, Ilorin Nigeria

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Introduction

- Despite global mass scale-up of interventions in malaria elimination, *falciparum* malaria still remains a significant public health issues in Nigeria (Shekarau *et, al*., 2024).

- Resistance to Artemisinin combination therapy (ACT) potentiates a delayed parasite clearance time (Alvarez *et. al*., 2022).

- Clearance of parasitaemia occurs 72hours post ACT regimen, except in situations of concomitant resistance to ACT partner drugs (GMP, 2016).

- The anti-malarial effect of ACT is best determined by the slope of the log-parasitaemia versus time (Flegg *et. al*., 2011; White, 2011)

Methods

- **Study Area**: This research was conducted in Ilorin among febrile/afebrile in-patients attending public health centres.

- **Study Design**: A follow-up research to assess the efficacy of ACT in treating clinical *P. falciparum* malaria. Volunteer patients were given free ACT medications after establishing clinical malaria and were enrolled for a participatory study to monitor parasite clearance over a 28day period.

- Following ACT treatment, thin and thick blood films were examined at these periods, 0, 24hrs, 48hrs, 72hrs and 28days post treatment. This was done to record parasitaemia decrease over the 72hrs therapy period and until two consecutive blood slides tested negative.

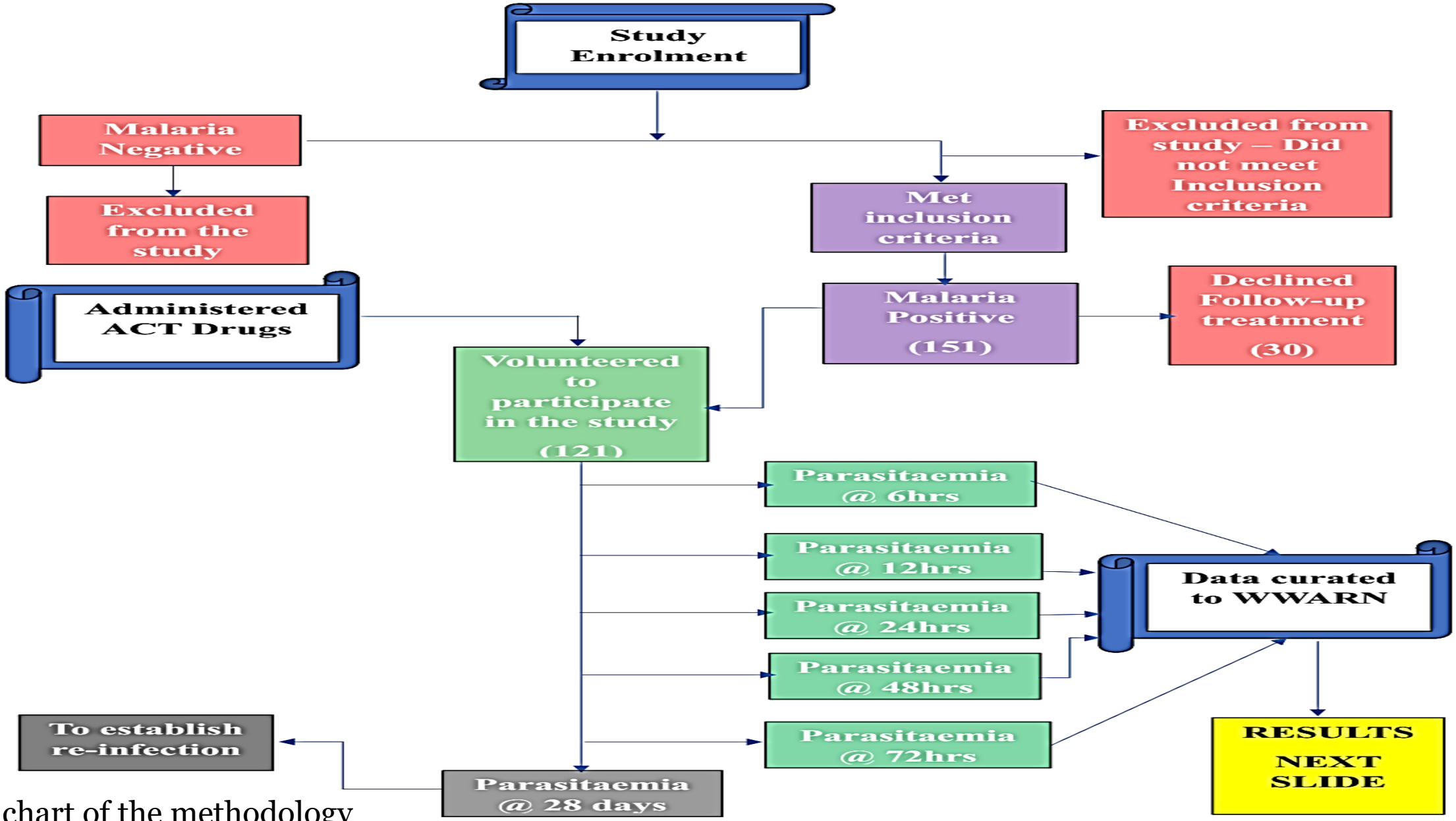

Fig. 1: Flow chart of the methodology

Algorithm used for model fitting

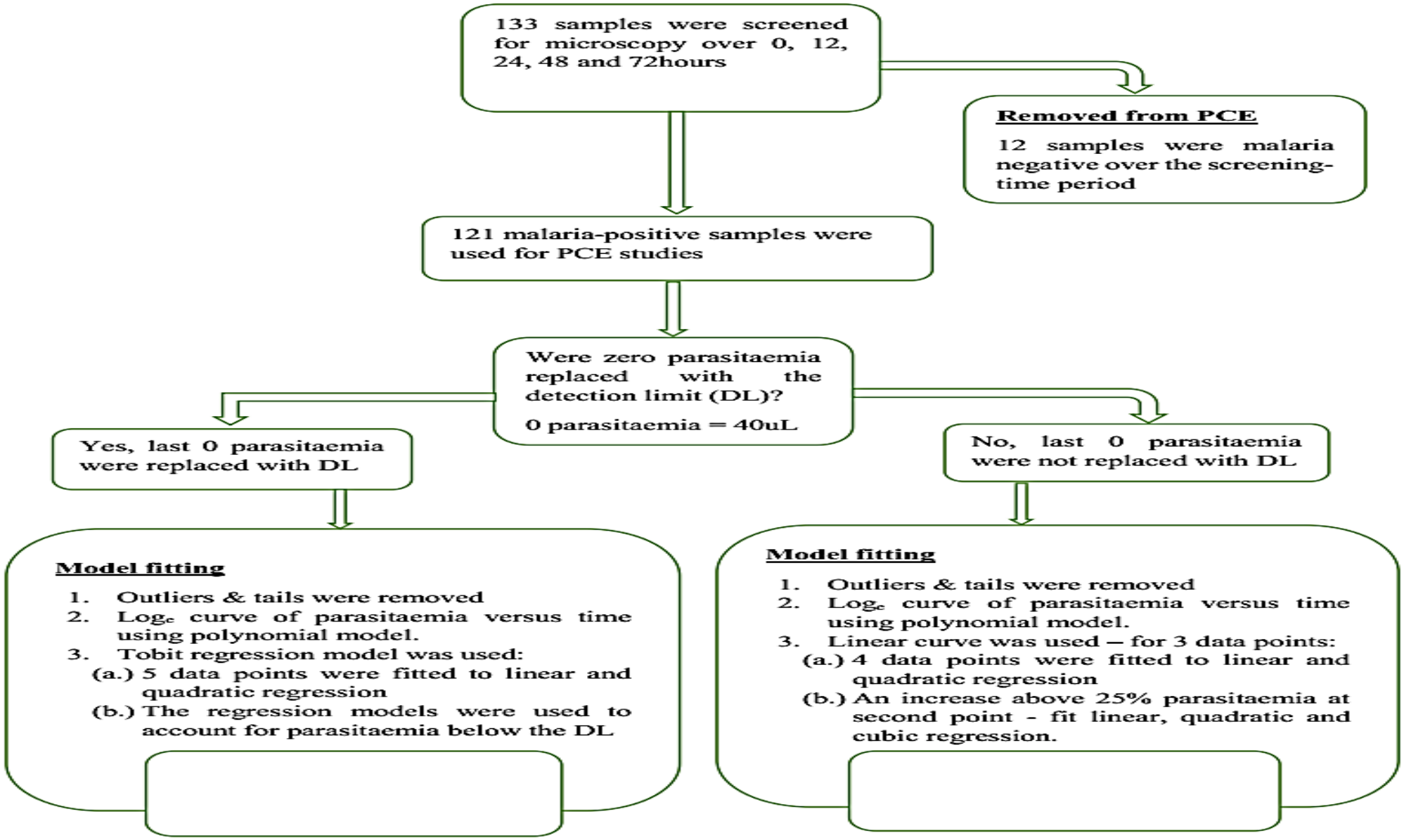

Figure 2: Flow chart of the models tested for establishing the best PCE over 72 hours for each individuals sampled

Results

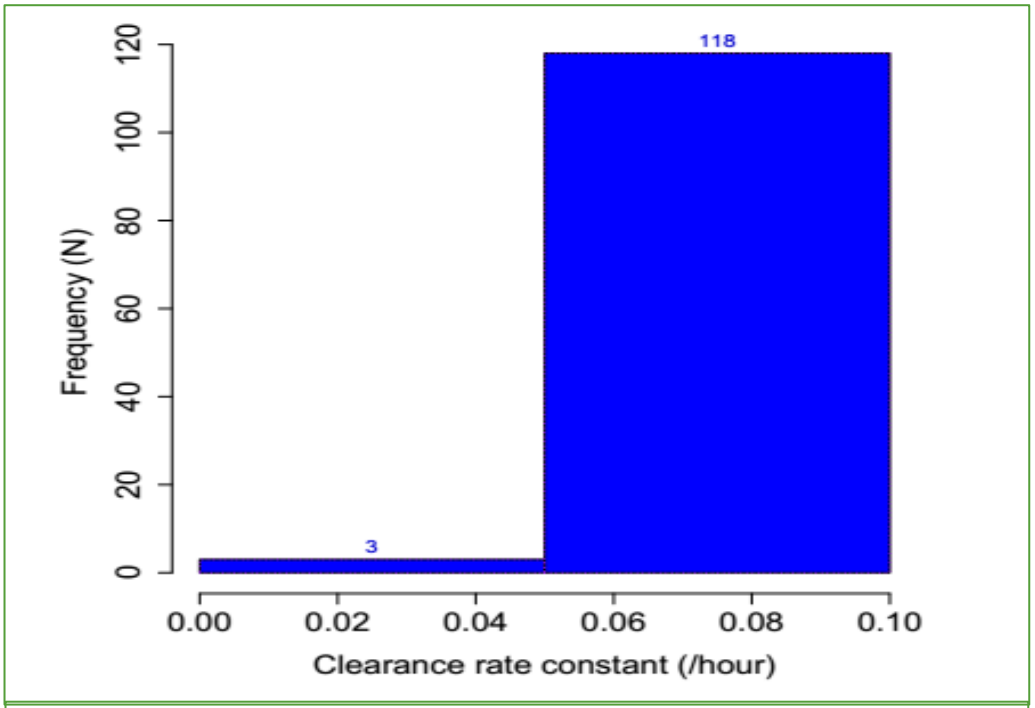

Figure 3: Distribution of clearance rate constant

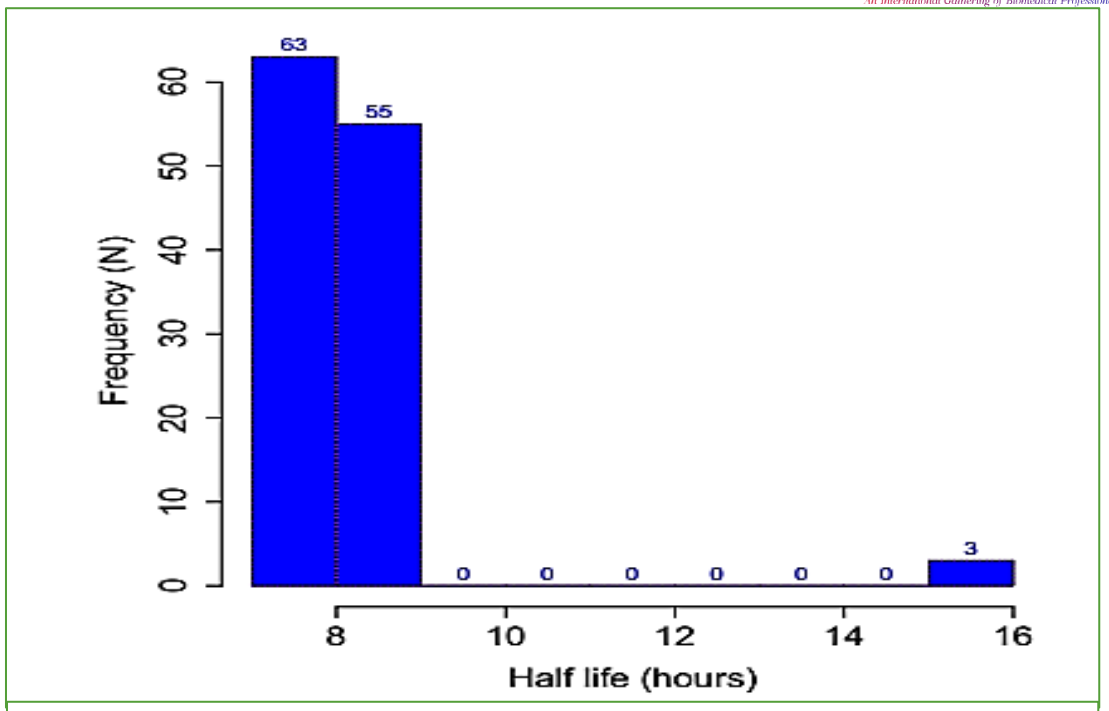

Figure 4: The distribution of the slope half-life/hour

Table 1: Duration of lag phase and percentage summary to clear parasitaemia (hours)

Parameters	No.	Median	Range: mini – maximum	IQR: 25 – 75Th centile
Profiles with lag phase	10	12.00	12.00 – 12.00	12.00 – 12.00
PC50		13.30	11.86 – 16.78	13.21 – 13.34
PC90		32.00	30.75 – 47.79	31.53 – 33.08
PC95		40.06	38.23 – 63.26	39.38 – 41.19
PC99		58.20	55.59 – 99.19	57.55 – 60.74

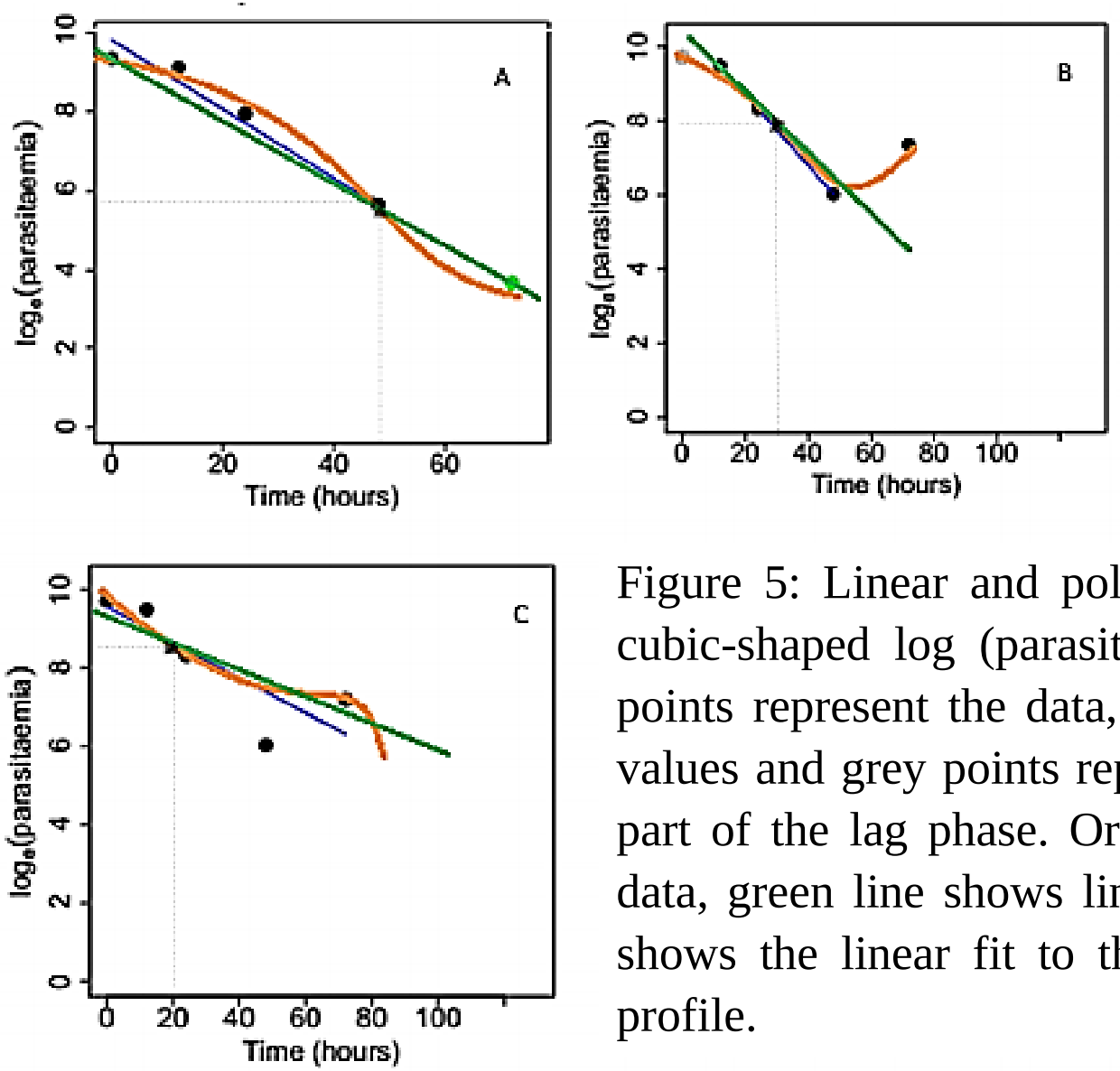

Figure 5: Linear and polynomial fits to the quadratic or cubic-shaped log (parasitaemia)-time profiles. The black points represent the data, green points represent censored values and grey points represent points identified as being part of the lag phase. Orange line shows cubic fit to the data, green line shows linear fit to the data and blue line shows the linear fit to the identified 'linear part' of the profile.

Discussion

- The exact determination of parasite clearance is essential to substantiate the spread of ACT resistance in malaria endemic populations.
- The study observed a clearance rate constant of 2.48% with parasitaemia after 72 hours post ACT regimen, a far cry from an early study where clearance rates were faster in high-transmission settings (Stepniewska *et al.*, 2011).
- The decline in parasite density was exponential, and similar to a first-order process, which is an indication that PCT was also directly proportional to the logarithm of the initial parasite count (Radohery, 2022)
- The slope of the log-parasitaemia with respect to timing was significant, the time frame from first ACT administration showed that over half of the samples (63, 52.07%) had more than 50% reduction in parasitaemia within the first 9 hours(Schneider *et al.*, 2023).

- The slope half-life observed in the present findings is useful for assessing resistance to ACT drugs acting on the ring stage parasites *in vivo* and it correlates best with heritability or at best with splenic clearance (Hastings *et al.*, 2015).
- In an earlier study, parasite clearance half-life in Ilorin, Nigeria was estimated at ≤5 hr. and a slight departure in Faladje, Mali with 2-8 hr. although the drug of choice was Artesunate (Ashley *et al.*, 2014; Kone *et al.*, 2020).
- Our findings on median PCT revealed that about 50% parasitaemia was cleared within 13.30 hours of ACT treatment at PC50 (IQR: 13.21-13.34) and by PC99 parasitaemia was cleared at 58.20 hours (IQR: 57.55-60.74) similar to Kone *et al.*, 2020.

Conclusion

- The delay in parasite clearance rate reported in this study does not point to the emergence of ACT resistance because the research did not identify phenotypic markers (Kelch 13) of parasite resistance as identified in other environs. The age and difference in host immunity along with the multiplicity of infection of the ring stage developing at different time may also have contributed to the delayed PCT.
- The minus slope of the Tobit regression revealed three models, viz; best fit at 50hours (Type I); 30hours (Type II) and 20hours (Type III).

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