



**RESEARCH ARTICLE**

**AN OBSERVATION ON THE EFFICACY AND OUTCOME OF ARTESUNATE VERSUS QUININE THERAPY IN COMPLICATED MALARIA PATIENTS: A HOSPITAL BASED STUDY**

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**ABSTRACT**

**Aim:** Our study was compared the efficacy and outcomes in artesunate in relation to quinine therapy in complicated malaria in reference to clinical and biochemical profile in children.

**Material & methods:** A total of 100 patients of complicated malaria due to *P. falciparum* were selected randomly into 2 groups. Group 1 – was given I.V. Quinine dihydrochloride 20 mg/kg (loading dose) in 10ml of isotonic fluids/kg by infusion over 4hours then 12 hours after the start of loading dose, a maintenance dose of 10mg salt/kg was given I.V. over 4 hours, every 8 hourly, until the patient could swallow, then quinine tab, 10mg/kg 8 hourly to complete 7 day course of treatment. Group 2 – was given I.V. artesunate 2.4 mg/kg dose at 0, 12 and 24 hours, then once a day for total 7 days. Supportive care like antibiotics, antipyretics, anticonvulsants, intravenous fluids, blood transfusion etc were given as and when required. The patients were assessed for:- Fever Clearance Time (FCT) in hours and Coma Resolution Time.

**Results:** The patients on quinine 50% developed nausea, 24% vomiting, 36% headache, 18% tinnitus, 8% vertigo, 4% hypoglycemia, 4% slurring of speech and 2% circulatory failure. Those patients who were treated with artesunate, only 4% developed nausea and 2% slurring of speech.

**Conclusions:** There is significant difference between the effectiveness of artesunate therapy and quinine therapy to clinical improvement of malaria children i.e artesunate is a better drug in complicated malaria in terms of clinical improvement and tolerability.

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**INTRODUCTION**

Malaria imposes great socioeconomic burden on humanity, affecting over 40-50 % of world population. Prevalence of malaria is estimated to be around of 124 million to 283 million people in world with a global death rate of estimated 584 000 per year.<sup>[1]</sup> In Asia maximum incidence is from South East Asian Region, among them is India. In India the prevalence of malaria has dropped from 1.6 million in 2010 to 1.07 million in 2014 but still it is a large number of cases.

*P. falciparum* is responsible for the most severe, complicated often fatal form of the disease. Multiple manifestations can occur singly or more commonly in combinations in the same patients. The recent rise in the incidence of malaria has been associated with the spread of drug resistant strains of *P. falciparum*. Chloroquine is now ineffective in many parts the world including Asia and South America and resistance to drug is emerging in Asia. Because of the emergence of resistance to

quinine, its effectiveness is declining in most parts of Africa and South East Asia.

Thousands years ago, quinghao (Sweet wormwood) was in use in China as a herbal remedy for fever. But during 1970s the Chinese scientists indentified the active antimalarial ingredient, quinghaosu (Extract of quinghao) or artemisinin. Since 1979 several derivatives have been synthesized and studied in China. Artemisinin compounds have shown great promise. Klayman Dh. Reported in 1985 in New England Journal of Medicine that derivatives of leafy portion of the plant *Artemisia annua*, a traditional Chinese medicine used for centuries as antimalarial drug in rural patients very rapidly restores the consciousness level in patients of cerebral malaria. Artemisinin suppositories, artesunate (oral or parenteral), intramuscular artemether and dihydroartemisinin tablets have all proved rapidly effective. Taylor *et al* and Murphy *et al* in their study of cerebral malaria in Malawian children and African children respectively had noted rapid coma resolution and parasite clearance with artemether compared to those treated with quinine.[2,3] Thus

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the aim of this study is to compare the efficacy of quinine and artesunate with reference to clinical and biochemical profile in children with severe malaria.

Malaria has been known and described since the times of Hippocrates in the fifth century B.C. Charaka and Sushruta gave vivid descriptions of disease associated with the bites of mosquitoes. It was Lancisi (1717), who linked malaria with poisonous vapours of swamps and thus came with the name 'malaria' meaning bad air. In 1880, Laveran, a French Physician working in Algeria, first identified the causative agent for human malaria while viewing blood slides under microscope.

There are four different species of genus plasmodium, namely plasmodium falciparum, P. vivax, P. malariae and P. ovale. Golgi identified P.vivax and P. malariae in 1885. P. falciparum was identified by Sakharov (1889) and Marchiafava and Celli (1890). In 1894, Manson hypothesized that mosquitoes transmit malaria, after that in 1897, Ronald Ross, a young Scottish Physician identified the anopheles mosquito as the vector of human malaria. Both Ross and Laveran received Nobel Prize for their respective discoveries.

In 1939, Paul Muller discovered the insecticidal properties of DDT. In 1948, Sweatt and Garnham discovered the tissue phase in monkey malaria which was soon established for human malaria.

According to WHO Regional publication of South East Asia Series no.9, P.falciparum and P.vivax account for more than 95% of the cases of malaria in the South East Asian region. In 1970, nearly 20% of confirmed cases were due to P.falciparum. However during subsequent years, P. falciparum showed a downward trend and in 1977 the percentage of P. falciparum was 12.90% of all confirmed cases of malaria. In 1987 and 1988 the same data stood at 38% and 37% respectively in the South East Asian Region. In India also percentage of P. falciparum cases decreased from 1.14 million in 1995 to 0.65 million in 2011.

P. falciparum causes multiple organ damage by heavy parasitisation of red cell, (usually in excess of 5%) which became sticky, deformed and adhere on the capillary endothelium in internal organs and get sequestered there and cause anoxic inflammatory damage to it.

The sequestration is greatest in brain which explains the coma in cases of P. falciparum malaria. Quinine is still very effective but studies in Bangkok Hospital for Tropical Diseases by Pukrittaya kamee J *et al* and elsewhere have shown a declining efficacy and delayed response to quinine.<sup>[4]</sup> Recent years have witnessed the increasing use of artemisinin derivatives (mainly artesunate) in the treatment of severe malaria.

The aim of the study was to compared the efficacy and outcomes in artesunate in relation to quinine therapy in complicated malaria, in reference to clinical and biochemical profile in children.

## METHOD AND MATERIALS

Subjects: A total of 100 subjects were selected on the basis of inclusion and exclusion criteria after signing the informed consent from guardian or attendant of patients, (50 for Quinine dihydrochloride therapy and 50 for artesunate therapy).

Subjects included were patients of complicated malaria caused by plasmodium falciparum recruited at pediatric unit of Katihar Medical Collage under department of Pediatrics after approval from the institutional ethical committee of Katihar Medical College & Hospital, Katihar was sought. Subjects meeting inclusion and exclusion criteria were selected for the study. They were informed in detail about the type and nature of the study, the consent was taken prior to the study. Design of Study: Prospective. Setting of Study: Hospital based study. Subject of Study: 100 cases of complicated malaria admitted in Department of Pediatrics, KMCH, Katihar. Cases will be proved as malaria by: Leishman stained peripheral blood smear – thick and thin smear film. Other investigation to detect concomittent complications and rule out other diseases with similar presentation. TC, DC of WBC, Hb%, IgM Anti-Pv, Pf, Serum Bilirubin- Total ,Direct ,Indirect Serum Enzyme Levels-SGPT,SGOT,ALP, CSF analysis to rule out meningitis, Chest X-ray PA view to know presence or absence of pulmonary edema and rule out other diseases., ECG after administration of drugs, Plasma glucose level random. Patient were assessed for (FCT) fever clearance time in hours, (CRT) Coma Resolution time, (PCT) Parasite Clearance Time in hours, Toxicity of Drugs, Neurological sequele in survivors, Mortality. Thick Film: A drop of blood placed at center of slide and immediately a glass slide is placed and drop is then spread quickly, The thickness of the film should be such as to allow newsprint to be read or hands of wrist watch to be seen through the dry preparation, The film is air dried or dried in an incubator. Thin film: A drop of blood (not larger than a pin head) is placed in the centre line of a slide about 1-2cm from one end, Immediately a glass slide is placed (spreader) with smooth edge at an angle of about 45° to the slide and moved back to make contact with the drop of blood, The drop is then spread out quickly along the line of contact of the spreader with the slide, A good thin film has following characteristics: Surface of the film is even and uniform, Margins of the film do not extend to the sides of the slide, The 'tails' end near about the centre of the slide, It consists of single layer of red cells, The film is dried and stained with Leishman's stain. Leishman's stain & method for parasite count: A thick & thin blood films were made from each patients. The films were dried and stained in the following way: The dried thick film was dehaemoglobinised by dipping in a glass cylinder containing distilled water for 5-10 minutes before staining with Leishman's stain. Dried thin film was directly stained with Leishman's stain, The dried film was placed on a staining rack, flooded with Leishman's stain and left for 1-2 minutes to fix, Two volumes of buffered distilled water (pH 7.2) were added drop by drop over the smear, The stain was then left for 10 minutes, The stain was then washed under tap water and dried in air, Slide was viewed under oil immersion microscope for identification of the parasite, Thick and thin smears were seen. Thick smear used to show the presence of parasite, Thin smear

was used for parasite count. Level of parasitemia was expressed as the number of parasitized RBCs per 1000 RBCs. This figure was then converted to number per microlitre of blood. Other investigations were done to detect concomitant complications and to rule out other diseases with similar presumptions. TC, DC of WBC, Hb% Blood urea, Serum Creatinine, Serum bilirubin- total, direct; SGPT, SGOT, Alkaline Phosphatase, CSF analysis to rule out meningitis, R/E of urine for proteinuria, RBC & casts, ECG after administration of drugs, X ray Chest PA view- to know the presence or absence of pulmonary oedema & rule out any other disease, Plasma glucose (R). Criteria for Exclusion: The case having no asexual form of *P. falciparum* in the peripheral smear were not taken into study, The cases showing multispecies forms of malaria parasite in peripheral smear were not taken into study, Patients with know G6PD deficiency were not taken into study, Hepatitis due to other causes. Renal failure due to other causes.

**Group 1** – was given I.V. Quinine dihydrochloride 20 mg/kg (loading dose) in 10ml of isotonic fluids/kg by infusion over 4hours then 12 hours after the start of loading dose, a maintenance dose of 10mg salt/kg was given I.V. over 4 hours, every 8 hourly, until the patient could swallow, then quinine tab, 10mg/kg 8 hourly to complete 7 days course of treatment.

**Group 2** – was given I.V. artesunate 2.4 mg/kg dose at 0, 12 and 24 hours, then once a day for total 7 days. Supportive care like antibiotics, antipyretics, anticonvulsants, intravenous fluids, blood transfusion etc were given as and when required. The patients were assessed for: Fever Clearance Time (FCT) in hours – Defined as the period from administration of first dose of antimalarial drug till the axillary temperature remained at or below 37°C for 72 hours. Coma Resolution Time (CRT) – Defined as time taken from the start of therapy till the patient had become fully conscious, and responded to verbal commands. Parasite Clearance Time (PCT) in hours – Defined as time taken from administration of first dose of antimalarial drug till parasites were undetectable in peripheral blood films and remained so for 7 days. Toxicity of drugs – Hypoglycemia, neurotoxicity, cardiotoxicity etc. Neurological sequelae in survivors. Mortality. Patients were followed up in the hospital at regular intervals. Their clinical examinations were done twice daily. Vitals were monitored 4 hourly, blood for malaria parasite was tested 8 hourly. Patients were discharged from hospital after completion of treatment, with instructions for follow-up in the outpatient clinic on day 14, 21, and 28. During these visits patient clinical status were assessed and blood samples were collected for hematological and biochemical test.

### Statistical Analysis

The data was analyzed by using the SPSS 18 software. The results were taken to be significant if  $P < 0.05$ .

### Observation

Table 1 to 8 details the result of present study. Table 1 shows the Median Coma Clearance Time for Quinine = 52.95 hours, Median Coma Clearance Time for Artesunate = 40.64 hours. The results show faster coma clearance time in patients treated with artesunate (40.64 hours) than the patients treated with quinine (52.94 hours),  $p < 0.05$ . Table 2 shows the Median fever

clearance time for quinine = 63.78 hours, Median fever clearance time for artesunate = 49.66 hours, Fever clearance time for artesunate (49.66 hrs) is better than for quinine (63.78 hrs). In quinine group 66% patients became afebrile by 72 hours while in artesunate group, 86% became afebrile by 72 hours. Table 3 shows the Median Parasite Clearance Time for quinine = 54.70 hours, Median Parasite Clearance Time for artesunate = 42.88 hours. The above results shows that Parasite clearance time for artesunate was (42.88 hrs) which is lower than for quinine which was (54.70 hrs) ( $p < 0.05$ ). It shows that 82% slides were clear of parasite within 72 hours in cases treated by artesunate. Only 72% slides were clear of parasite in cases treated with quinine within 72 hours. Table 4 shows that there is definite improvement of renal function in both groups, but the difference of improvement was not statistically significant ( $p > 0.05$ ). Renal function is assessed on the basis of blood urea and serum creatinine. Both were estimated before treatment (BT) and after treatment (AT). Table 5 shows the The table the value of serum bilirubin and SGPT level before and after treatment with quinine and artesunate does not vary significantly. Improvement in liver function test is significant difference after treatment with both quinine and artesunate group ( $p > 0.05$ ). Table 6 shows that, in patients with MGCS  $< 7$  mortality was 34.30% and the statistical difference between quinine and artesunate was not significant ( $p > 0.05$ ). In patients with MGCS (7-10), only two died in quinine group whereas none in artesunate group. There was only one mortality in patients treated with quinine, and having MGCS  $> 10$ , while none died in artesunate group with MGCS  $> 10$ . Table 7 shows that majority of the deaths were in patients presenting with features of cerebral malaria and anaemia in both groups. While one mortality in quinine group was associated with ARF, along with the features of coma and anaemia; one died due to associated shock and coma; one with features of DIC. In cases treated with artesunate, one mortality was due to severe anaemia and one due to associated coma with anaemia and jaundice. Table 8 shows that of the patients on quinine 50% developed nausea, 24% vomiting, 36% headache, 18% tinnitus, 8% vertigo, 4% hypoglycemia, 4% slurring of speech and 2% circulatory failure. Those patients who were treated with artesunate, only 4% developed nausea and 2% slurring of speech. This shows that the incidence of side effects with quinine therapy is definitely higher but was of milder form i.e. cinchonism. Whereas the incidence of side effect in artesunate group was insignificant and was of milder form.

### DISCUSSION

In the present study 100 cases of complicated malaria were selected on the basis of clinical features and laboratory confirmation of *Plasmodium falciparum* in thick and thin smears of blood film, from the patients admitted in the Department of Pediatrics, KMCH, Katihar, Bihar, India. The level of consciousness was assessed using Modified Glasgow Coma Scale for infants and children. It was found that 24% cases were conscious at the time of admission (MGCS = 15,) while 76% cases were either unconscious (35%) with MGCS  $< 8$ , or in altered sensorium (41%) with MGCS  $> 8$  but  $< 15$ . The may be due to high parasitemia or high antigenic load, resulting in observation of microvasculature and CNS involvement (Table-1).

**Table 1** Coma Clearance Time in Hours, in patient treated with Quinine & Artesunate (n=100)

Sl. No.	Time in Hrs	Quinine		Artesunate	
		No. of cases	%	No. of cases	%
1.	6 – 24 hours	3	8.82	6	18.75
2.	24 – 48 hours	9	26.47	14	43.75
3.	48 – 72 hours	22	64.70	12	37.50
	Total	34	100	32	100

The pattern of haemoglobin distribution was also studied and it was found that out of 100 cases under study, only 8% had haemoglobin level >10 gram/dl, 37% had haemoglobin level between 7 – 10 gram/dl, while majority (55%) of patients had haemoglobin level <7 gram/dl (**Table-2**). The degree and severity of anaemia may be due to obligatory destruction of parasitized as well as non parasitized RBC. The anaemia further may be compounded by dyserythropoietic bone marrow and shortened red cell survival in malarial infection. The finding was comparable with the finding of Biemba G, et al., 2000.<sup>[5]</sup>

**Table 2** Fever Clearance Time in hours in patient treated with Quinine & Artesunate (n=100)

Sl. No.	Time in hours	Quinine		Artesunate	
		No. of Cases	%	No. of cases	%
1.	24 – 48 hours	3	6	21	42
2.	48 – 72 hours	28	56	22	44
3.	72 – 96 hours	9	18	3	6
4.	96 – 120 hours	4	8	0	0
5.	Death	6	12	4	8
6.	Total	50	100	50	100

It was found that most cases recovered within 72 hours or succumbed to their illness. Coma resolution time varied from 6 to 72 hours for both the groups of patients receiving quinine (median = 52.95 hours) and artesunate (median = 40.64 hours). Maximum number of patients recovered within 24–48 hours in artesunate group (43%), while only 26% in quinine group (**Table-3**). This clearly shows that coma resolution time was faster in patients treated with artesunate than with quinine. This work corresponds to the work of Mohanty A.K et al. 2004, who reported a coma clearance time in 40 patients treated with quinine to be  $70.15 \pm 17.56$  hrs, and  $50.4 \pm 31.49$  hrs in 40 patients treated with artesunate respectively.<sup>[6]</sup>

**Table 3** Parasite Clearance Time in hours in Patient treated with Quinine & Artesunate (n=100)

Sl. No.	Time in hours	Quinine		Artesunate	
		No. of cases	%	No. of Cases	%
1.	6 – 24 hours	0	0	2	4
2.	24 – 48 hours	16	32	26	52
3.	48 – 72 hours	20	40	18	36
4.	72 – 96 hours	8	16	0	0
	Death	6	12	4	8
	Total	50	100	50	100

The significant less coma resolution time in patients treated with artesunate could be due to its rapid schizonticidal effect leading to inhibition of cytokines and ultimately release of nitric oxide (which is neurotoxic). Also it prevents the rosette formation in the cerebral circulation. Taylor et al, 2004<sup>[7]</sup> in their study of cerebral malaria in Malawian children and Salako

et al 1989,<sup>[8]</sup> in a study of cerebral malaria in Nigerian children had found similar results with artesunate.

Faster fever clearance time was noted with artesunate (median = 49.66 hours) than with quinine (median= 63.78 hours) (**Table-4**). This work corresponds to the work of Li G.Q. et al. 1994, in China who reported the fever clearance time with quinine to be  $63 \pm 40$  hrs.<sup>[9]</sup> and with artemisinin derivatives to be  $30 \pm 22$  hrs. The significantly lower fever clearance time for artesunate could be due to its rapid schizonticidal effect leading to suppression of cytokines and TNF- production, which are responsible for fever.

**Table 4** Renal Function Test on the basis of blood urea & serum creatinine. (N=13)

Group	No. of cases	Mean Blood Urea mg%		Mean Serum Creatinine mg/dl	
		BT	AT	BT	AT
Quinine	7	99.95	38.15	3.17	2.14
Artesunate	6	98.10	38.53	3.43	2.36

The parasite clearance time was significantly less in artesunate group (median=42.88 hours) as compared to quinine group (median = 54.7 hours), (**Table – 5**).

**Table 5** Liver Function Test on the basis of serum bilirubin & SGPT LEVEL (n=19)

Group	No. of cases	Mean Serum Bilirubin (mg/dl)		Mean SGPT(IU/I)	
		BT	AT	BT	AT
Quinine	10	3.87	2.17	93.3	60.2
Artesunate	10	3.67	2.07	92.7	57.6

This work corresponds to the work of Mohanty A.K, et al (2004)<sup>[6]</sup> who found that the parasite clearance time with artesunate was  $41.67 \pm 16.78$  hrs, as compared to quinine which was  $52.24 \pm 12.69$  hrs. There was definite improvement of renal function and liver function after treatment with quinine and artesunate groups, but the difference of improvement was not statistically significant (**Table 6 & 7**). Toxicity and side effects of drugs were much less in patients taking artesunate than those taking quinine. This corresponds to the work of Cae-Xuan-Thanh-Phoung, et al 1997.<sup>[10]</sup> In Quinine treated group side effects like nausea (50%), vomiting (24%), headache (36%), tinnitus (18%), vertigo (8%), circulatory failure (2%), slurring of speech (4%) and hypoglycemia (4%) were observed, whereas no significant side effect was observed in artesunate group except for slurring of speech in one case and nausea in two cases. Price R et al.1999, had similar observation that quinine was associated with a wide range of common side effects at therapeutic drug concentration, whereas artesunate had none.<sup>[11]</sup>

Mortality in relation to GCS showed better survival rate in all patients treated with both artesunate and quinine. Six patients died in quinine group and 4 patients in the artesunate group, but the difference was not statistically significant (**Table – 8**). The mortality was highest with MGCS <7. Mortality with GCS between 7-10 and >10 were 30% and 10% respectively. The result of the present study has supported the results of the above mentioned worker.

**Table 6** Mortality in relation to Modified Glasgow Coma Scale (n=100).

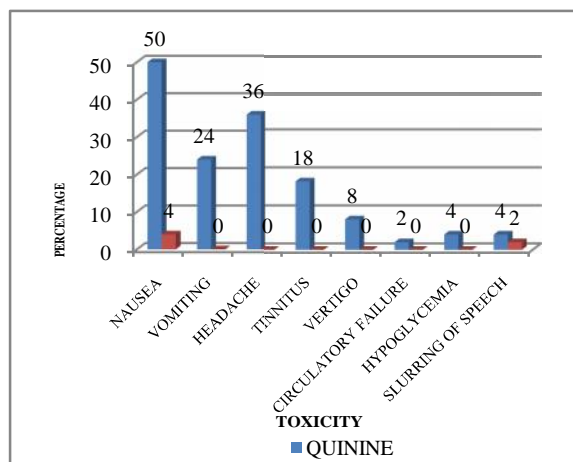
Sl. No.	MGCS	Quinine group					Artesunate group				
		No. of cases	No.		%	D	No. of cases	No.		%	D
			S	D				S	D		
1.	<7	18	15	3	83.34	16.66	17	14	3	82.36	17.64
2.	7 – 10	19	17	2	89.48	10.52	23	22	1	95.66	4.34
3.	>10	13	12	1	92.31	7.69	10	10	0	100.0	0.00
	Total	50	44	6	88	12.00	50	46	4	92.0	8.00

**Table 7** Mortality in relation to clinical manifestations (n=10)

Sl. No.	Presentation	Quinine group	Artesunate group
1.	Anaemia only	0	1
2.	Cerebral malaria + anaemia	3	2
3.	Cerebral malaria + anaemia + jaundice	0	1
4.	Cerebral malaria + anaemia + ARF	1	0
5.	Cerebral malaria + anaemia+shock	1	0
6.	DIC	1	0
	Total	6	4

**Table 8** Side effects of drugs in treatment of complicated malaria (n= 50).

Sl. No.	Toxicity	Quinine		Artesunate	
		No. of cases	%	No. of cases	%
1.	Nausea	25	50	2	4
2.	Vomiting	12	24	0	0
3.	Headache	16	36	0	0
4.	Tinnitus	8	18	0	0
5.	Vertigo	4	8	0	0
6.	Circulatory failure	1	2	0	0
7.	Hypoglycemia	2	4	0	0
8.	Slurring of speech	2	4	1	2



**Figure 2** Side effects of drug in treatment of complicated malaria

**Clinical Implication**

This study has shown that artesunate is a better drug in complicated malaria in terms of clinical improvement and tolerability. Artesunate therapy is to be a promising method for treatment of complicated malaria patients, which was found to be more effective than quinine therapy. Thus, earlier application of such treatment methods can prove very crucial in preventing the mortality of complicated malaria children patient, so that a good quality of life can be enjoyed by our patients. Hence, this novel treatment must be inculcated into our treatment program to gain maximum benefit for the patients.

**CONCLUSION**

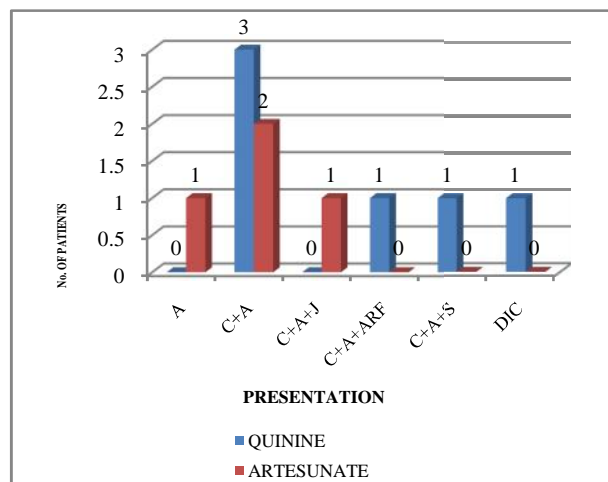
The findings of this study concluded that the artesunate is a better drug in complicated malaria caused by Plasmodium Falciparum in terms of clinical improvement and tolerability than quinine dihydrochloride therapy.

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**Bibliography**

1. WHO, Factsheet on the World Malaria Report 2014.
2. Taylor TE, Willis BA, Kazembe P *et al.* Rapid coma resolution with artemether in Malawain children with cerebral malaria. Lancet 1993; 341: 661-2.



**Figure 1** Correlation of mortality with clinical manifestation.

A = Anaemia, J = Jaundice, DIC = Disseminated intravascular coagulation, C = Cerebral malaria, ARF = Acute Renal Failure.

Paul Newton, *et al.* 2003 reported that mortality was 12% with artesunate and 22% with quinine.<sup>[12]</sup> Among the cases who succumbed to illness, presented with complication of falciparum malaria like cerebral malaria, severe anaemia, Acute renal failure, shock and DIC.

With the present study we found that artesunate is a better drug in complicated malaria in terms of clinical improvement and tolerability.

3. Murphy S, Watkins WM, Bray PG. Parasite viability during treatment of severe falciparum malaria: differential effects of artemether and quinine. *Am J Trop Med Hyg.* 1995;53:303–305. [PubMed]
4. Pukrittayakamee S, Supanaranond W, Looareesuwan S, Vanijanonta S, White NJ. Quinine in severe falciparum malaria: evidence of declining efficacy in Thailand. *Trans R Soc Trop Med Hyg.* 1994 May-Jun;88(3):324-7[PubMed]
5. Biemba G; Dolmans D; *et al.* Severe anemia in Zambian children with *P. falciparum* malaria – *Trop. Med. Int Health* 2000 Jan.
6. Mohanty AK, Rath BK, Mohanty R, Samal AK, Mishra K. Randomized control trial of quinine and artesunate in complicated malaria. *Indian J Pediatr.* 2004 Apr;71(4):291-5.
7. Taylor WR, White NJ. Antimalarial drug toxicity: a review. *Drug Safety,* 2004, 27:25-61.
8. Salako LA, Sowunmi A, Akinbami FO. Pharmacokinetics of quinine in African children suffering from kwashiorkor. *British Journal of Clinical Pharmacology,* 1989, 28:197-201.
9. Li GQ, Guo XB, Fu LC, Jian HX. Clinical trials of artemisinin and its derivatives in the treatment of malaria in China. *Trans R Soc Trop Med Hyg* 1994, 88 Suppl 1:S5-6.
10. Bethell DB *et al.* Pharmacokinetics of oral artesunate in children with moderately severe *Plasmodium falciparum* malaria. *Transactions of the Royal Society of Tropical Medicine and Hygiene,* 1997, 91:195-198.
11. Price R *et al.* Adverse effects in patients with acute falciparum malaria treated with artemisinin derivatives. *American Journal of Tropical Medicine and Hygiene,* 1999, 60:547-555.
12. Paul N. Newton, Brian J. Angus, Wirongrong Chierakul, Arjen Dondrop, Ronatrai R, K. Silamut, P. Teerapong, Yupin S, Sornchai L, and N. J. White. Randomized comparison of artesunate and quinine in the treatment of severe falciparum malaria. *Clin. Infect Disease,* Vol 37 (2003), Pg: 7 – 16.

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