Ernstige malaria

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Jaarvergadering NVP

Disclosure belangen spreker

Geen (potentiële) belangenverstrengeling	
Voor bijeenkomst mogelijk relevante relaties[1]	Bedrijfsnamen
• **Sponsoring of onderzoeksgeld[2]** • **Honorarium of andere (financiële) vergoeding[3]** • **Aandeelhouder[4]** • **Andere relatie, namelijk …[5]**	• • • •

Casus

<u>SEH</u>

53-jarige antropologe

VG/ 1998 *P. ovale*-infectie

Anamnese:
Koorts, koude rillingen, hoofdpijn, geen focale klachten
10dagen terug uit India
6wkn in New Delhi en Udaipur geweest
Via GGD vaccinatie gehad, geen malariaprofylaxe

Casus

Lichamelijk onderzoek:
Niet acuut ziek, temp 38.7, systolische souffle

Malariadiagnostiek: *P. vivax*

Start chloroquine

Hemoglobine	8.0	
Leucocyten	3.2	
Neutrofielen	2.5	
Lymfocyten	0.4	
Monocyten	0.2	
Eosinofielen	0.00	
Trombocyten	45	
Opm trombocyten	Zie opm.	
nie		
Glucose	5.4	
Albumine	41	
Ca (alb. Correct)	2.32	
Natrium	135	
Kalium	3.7	
Kreatinine	59	
eGFR (CKD-EPI)	>90	
Bilirubine Totaal	21	
Bilirubine Direct	11	
GGT	79	
ASAT	109	
ALAT	91	
LD	437	
Glucose POC		
CRP	69	
e		
Soortelijk gewicht		1015
Albumine		+
Totaal eiwit		0.44
Eiwit/kreat(EKR)		0.02
Glucose		Neg.
Ketonen		+++
Leukocyten strip		5-15
Erytrocyten strip		5-15
Nitriet		Neg.

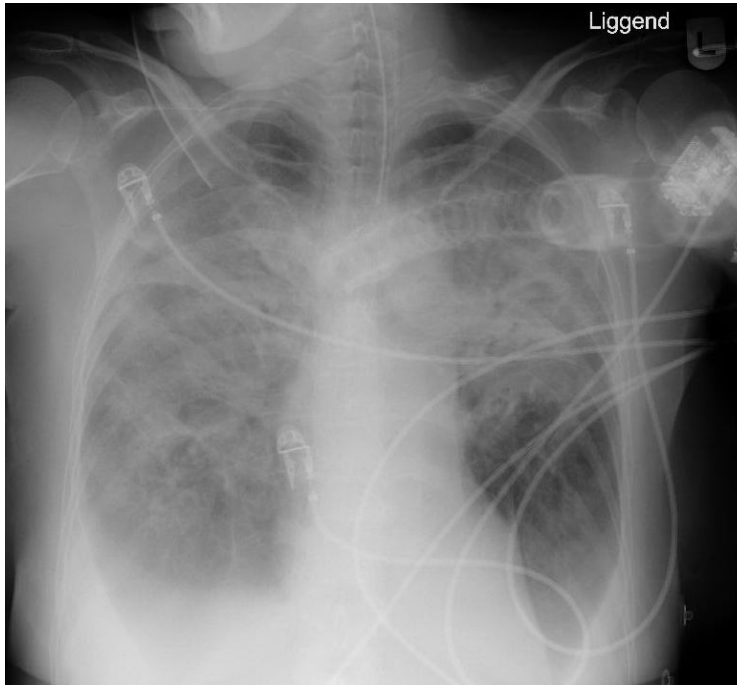
Casus

≥ 18 jaar

Prioriteit	Medicatie	Opmerking
1e keus	chloroquine po 10mg/kg 1dd 2 dagen gevolgd door chloroquine po 5mg/kg eenmalig	Cave: chloroquine resistente P.vivax ZO-Azie
1e keus alternatief	mefloquine po 10mg/kg eenmalig	

Casus

Na 24 uur klinische verslechtering:
Respiratoire insufficiëntie, hypotensie, koorts en stijgende infectieparameters



Opname IC:
Intubatie bij ARDS-beeld
Nieuwe bloedkweken, BAL

Casus

Overwegingen:
- Kleine kans chloroquineresistentie
- Behandeling vivax reeds >24h
- Waarschijnlijk bijkomende sepsis

Beleid
- Geen switch naar artesenaat i.v. (ernstige malaria)
- Meropenem bijstarten (ESBL, *Burkholderia*)

Casus

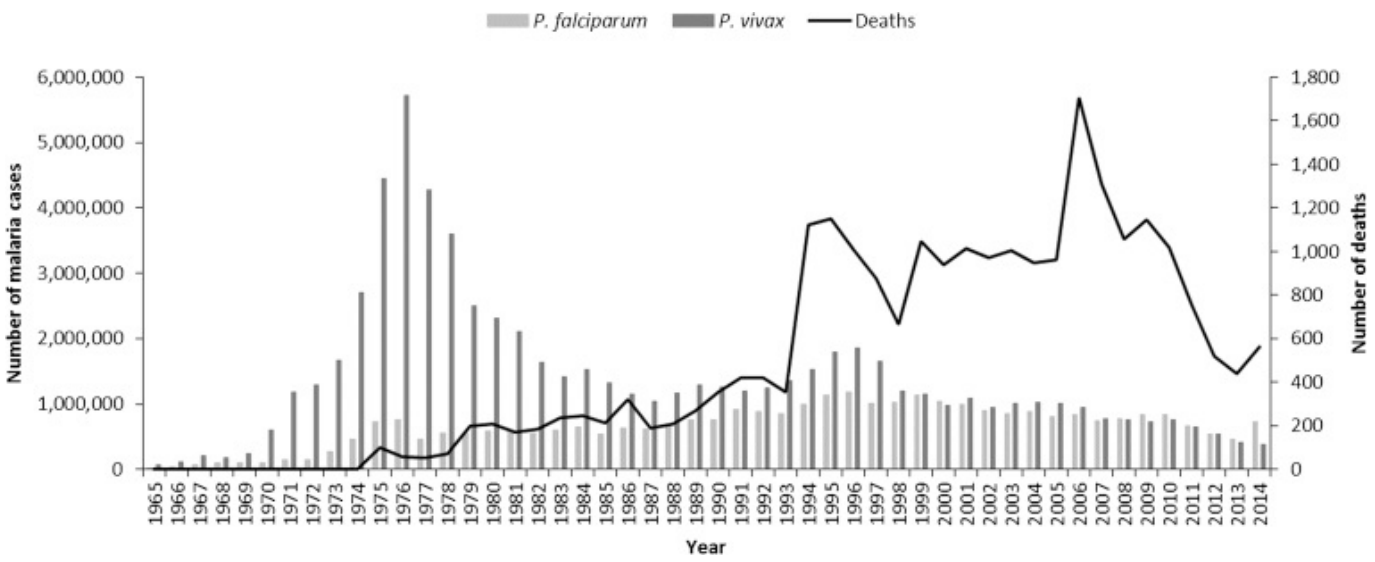
Beloop:
Na een week klinisch beter. Detubatie.

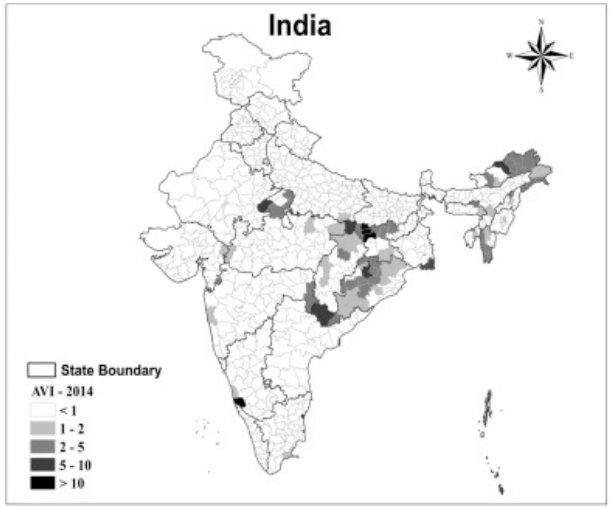
Bloedkweken: negatief
Dengue, EBV, CMV, chikungunya, hepatitis B, leptospirose, TB en PJP: negatief

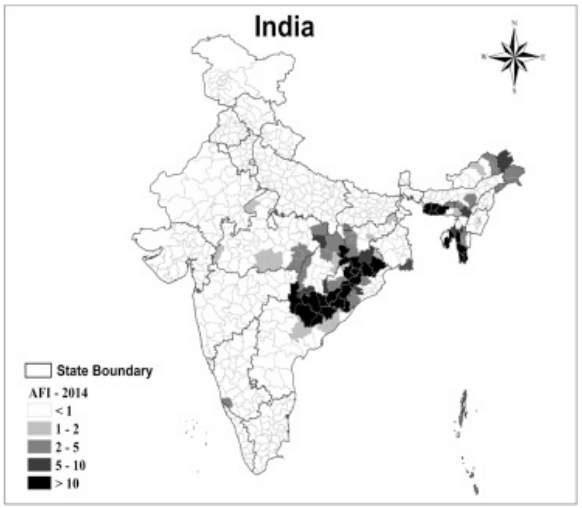
Conclusie: Ernstige *P. vivax*-infectie

Poliklinisch:
G6PD-deficiëntie uitgesloten. Primaquine 1dd30mg 14 dgn

India





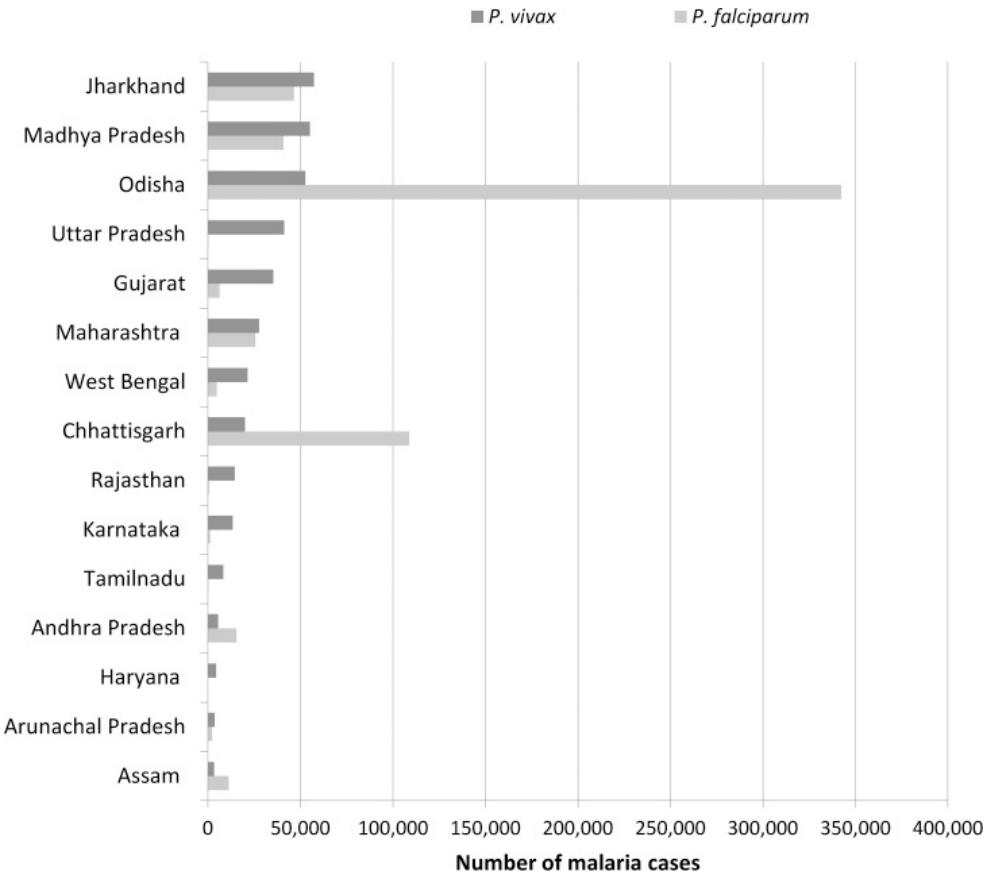


Anupkumar, Am J Trop Med Hyg, 2016

P. vivax

P. falciparum

India



Chloroquineresistentie laag in India, enkele case reports

Anupkumar, Am J Trop Med Hyg, 2016

Table 2. Characteristics of Patients with Severe Malaria

	Survived (n = 227)	Died (n = 74)	Relative Risk (95% CI)	p Values
Age				
≤45 yrs	174	35		< .001
>45 yrs	53	39	2.5 (1.7–3.7)[a]	
Gender				
Male	158	52	1.01 (0.85–1.2)	NS
Female	69	22		
Fever duration prior to admission (days)[b]	5 (4–8)	7 (4–8)		NS[c]
APACHE II score on day 1[b]	19 (14–24)	30.5 (25–37.3)		< .001[c]
Parasite index[b]	5 (2–10)	4.5 (1.8–15)		NS[c]
Organ failure[d]				
CNS	68	53	3.8 (2.4–5.9)	< .0001
Renal	43	48	4.3 (2.8–6.4)	< .0001
Respiratory	7	36	5.7 (4.7–7.8)	< .0001
Cardiovascular	7	44	7.2 (5.1–10.2)	< .0001
Hepatic	39	38	3.1 (2.1–4.5)	< .0001
Hematological	85	48	2.3 (1.5–3.6)	< .0001
Other features				
Metabolic acidosis	105	62	1.8 (1.5–2.2)	< .0001
Convulsions	24	30	3.8 (2.4–6.1)	< .0001
Hypoglycemia	54	34	1.9 (1.4–2.7)	.0003
Hemoglobinuria	127	63	1.5 (1.3–1.8)	.0006
Blood transfusions	164	65	1.2 (1.1–1.4)	.006
Pregnant women	19	4		NS
Preexisting chronic disease	33	20	1.9 (1.1–3.0)	.014
Nosocomial pneumonia	5	29	17.8 (7.2–44.3)	< .0001
Sepsis	4	35	26.9 (9.9–73.0)	< .0001

CI, confidence interval; NS, not significant; APACHE, Acute Physiology and Chronic Health Evaluation; CNS, central nervous system.

[a]Relative risk of death vs. patients aged ≤45 yrs; [b]values are median (interquartile range); all other values are number of patients; [c]differences were compared by Mann-Whitney test; [d]SOFA score ≥3 during the first 48 hrs of stay in the intensive care unit was considered as organ failure due to malaria.

Table 3. Glasgow Coma Score (GCS) and Mortality Rate in 301 Patients with Severe Falciparum Malaria

GCS	No. Patients	Died (%)
15	92	5 (5.4)
10–14	88	16 (18.2)
6–9	81	27 (33.3)
<6	40	26 (65)

Chi-square test for trend in proportions of mortality vs. decreasing GCS: $p < .0001$.

nal dysfunction occurred a mean of 1.6 curred in the 101 patients with one or with 16.1% in patients without hepatic failure (Table 2). Twenty-two deaths occurred in the 33 patients who had elevation of transaminases, whereas 19 of 45 patients with hyperbilirubinemia but no hepatic enzyme elevation died ($p = .033$). Hepatic failure was seen in isolation in only 11 patients with one death, whereas failure of at least one other organ was present in the remaining 66 patients (37 deaths).

Respiratory Failure. On admission, 84 patients had mild hypoxia (Pao_2/FIo_2 <400, SOFA score 1), 18 had acute lung injury (Pao_2/FIo_2 <300, SOFA score 2), and ten were classified as respiratory failure (Pao_2/FIo_2 <200). Respiratory failure occurred within the first 48 hrs in another 33 patients. A further 36 patients developed respiratory failure after 48 hrs. Thus, 79 patients had respiratory failure with acute respiratory distress syndrome

Krishnan en Karnad, Crit Care Med, 2003

Frequency and case fatality rate of ARDS among patients with Pv malaria according to age groups in hospital-based studies

First author, year (reference)	Location	Study population	No. of Pv patients				Frequency (%)		
			Total	Severe	ARDS	Deaths	ARDS /total	ARDS /severe	ARDS mortality
Studies with pediatric population (children under 18 years)									
Kochar, 2010[27]	India	Malaria hospitalizations	103	65	1	–	0.9	1.5	–
Singh, 2011[33]	India	Patient hospital presentations	108	23	0	0	0	0	0
Lança, 2012[28]	Brazil	Pv pediatric hospitalizations	24	24	3	0	12.5	12.5	0
Sharma, 2012[29]	India	Patients admitted to hospital	105	46	9	7	8.5	19.5	77.8
Yadav, 2012[30]	India	Severe vivax malaria	131	131	3	2	2.2	2.2	66.7
Gehlawat, 2013[32]	India	Severe vivax in children	18	18	1	1	5.5	5.5	100
Bhattacharjee, 2013[34]	India	Pv pediatric hospitalizations	168	168	2	0	1.1	1.1	0
Singh, 2013[35]	India	Patients admitted to hospital	61	38	5	3	8.2	13.1	60
Sharma, 2013[36]	India	Pv pediatric hospitalizations	261	54	3	–	1.1	5.5	0
Goyal, 2014[37]	India	Pv hospital admissions	47	–	2	1	4.2	–	50
Total			1026	567	29	14	2.8	5.1	48.2
Studies with adult population									
Kotwal, 2005[57]	Afghanistan	American soldiers	38	1	1	0	2.6	100	0
Sharma, 2009[60]	India	Records of malaria cases	221	–	3	3	1.3	–	100
Kochar, 2009[61]	India	Patients admitted to hospital	456	40	4	2	0.8	100	50
George, 2010[71]	India	Severe Pv admissions	30	30	1	1	3.3	3.3	100
Nayak, 2011[62]	India	Severe malaria cases	80	80	4	4	5	5	100
Srivastava, 2011[63]	India	Patient hospital presentations	50	41	3	0	6	7.3	0
Limaye, 2012[64]	India	Patients admitted to hospital	336	50	10	6	2.9	20	60
Mehmood, 2012[65]	Pakistan	Pv cases in Emergency Dept.	97	–	1	0	1	–	0
Singh, 2013[56]	India	Patients admitted to hospital	140	63	3	2	2.1	4.7	66.7
Rizvi, 2013[67]	India	Patients admitted to hospital	172	62	6	2	3.5	9.7	33.3
Muley, 2014[70]	India	Hospital admissions	100	–	6	1	6	–	16.6
Siqueira, 2015[26]	Brazil	Patients admitted to hospital	316	40	7	1	22.2	17.5	14.2
Siqueira, 2015[26]	India	Patients admitted to hospital	462	157	5	5	1.1	3.1	100
Jain, 2016[72]	India	Patients in Emergency Dept.	48	25	2	1	4.1	8	50
Total			2548	589	56	28	2.2	9.5	50

ARDS = acute respiratory distress syndrome; Dept. = department; Pv = *Plasmodium vivax*. Blank spaces mean no data was available in original paper.

Val et al. Am J Trop Med Hyg, 2017

Ernstige vivax, verraderlijk?

Criteria ernstige malaria:

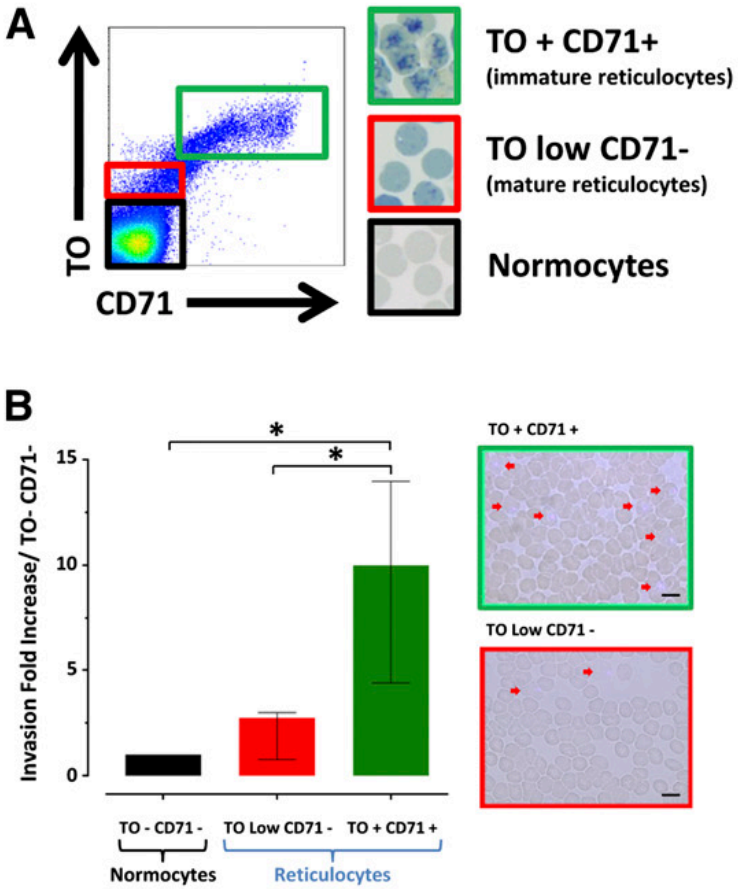
Parasitaemie > 5%

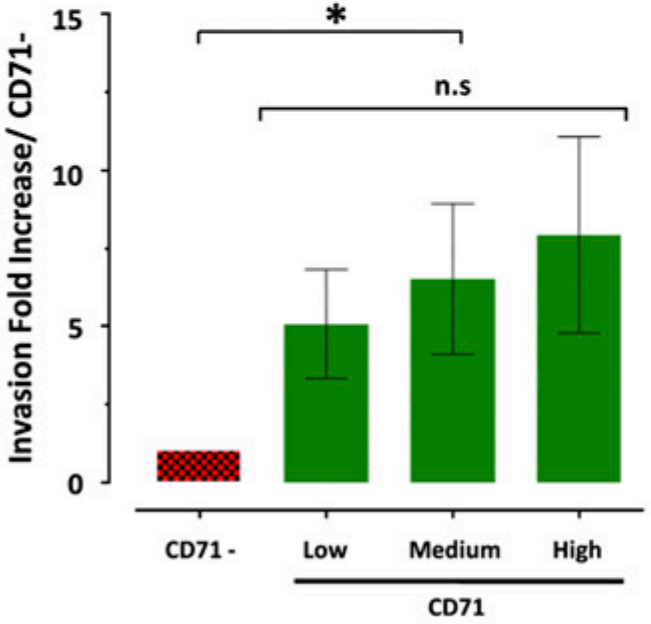
Table 4 Epidemiological and research definition of severe falciparum malaria

For epidemiological and research purposes, severe malaria is defined as one or more of the following, occurring in the absence of an identified alternative cause, and in the presence of *P. falciparum* asexual parasitaemia:

Impaired consciousness:	A Glasgow Coma Score <11 in adults or a Blantyre coma score <3 in children
Acidosis:	A base deficit of >8 meq/l or, if unavailable, a plasma bicarbonate of <15 mM or venous plasma lactate >5 mM. Severe acidosis manifests clinically as respiratory distress – rapid, deep and laboured breathing
Hypoglycaemia:	Blood or plasma glucose <2.2 mM (<40 mg/dl)
Severe malarial anaemia:	A haemoglobin concentration <5 g/dl or a haematocrit of <15% in children <12 years of age (<7 g/dl and <20%, respectively, in adults) together with a parasite count >10 000/μl
Renal impairment (acute kidney injury):	Plasma or serum creatinine >265 μM (3 mg/dl) or blood urea >20 mM
Jaundice:	Plasma or serum bilirubin >50 μM (3 mg/dl) together with a parasite count >100 000/μl
Pulmonary oedema:	Radiologically confirmed, or oxygen saturation <92% on room air with a respiratory rate >30/min, often with chest indrawing and crepitations on auscultation
Significant bleeding:	Including recurrent or prolonged bleeding from nose gums or venepuncture sites; haematemesis or melaena
Shock:	Compensated shock is defined as capillary refill ≥3 s or temperature gradient on leg (mid to proximal limb), but no hypotension. Decompensated shock is defined as systolic blood pressure <70 mm Hg in children or <80 mm Hg in adults with evidence of impaired perfusion (cool peripheries or prolonged capillary refill)
Hyperparasitaemia:	*P. falciparum* parasitaemia >10%

WHO criteria





Malleret et al, Blood, 2015

Conclusie

-*P. vivax* is over het algemeen mild;

-Parasitaemie is geen goede maat voor de ernst;

-Ernstige symptomen kunnen pas laat ontstaan;

-Een ernstige *P. vivax* met artesunate iv gevolgd door een volledige orale ACT kuur, en bij *P. vivax* tevens primaquine

Vragen