Management of Severe Malaria

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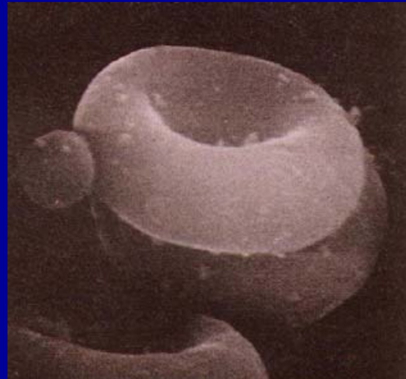
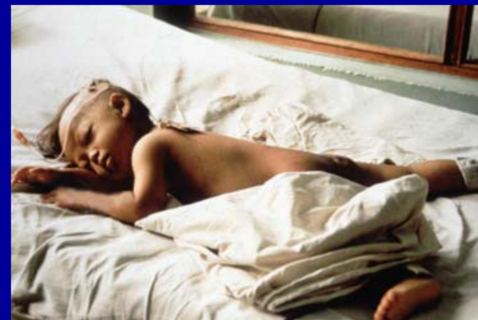
Determinants of Severe Malaria



Parasite ⟷ Vector

Environment

Host



Finger prick for blood slide in a child with non-severe Malaria. Mortality 0.1%

A child with severe Malaria in Coma. Mortality 15-20%

The facts

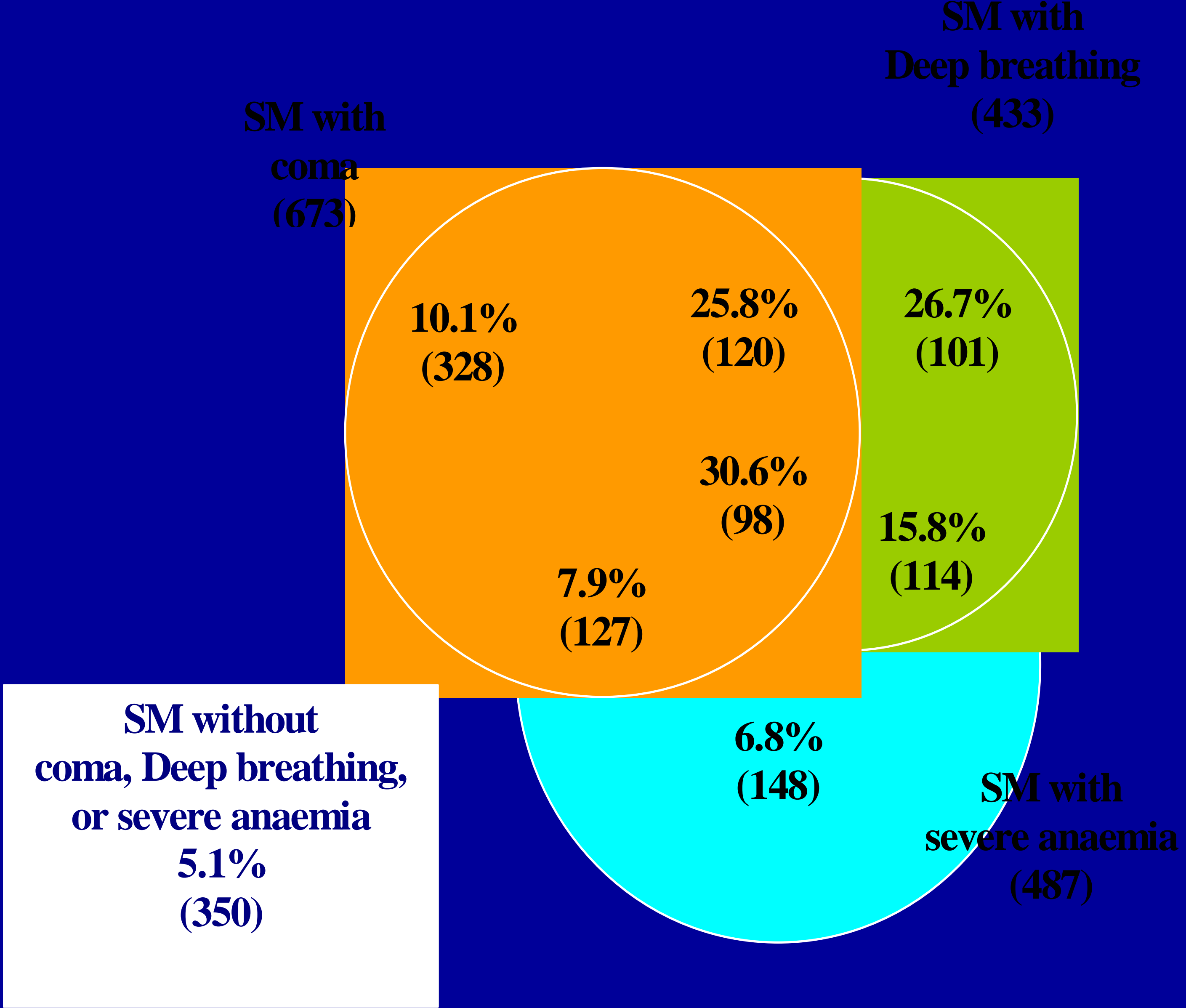
- In severe disease the imminent cause of death is the deranged homeostasis
- Most deaths within hours of admission
- Will new antimalarials result in reduction of mortality or neurological consequences
- Supportive care the cornerstone of preventing deaths in severe malaria

Severe malaria is an emergency and requires high dependency or ICU care unless in situations of resource scarcity

Prognostic Value		Clinical manifestations or Laboratory findings	Frequency	
Children	Adults		Children	Adults
+	?	Prostration	+++	+++
+++	++	Impaired consciousness	+++	++
+++	+++	Respiratory distress (acidotic br)	+++	+
+	++	Multiple convulsions	+++	+
+++	+++	Circulatory collapse	+	+
+++	+++	Pulmonary oedema	+/-	+
+++	++	Abnormal bleeding	+/-	+
++	+	Jaundice	+	+++
+	+	Haemoglobinuria	+/-	+
+	+	Severe anaemia	+++	+

On scale from + to +++; +/- indicates infrequent occurrence

? Data not available



SM with
Deep breathing
(433)
SM with
coma
(673)
10.1%
(328)
25.8%
(120)
26.7%
(101)
30.6%
(98)
15.8%
(114)
7.9%
(127)
6.8%
(148)
SM with
severe anaemia
(487)
SM without
coma, Deep breathing,
or severe anaemia
5.1%
(350)

Definition of CM

- Encephalopathy with coma (BCS $\leq$ 2) in the presence of peripheral parasitemia in the absence of any other identifiable cause
- Alterations in the level of consciousness in the presence of peripheral parasitemia in the absence of any other identifiable cause

Variants of CM

- CM
- Constitutional Coma
- Biphasic

Dilemmas

- Syndromic definitions
- Burden
- Pathogenesis
- Interventions

Principles of Management

- Detailed clinical evaluation
- Complications directed interventions
- Identify treatable complications i.e, hypoglycaemia,ARF, bacterial infections, hyperparasiteamia, acidosis, anemia
- Continuous monitoring
- Education of care taker
- Follow up

Investigations

- Haematological
- Clinical chemistry
- Roentography

General Severe disease care

- ABC
- Restriction in bed
- Skin care
- Bladder care
- Chest physiotherapy
- Nutritional support
- Family therapy
- Long term care plan

Acidosis

- Treat the underlying cause
  - Antimalarials
  - Correct hypoglycaemia
  - Stop seizures
- Think about the mechanisms
  - hypovolemia
  - anaemia
  - impaired perfusion
  - salicylates

Acidosis

- Fluid replacement
  - Which fluid
  - How much
- Close monitoring
  - Check Hb
  - When to change fluid regimen
- Bicarbonate
  - Not indicated unless blood gas ??

Severe Anaemia

- Indications for blood transfusion
    - Hb < 5 g/dl + respiratory distress
    - Hb < 4 g/dl
- Haematinics
    - folate
    - iron
- Other treatments
    - antioxidants
- Artificial blood

Bacterial Infections

- Bacteraemia in children with severe malaria
  - incidence
    - 7.8% (95% CI 5.5-10.0)
    - < 30 months: 12.0% (95% CI 8.3-15.7)
  - mortality
    - 33.3% vs 10.4%
  - organisms:
    - *S.pneum, S.aureus, Salmonella sp, Strept. sp, H.influ, Pseudomonas,* gram negative
- Other infections
  - lung, UTI
  - **Appropriate antibiotic cover from admission**

Meningitis

- incidence
  - 4%
  - < 13 months: 14.0%
  - Stormy inpatient period
- mortality
  - High, soon after admission and is sudden
- organisms:
  - *S.pneum, H.influ, Pseudomonas, Strept. sp,* gram negative organisms

Appropriate antibiotic cover from admission

What next

- Other pathogens
  - Parasites
  - Viruses

Hypoglycaemia

- Associated with death and neurological sequelae
- ?0.5-1.0 ml/Kg 50% dextrose
  - rebound phenomenon
- ?Bolus of 10% dextrose at 2ml/kg, followed by an infusion of 10% dextrose at 4.0mls/hr
- ?Continuous infusions of 10% dextrose titrated to provide 5-8mg/kg/min have been used to maintain normoglycaemia
- NGT, Hyperalimentation

Acute seizures

- When to terminate seizure
  - After 5 minutes
- Diazepam - IV 0.3 mg/Kg or PR 0.5 mg/Kg
- Paraldehyde - IM 0.4 ml/Kg or PR 0.8ml/Kg
- Lorazepam - IV
- Midazolam - IV or buccal, IM

Status Epilepticus

- Phenobarbitone IV 15 mg/kg infusion over 20 min
  - Maintenance 2.5 mg/kg/day for 48 hrs
- Phenytoin IV 18 mg/kg over 20 min / Fosphenytoin IV/IM 27 mg/kg OVER 3 min
  - Maintenance 5 mg/kg 2 hourly for 48 hrs

Limited data

Seizure Prophylaxis

- Phenobarbitone ! What next?
  - Thai adults 3.5 mg/Kg
  - Kenyan children
    - 20 mg/Kg IMI on admission to 440 children
    - decrease in seizures: 11% vs 27%
    - increase mortality:
      - diazepam 3 doses OR 31.7 (1.2-81.4)
    - no reduction in sequelae
    - 15 mg/Kg IV on admission to 15 children
- Fosphenytoin (Phenytoin) in 29 Kenyan children
- Other anticonvulsants

Fever

- May be beneficial
  - synchronises infections
  - paracetamol prolongs parasitaemia in non-severe malaria
- May be detrimental
  - Precipitates seizures
  - Contributes to neurological damage

ROS in Falciparum malaria

- Administration of Vit E unlikely to prevent fall in Haemoglobin
- Would substances that promote uptake by Vit E by RBC membranes e.g. ascorbate work?
- Does ROS contribute to decreased RCD?
- Are ROS involved in the pathogenesis of neurological damage?

HIV

- Drug interaction
  - ARVs
  - Other drugs
- Pathogens
  - Viral, Bacterial, parasitic, fungal
- Nutritional supplements
- Long term complications

Antimalarial Treatment

Monotherapy

- QN 7 days
- ARTM, ART 5-7 days

Combination therapy

- QN/SP - days ?
- QN/CLIND 7 days
- ARTM/MQ 5-7 days
- QN/ARTM/LUM?
- ARTM/ARTM/LUM?
- ART/ARTM/LUM?
- ART/MQ 5-7 ?
- QN/LAPDAP ?
- ART/LAPDAP ?

The dichotomy

- In intensive follow up studies severe disease disappears
- Is severe disease on the decline

Malaria MX commandments

- HDU or ICU management protocol
- Appropriate & Effective Antimalarial (s)
- Fluids
- Glucose
- Safe Blood
- Anticonvulsants
- Monitoring
- Parental counseling
- Follow up

Future control Strategy?

- Partially effective vaccine
- Effective first line
- IPT in pregnancy
- IPT in children
- Prophylaxis for vulnerable groups
- Reduction of Vector – Man contact
  - ITN, Residual spraying, laviciding
- Functional health infrastructure

Ero kamano uru