Shiga toxin-producing Escherichia coli (STEC) hemolytic uremic syndrome (HUS) in children

General department

INTRODUCTION

- The hemolytic uremic syndrome (HUS): microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury
- One of the main causes of acute kidney injury in children < 3 years.
- Mortality: 3 - 5 %, long-term renal 39 % , require dialysis during the acute phase 50%, neurologic sequelae 4 %

CLASSIFICATION

- Primary causes:
  Complement dysregulation (50% of non-Shiga toxin-producing E. coli)
- Secondary causes:

  - Infection: STEC,Strep.pneumonie (5-15%), HIV, H1N1 influenza A

  - Inborn error of cobalamin C metabolism

  - Drug toxicity, cancer or solid organ transplant recipients

  - Rare: pregnant, autoimmune disorders (eg, systemic lupus erythematous)

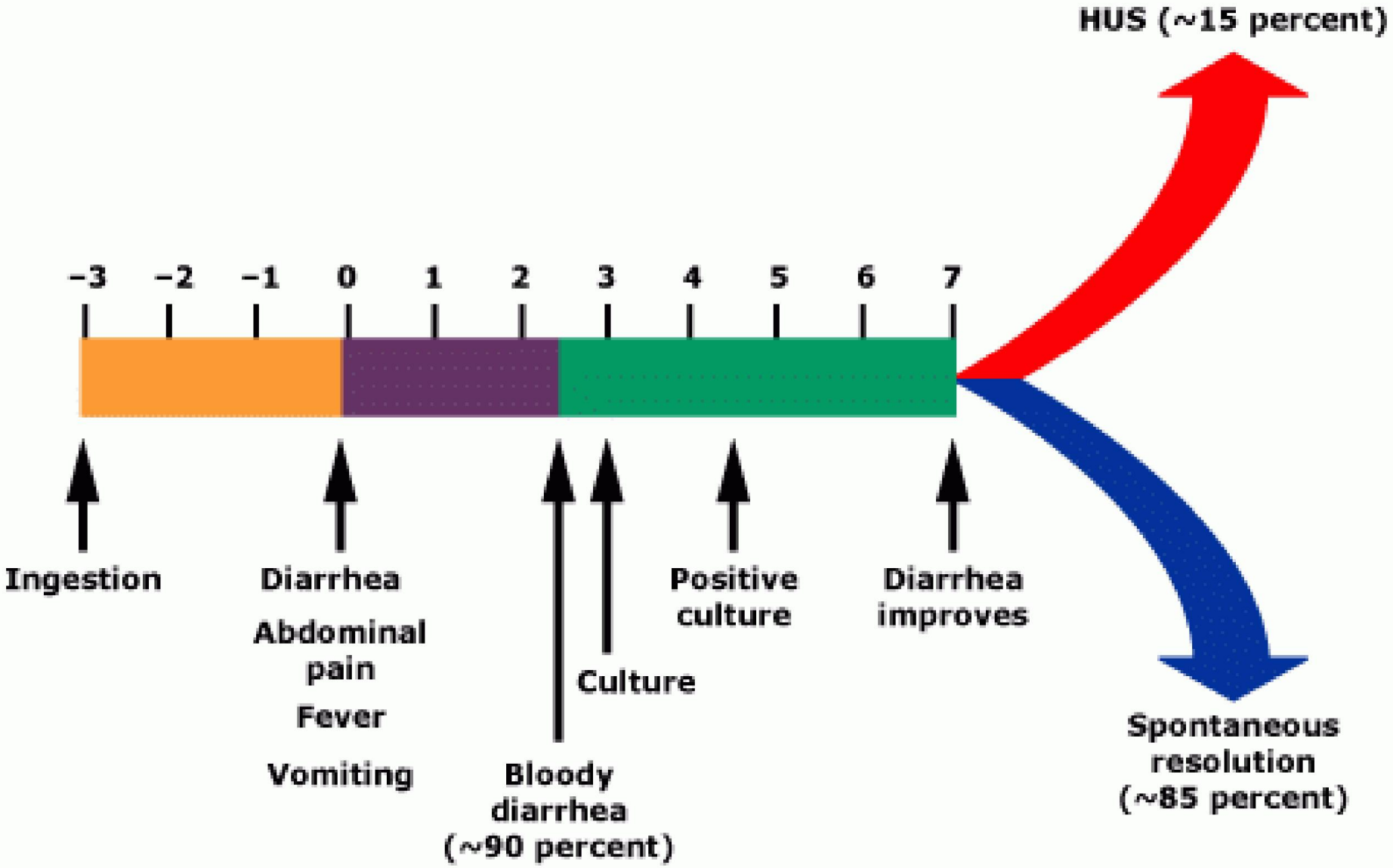
STEC HUS

- Over 90% of cases of HUS, < 5 years
- Occurs after an infection with Shiga toxin-producing enterohemorrhagic E. coli (EHEC) or Shigella
- Enterohemorrhagic E. coli — EHEC: the most common cause, over 70% of cases of postdiarrheal HUS.
- Shigella: in India, Bangladesh, and southern Africa, more severe, with an acute mortality rate of 15 %

CLINICAL MANIFESTATIONS

- History of bloody diarrhea, a visibly bloody stool specimen, no reported fever, abdominal tenderness, a peripheral WBC >10,000/microL,
- HUS complicates: 6 to 9 % of EHEC infections , typically begin 5 to 10 days after the onset of diarrhea

CLINICAL MANIFESTATIONS



CLINICAL MANIFESTATIONS

- **Hemolytic anemia**: Hb < 8 g/dL.
- **Thrombocytopenia**: <140,000/mm^3, usually about 40,000/mm^3 , no purpura or active bleeding.

  No correlation between the severity of anemia, thrombocytopenia and the severity of renal disease
- **Acute kidney injury (AKI)**: occurs in 50% of cases, hypertension is common

CLINICAL MANIFESTATIONS

Other organ involvement

- Central nervous system: up to 20 % of cases due to E. coli .

  Severe CNS involvement is associated with increased mortality.

- Gastrointestinal tract, Cardiac dysfunction, Pancreas, Liver, Hematology

LABORATORY

- Blood count, Haptoglobuline, blood group
- AST/ ALT, ure/creatinin, LDH, Glycemia, Lipase, Amylase
- Urinalysis , protein/creatinin urine
- Stool exam – stool culture
- Test Coombs
- Chest-abdominal X-ray , ultrasonogram , abdominal CT scan
- ECG
- EEG, brain MRI

DIAGNOSIS

- Diagnosis of STEC HUS in children: clinical + laboratory findings of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury following a diarrheal prodrome due to STEC

DIFFERENTIAL DIAGNOSIS

- Enteric infections
- Henoch-Schönlein purpura (IgA vasculitis)
- Systemic vasculitis
- Disseminated intravascular coagulation
- Non-STEC HUS.

MANAGEMENT

The management primarily based on supportive care

- Anemia: Transfuse when Hb< 6 g/dL
- Thrombocytopenia: platelet transfuse when PLT < 30,000/mm^3 and active bleeding or prior to a required invasive procedure
- Fluid and electrolyte disturbances: Monitoring to detect hyperkalemia, hyperphosphatemia, and metabolic acidosis.

MANAGEMENT

The management primarily based on supportive care

- Hypertension: calcium channel blockers (such as nifedipine or nicardipine)
- Neurologic dysfunction
- Plasma exchange
- Antibiotics ???

Antibiotics in STEC HUS?

- Bloody diarrhea = give antibiotic ???

Antibiotics in STEC HUS?

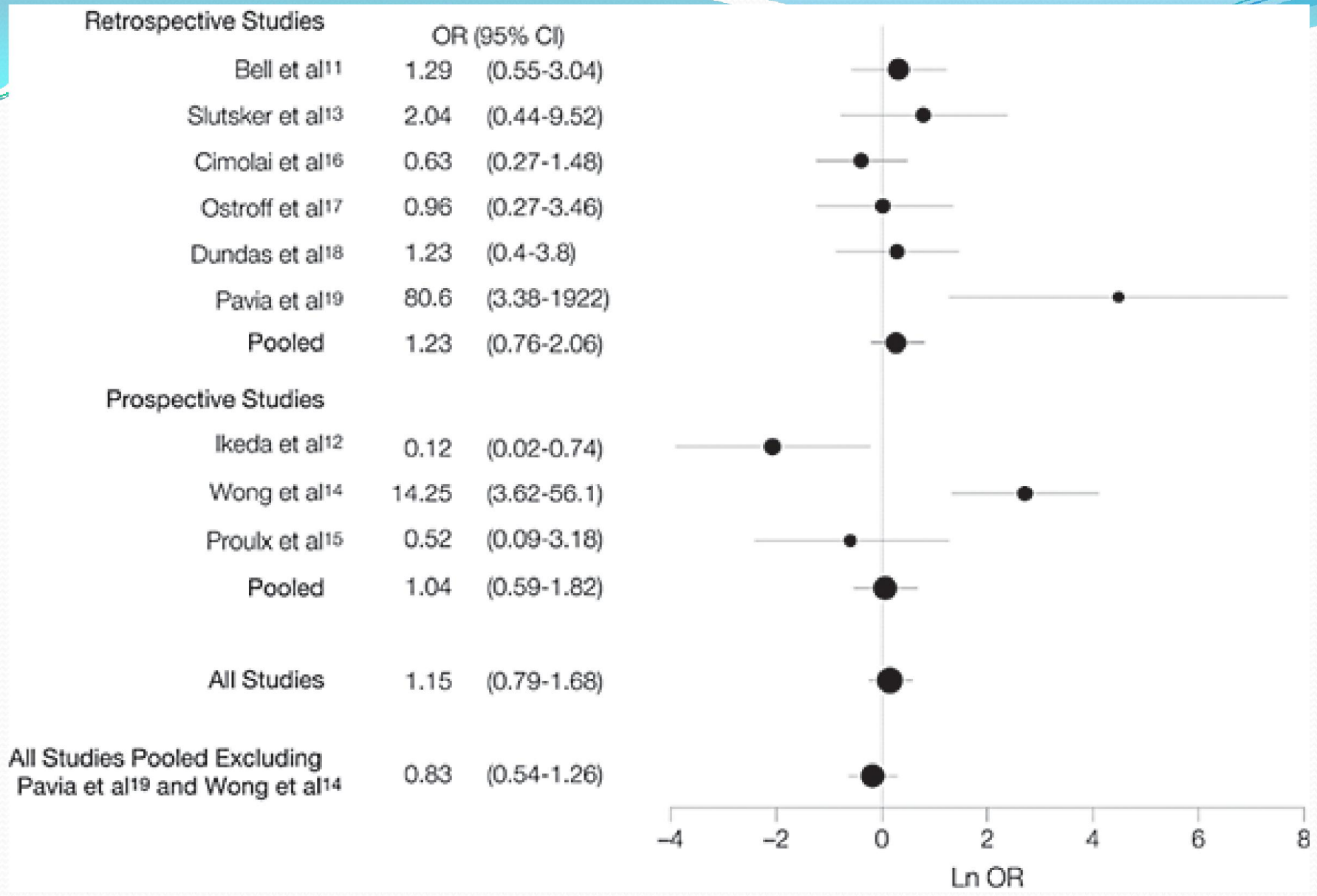
- The risk of the hemolytic-uremic syndrome after antibiotic treatment of Escherichia coli O157:H7 infections. Wong CS, Jelacic S, Habeeb RL, Watkins SL, Tarr PI (N Engl J Med. 2000)
- METHODS: Prospective cohort study of 71 children younger than 10 years of age
- RESULTS: Antibiotic administration remained a risk factor for the development of the HUS (RR 14.3; 95 percent confidence interval, 2.9 to 70.7)

Antibiotics in STEC HUS?

- Risk factors for the hemolytic uremic syndrome in children infected with Escherichia coli O157:H7: a multivariable analysis. Wong CS, Mooney JC, Brandt JR, Staples AO, Jelacic S, Boster DR, Watkins SL, Tarr PI (Clin Infect Dis. 2012)
- METHODS: prospective cohort study, 259 children
- RESULTS: children who received antibiotics more frequently developed HUS than those who did not (36% vs 12%; P = .001).

Antibiotics in STEC HUS?

- Risk of Hemolytic Uremic Syndrome After Antibiotic Treatment of *Escherichia coli* O157:H7 Enteritis. A Meta-analysis**,** Nasia Safdar, MD; Adnan Said, MD; Ronald E. Gangnon, PhD; Dennis G. Maki, MD (*JAMA.* 2002)
- **Data Sources:** PubMed and MEDLINE computer searches were performed for studies published from January 1983 to February 2001



Our analysis does not show an increased risk of HUS after antibiotic treatment of *E coli* O157:H7 infection

RECOMMENDATIONS

- **Not** be given antibiotics and antimotility agents in EHEC (**Grade 1C**)
- Early parenteral volume expansion to avoid renal hypoperfusion during the diarrheal phase of STEC(**Grade 2B**).
- Platelet transfusion only if there is active bleeding or prior to a required invasive procedure with PLT < 30,000/mm^3 (**Grade 2C**).

RECOMMENDATIONS

- Hypertension is managed by fluid restriction, antihypertensive agents, and dialysis if needed. We suggest the use of calcium channel blockers as the initial choice (**Grade 2C**)
- Plasma exchange be used in patients with significant neurologic symptoms, such as seizures or strokes (**Grade 2C**)

Thank you!