CHARACTERISTICS OF MENINGITIS CAUSED BY *ESCHERICHIA COLI* IN CHILDREN OLDER THAN ONE MONTH IN THE INFECTIOUS DISEASE WARD OF CHILDREN'S HOSPITAL 1 FROM 2013 TO 2018

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OUTLINE

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1. INTRODUCTION

- *E. coli* meningitis: neonates (premature/low birth weight) and infants (with/without risk factors).

This study was conducted to answer the question:

What were the features of *E. coli* meningitis in children >1 month of age in Children's Hospital 1 from 2013 to 2018?

- *Basmaci et al.* (2015) *E. coli* meningitis mortality 9.2%.
- *E. coli* meningitis: important cause of mortality, high incidence, severe neurologiacl sequelae in children globally
- **Vietnam:** limited contemporary data on *E. coli* meningitis

OBJECTIVES

Primary objective

To identify the clinical features, laboratory findings, treatment, and outcome of *E. coli* meningitis in children >1 moth old admitted to Children's Hospital 1 from 2013 to 2018

Secondary objective

- To determine the proportion of *E. coli* among bacterial pathogens of meningitis in children in our setting
- To describe the clinical features, laboratory findings, treatment, and outcome of *E. coli* meningitis in children in our setting
- To identify the proportion of factors that were potentially associated with mortality of children with *E. coli* meningitis

2. MATERIALS AND METHODS

- **STUDY DESIGN:**

  Case series

- **STUDY POPULATION:**

✓ **Target population:** hospitalised children >1 month of age having a diagnosis of *E. coli* meningitis

✓ **Sampling population:** hospitalised children >1 month of age having a diagnosis of *E. coli* meningitis in Children's Hospital 1 from 1st Jan 2013 to 30th Jun 2018

2. MATERIALS AND METHODS

- **PARTICIPANT RECRUITMENT:** all hospitalised children fulfilling the
  - **Inclusion criteria:** In-patient children >1 moth, admitted to Children Hospital 1, with *E. coli* identification.
  - **Exclusion criteria:** Informed consent were not provided.

➢ **Diagnostic criteria for confirmed *E. coli* meningitis**

Clinical relevance: fever and meningitis syndrome, **and**
CSF ≥10 leucocytes/mm^3, **and**
Positive CSF culture with *E. coli* identification.

➢ **Diagnostic criteria for suspected *E. coli* meningitis**

Clinical relevance: fever and meningitis syndrome, **and**
CSF ≥10 leucocytes/mm^3, **and**
CSF Latex with detected *E. coli* **and**
Negative CSF culture.

2. MATERIALS AND METHODS

- **DATA COLLECTION**

  An investigator recorded and collected information to case report forms

- **DATA ANALYSIS**

  ✓ Data from these records were subsequently entered into **EpiData 3.1**

  ✓ Data were analysed using **Stata 13.0**

  ✓ Continuous variables were presented in the forms of mean, SD, median, IQR

  ✓ Categorical variables were presented in percentage

3. RESULTS AND DISCUSSION

3.1. Proportion of *E. coli* among pathogens of menigitis

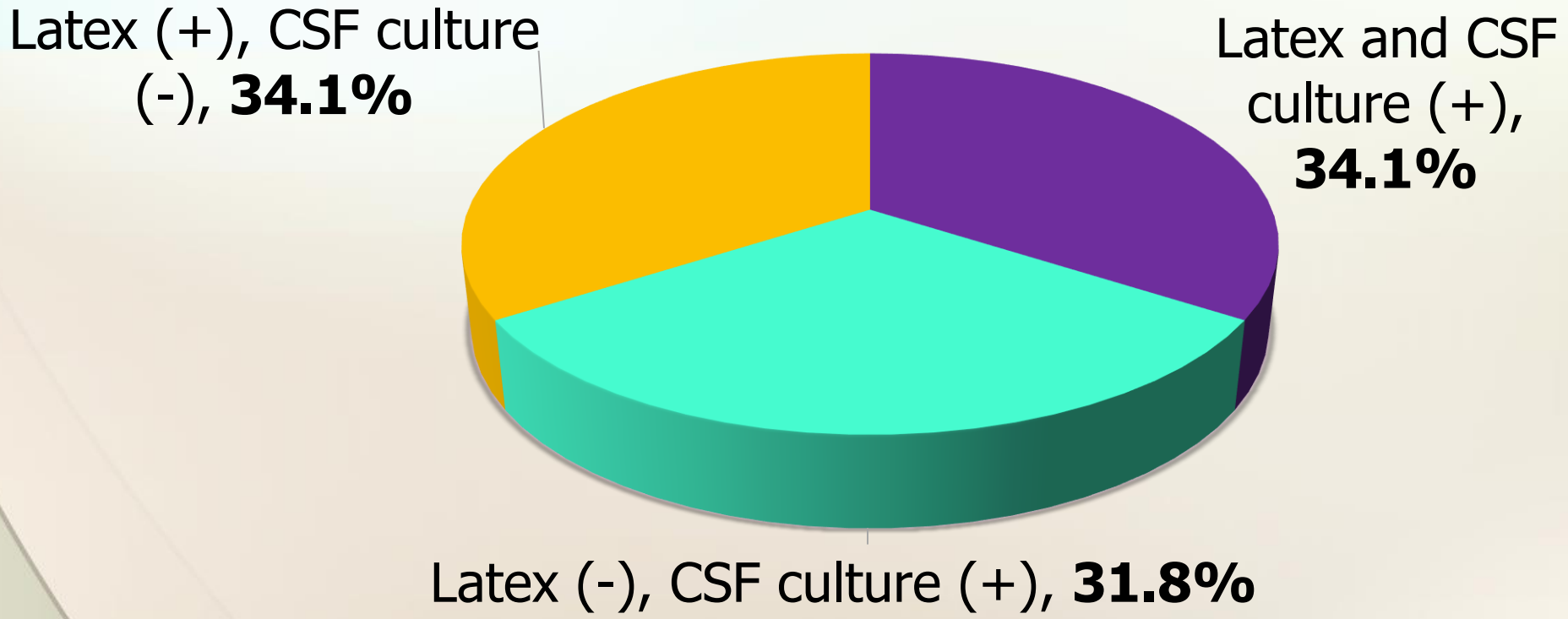
3.2. Clinical features of *E. coli meningitis*

- Administrative and demographic information
- Clinical manifestation
- Laboratory and imaging findings
- Treatment
- Comparisons of features between died and survival groups

3.3. Factors potentially associated with mortality in *E. coli* meningitis

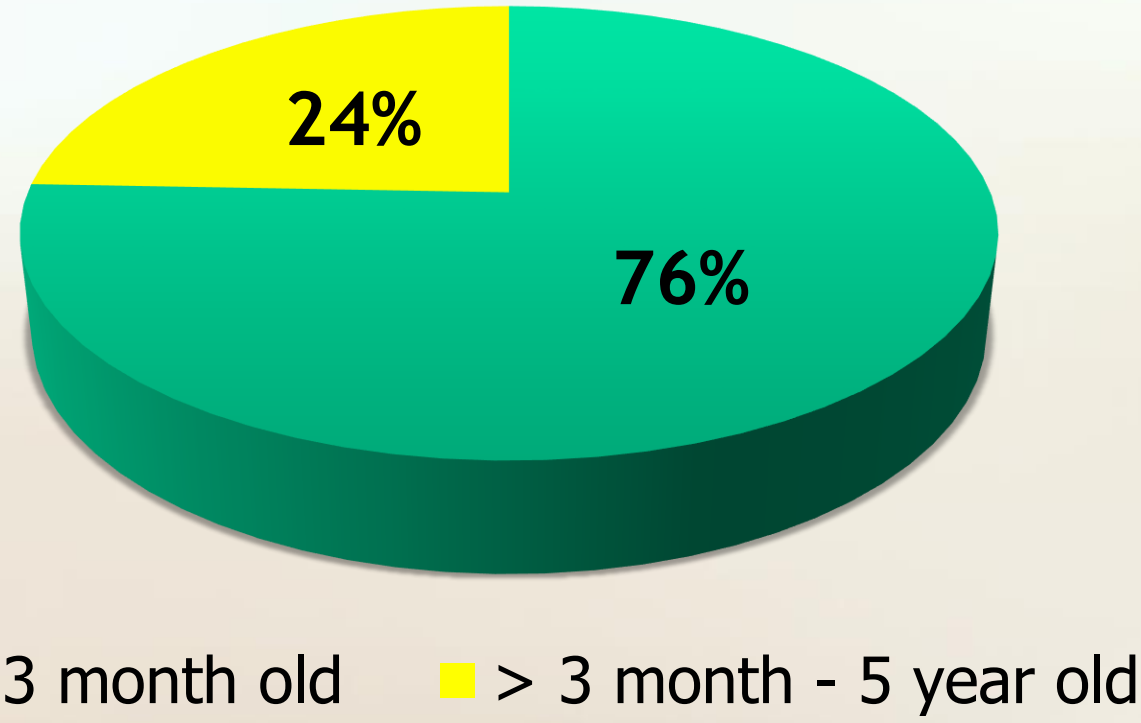
PROPORTION OF *E. COLI* MENIGITIS

- 144 confirmed bacterial meningitis in children
- 41 confirmed *E. coli* meningitis: 28.4%



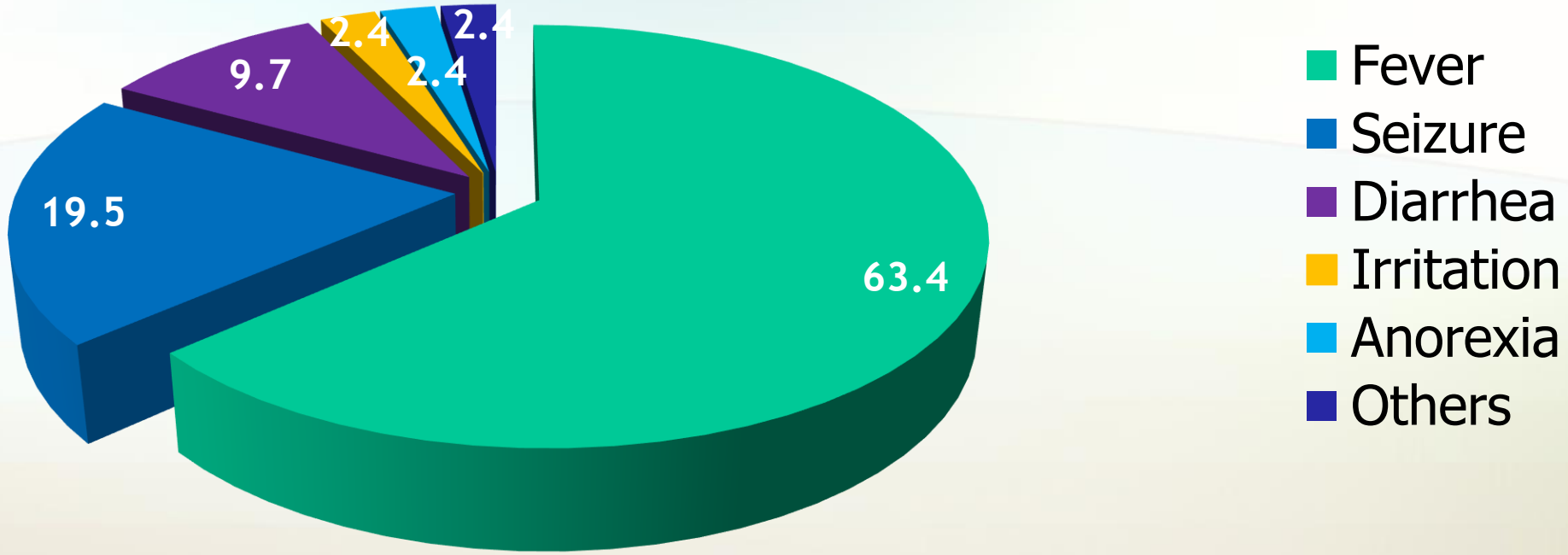
DEMOGRAPHIC FEATURES

- Age: 3,4 ± 3,3 months old
- Male:female ratio = 2,7



CLINICAL FEATURES

CHIEF COMPLAINTS(%)

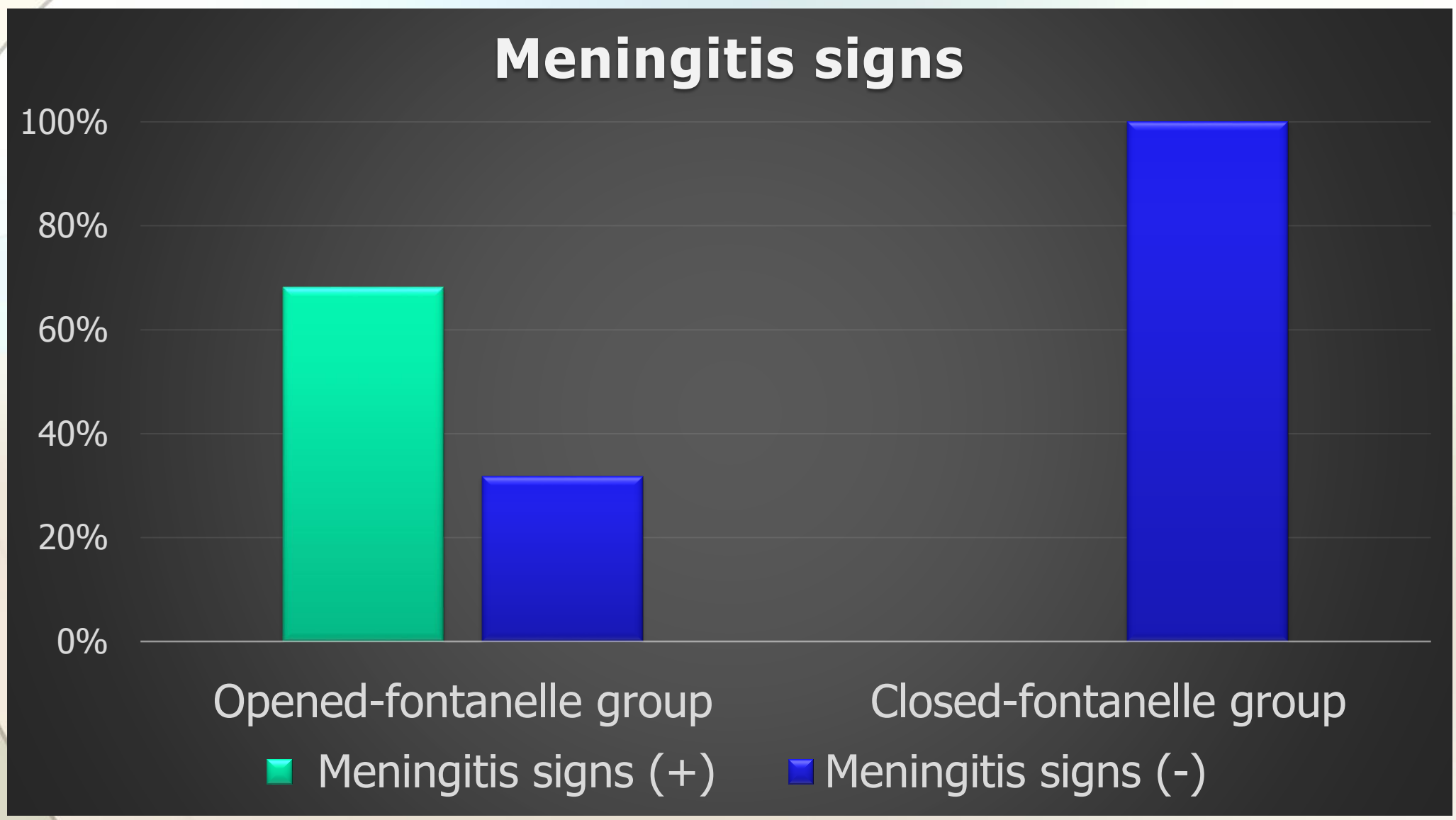


- 100% patients continued to have fever after admission
- Time from fever onset to admission: 3 days (2-5 days); min 1 day, max 16 days
- Fever duration: 12 days (9-19 days), min 5 days, max: 27 days
- **80%** had high fever (≥39°C) with body temparature 39,5±0,5°C

CLINICAL FEATURES

Features (N=41)	n (%)
Seizure	28 (68.2%)
Localised seizure	21 (75.0%)
Generalised seizure	24 (85.7%)
Post-seizure impaired consciousness	26 (92.8%)
Impaired consciousness	14 (34.1%)
Lethargy	10 (71.4%)
Coma	3 (21.4%)
Semi-coma	1 (7.1%)

CLINICAL FEATURES



LABORATORY FINDINGS

FULL BLOOD COUNT

	N	n(%)/Median (IQR)	Min	Max
Leucocytes (1000/mm^3)	41	10.59 (6.21-12.32)	2.28	28.31
Neutrophil (1000/mm^3)	41	3.50 (1.58-5.15)	0.49	19.66
Hemoglobin (g/dL)	41	9.10 (8.3-9.8)	7.2	25
Hematocrit (%)	41	26.9 (24.4-29.7)	22.4	83.1
Platelet (1000/mm^3)	41	376 (206-519)	25	940
C-RP hs (mg/L)	40	178.25 (107.25-187.25)	0.7	197.6

LABORATORY FINDINGS

BIOCHEMISTRY

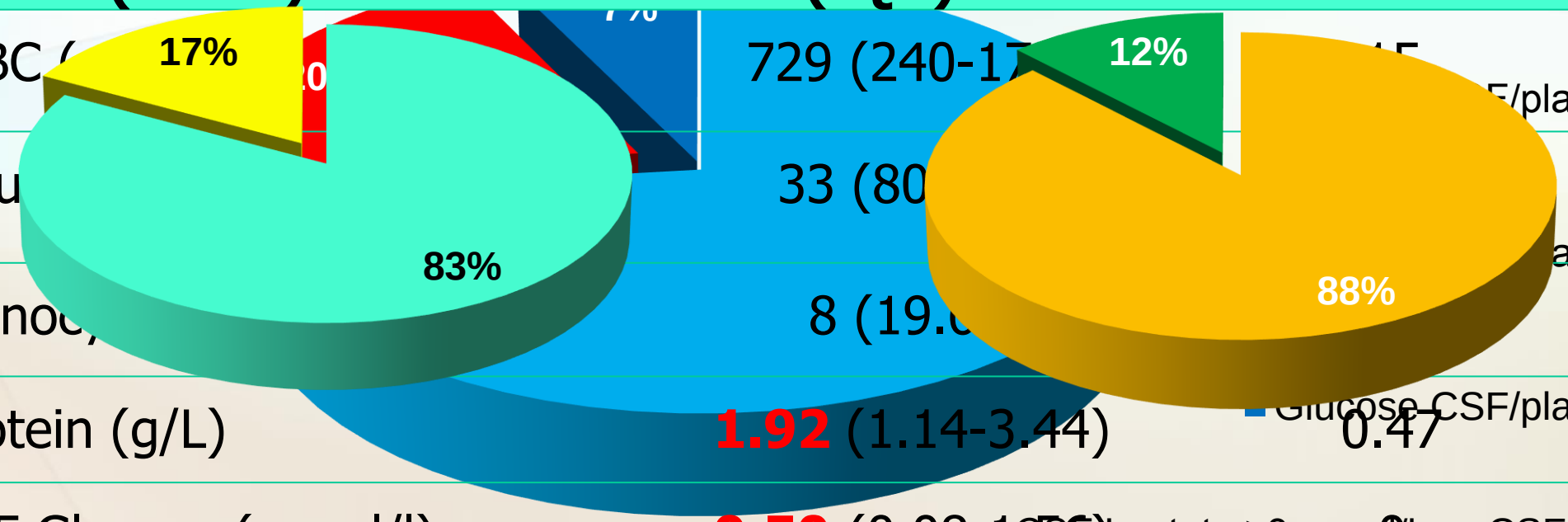
Arterial blood gases (ABG)	n (%)
Normal ABG	28 (68.3%)
Abnormal ABG	13 (31.7%)
Abnormal ABG (n=13)	
Metabolic acidosis	6 (46.1%)
Respiratory acidosis	4 (30.8%)
Respiratory alkalosis	2 (15.3%)
Elevated $AaDO_2$	1 (7.8%)

Blood electrolyte panel	n (%)
Abnormal	27 (65.8%)
Normal	14 (34.2%)
Electrolyte disturbance	
Hyper K^+	16 (59.2%)
Hypo Na^+	6 (22.2%)
Hypo K^+	2 (7.4%)
Hyper Na^+ and hypo K^+	2 (7.4%)
Hyper K^+ and hypo Na^+	1 (3.7%)

LABORATORY FINDINGS

CSF FEATURES

CSF features (N=41)	n(%)/ Median (IQR)	Min	Max
WBC (	729 (240-17		71111
Neu	33 (80		
Monoc	8 (19.0		
Protein (g/L)	**1.92** (1.14-3.44)	0.47	8.17
CSF Glucose (mmol/l)	**0.50** (0.08-1.56)	0	3.72
Lactate (mmol/L)	**7.88** (5.60-9.55)	1.12	15.6



CSF Protein

Glucose CSF/Plasma

CSF Lactate

LABORATORY FINDINGS

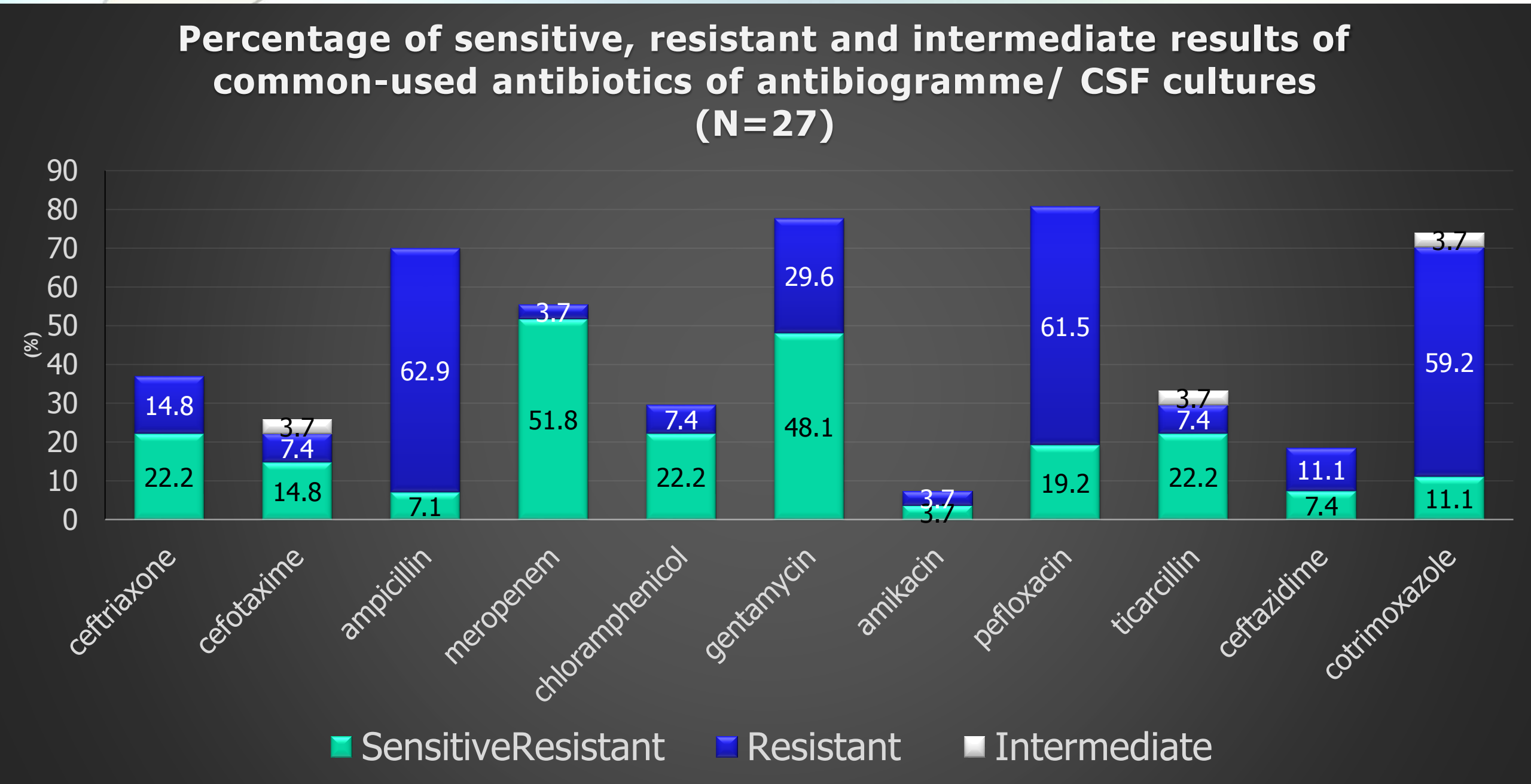
CSF FEATURES

CSF Culture / CSF Gram Stain	Negative	E. coli K1
Negative	11 (26.8%)	11 (26.8%)
Gram(-) bacillus	2 (4.8%)	**16 (39%)**
Others bacteria	**1 (2.4%)**	0 (0.0%)

LABORATORY FINDINGS
CSF FEATURES

		Blood culture *E.coli* (+) n (%)	Blood Culture (-) n (%)	Blood Culture (+) w other bacteria n (%)
Latex (+)	CSF Culture (+)	**8 (19.6%)**	6 (14.5%)	0 (0%)
	CSF Culture (-)	1 (2.4%)	13 (31.8%)	0 (0%)
Latex (-)	CSF Culture (+)	5 (12.1%)	6 (19.6%)	2 (4.8%)
	CSF Culture (-)	0 (0%)	0 (0%)	0 (0%)

LABORATORY FINDINGS



INVESTIGATION

IMAGING STUDIES

Ultrasounds	**n (%)**
Not performed	2 (4.8%)
Performed	**39 (95.2%)**
Results (n=39)	
Normal	6 (15.4%)
Subarachnoid effusion	2 (5.1%)
Subarachnoid empyema	7 (17.9%)
Subdural effusion	12 (30.8%)
Subdural empyema	9 (23.1%)
Ventricular dilation	3 (7.7%)

INVESTIGATION

	1st CT scan, n (%)	2nd CT scan, n (%)
Performed	**31 (75.6%)**	23 (56.1%)
Not performed	10 (24.4%)	18 (43.9%)
Days after disease onset (days)	9 (6-13)	25,5 (18-33)
(Min-max)	(2-45)	(1-65)
Normal	2 (6.4%)	1 (5.56%)
Abnormal	**29 (93.5%)**	17 (94.4%)
Subdural effusion	10 (34.4%)	4 (23.5%)
Subdural empyema	16 (55.2%)	7 (41.1%)
Cerebral Infarction	1 (3.5%)	**2 (11.7%)**
Ventricular dilation	1 (3.5%)	**1 (5.8%)**
Others	1 (3.5%)	3 (17.6%)

ĐẶC ĐIỂM ĐIỀU TRỊ

KHÁNG SINH ĐẦU TIÊN

- 16/19 cases transferred to Children's Hospital 1 had been previously prescribed IV antibiotics before admission (**84.1%)**

- Timing of first use of antibiotics:
  - ✓Before lumbar puncture **(73.17%)**
  - ✓After lumbar puncture (26.8%)

    (2 hours (0-4 hours), latest 7 hours, earliest <1 hour)
- **Cefotaxime** was the most commonly used antibiotics

TREATMENT

REASONS FOR CHANGES IN THE USE OF ANTIBIOTICS

	n (%)
No clinical response after 48h	21/40 (52.5%)
No CSF response after 48h	1/41 (2.5%)
Microbiologically confirmed *E. coli* K1 (Latex and/or CSF culture)	16/40 (40.0%)
Co-infections	2/40 (5.0%)

TREATMENT

Alternative/combined antimicrobial therapy

	n (%)	
Combined antibiotics	4 (9.7%)	
Alternative antibiotics	37 (90.2%)	
Percentage of alternative antibiotics		Doses (mg/kg/d)
meropenem	35 (85.3%)	120
chloramphenicol	17 (41.4%)	100
ceftriaxone	16 (39.0%)	100
pefloxacin	6 (19.3%)	45
ciprofloxacin	5 (12.1%)	45

OUTCOMES

- Discharge: 36 cases (87.8%)
- Length of stay: 41 (18-59) days, min 7 days, max 103 days
- Septic shock: 5 cases (12.2%)
- Respiratory support: 14 case (34.1%) (ventilator (31.7%), oxygen cannula (34.1%), nCPAP (31.7%))
- Imaging abnormality and/or clinical impairment at discharge: 20/41 cases (51.2%)
- Coma (GCS <3) and deaths: 5 cases (12,2%)
- Transferred to other centres for treatment of complications (subdural empyema with midline shift and/or brain herniation): 5 ca (12,2%)
- Hospital-acquired infections: 20 cases (48.7%) (pneumonia, sepsis, skin, GI infections)

Comparisons of features between died and survival groups

	Died (n=5) n (%)/mean±SD	Survival (n=36) n (%)/mean±SD
Fever before admission	**5 (100%)**	28 (77.8%)
Duration of fever before admission	7.6±2,1	3.5±0.3
Duration of fever	20.4±8.2	14.9±1.4
Fever	3 (60%)	25 (69.4%)
Bulging fontanelle	3 (60%)	25 (69.4%)
Abnormal consciousness	4 (80%)	10 (27.8%)
Consciousness evalustion		
Semi-coma	1 (10%)	1 (10%)
Coma	2 (50%)	1 (10%)
Shock	5 (100%)	0 (0%)
Respiratory distress	5 (100%)	9 (25%)
Associated hospital-acquired infections	2 (40%)	18 (80%)

Comparisons of features between died and survival groups

	Died (n=5) n (%)/mean±SD	Survival (n=36) n (%)/mean±SD
FBC	n=5	n=36
WBC (/mm^3)	15.8±4.3	9.6±0.8
Neutrophils (/mm^3)	9.2±3.4	3.9±0.4
C-RP (mg/L)	81.7±36.5	148.0±11.3
Abnormal ABG	**5 (100%)**	8 (22.2%)
Metabolic acidosis	1 (20%)	5 (62.5%)
Respiratory acidosis	4 (80%)	0 (0%)
Electrolyte disturbances	4 (80%)	23 (63.8%)

Comparisons of features between died and survival groups

Imaging investigation	Died (n=5) n (%)/mean±SD	Survival (n=36) n (%)/mean±SD
Abnormal US	**3/3 (100%)**	30 (83.3%)
Ventricular dilation	2 (66.7%)	1 (2.78%)
1st Abnormal CT scan	**2/3 (66.7%)**	27 (75%)
Ventricular dilation	1 (50%)	0 (0%)
Brain herniation	1 (50%)	0 (0%)

4. CONCLUSION

- Lesions on imaging studies at discharge or transfer: 51.2 %
- **3 clinical factors** had significant difference between died and survival groups, and potentially associated with mortality:
  - **Respiratory failure**
  - **Shock**
  - **Abnormal consciousness**
- **3 investigations** had significant difference between died and survival groups, and potentially associated with mortality :
  - **Abnormal arterial blood gases, particularly metabolic acidosis**
  - **Abnormal 1st brain ultrasound**
  - **Abnormal 1st brain CT scan**

5. SUGGESTION

- Severe meningitis: initial antibiotics with **broad coverage** and with high susceptibility to ***E. coli.*** Early use of meropenem might be necessary.
- Other antimicrobials including **meropenem, ceftriaxone and chloramphenicol** might be considered in the setting that antimicrobial resistant *E. coli* meningitis has been emerged.
- **Early imaging investigation**, e.g. **brain ultrasound** for lesions detection and follow-up. Next comes **brain CT-scan** for complication, particularly subdural empyema.
- **Close follow-up** *E. coli* meningitis cases with high risk of treatment failure, e.g. deterioration of consciousness, respiratory failure, and shock.

Thank you for listening!