Non-invasive screening for meningitis via high-frequency transfontenellar ultrasound: Results from the UNITED-Meningitis study in Mozambique

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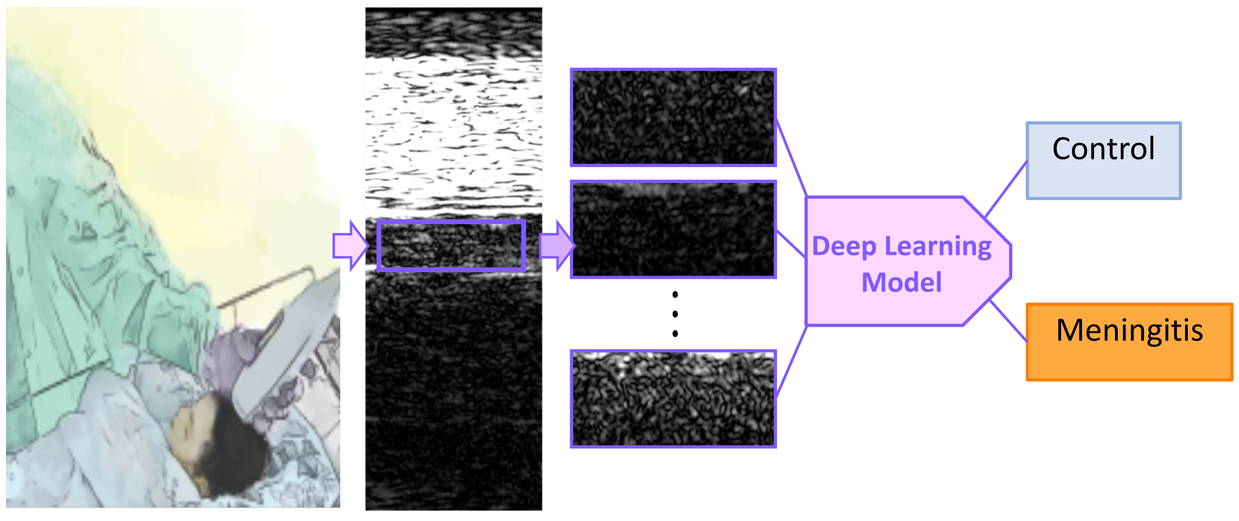
Background

- **Neonatal and infant meningitis** is a life-threatening disease, with significant **risk of death** or permanent neurologic **disability**.
- **Analysis of cerebrospinal fluid** (CSF) obtained through lumbar punctures (LP) continues to be the **gold standard** for diagnosing meningitis.
- In **resource-limited settings,** conditions may not allow LP to be performed or CSF to be analysed for white blood cells (WBC).
- **Alternative screening tools** could help overcome this obstacle by detecting at-risk infants who may benefit from presumptive treatment and/or early referral.
- **UNITED-Meningitis** is a prospective diagnostic study evaluating a **novel non-invasive, high-frequency ultrasonography (HFUS)** exam for transfontanellar imaging using deep learning (DL) models for the detection of very low concentrations of WBCs in CSF.

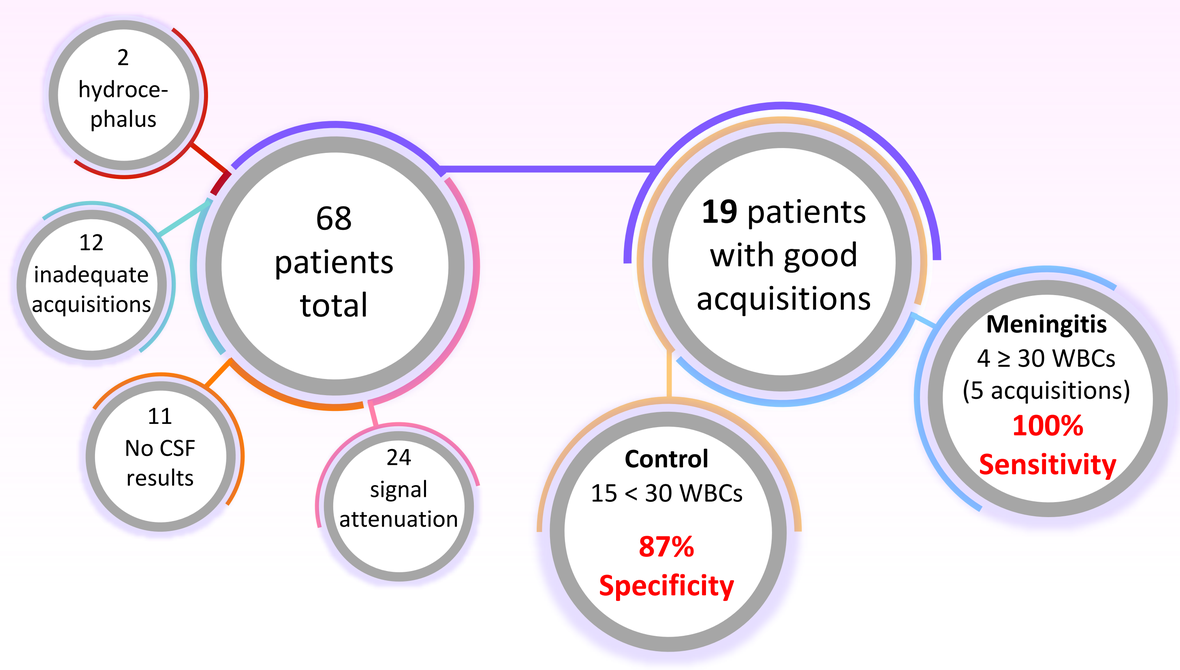
Methods

- Neonates and infants hospitalized at Hospital Central de Maputo with **suspected meningitis** (with/without pre-LP antibiotics) and an **open anterior fontanelle** were eligible for inclusion after informed consent.
- Known hydrocephalus and central nervous system malformations were **exclusion criteria**.
- **LP** was performed with **CSF testing** for cell counts, protein, and bacteriological exams (culture and latex agglutination).
- **HFUS** was performed at recruitment, with follow-up exams for participants with elevated WBC counts.
- HFUS images were processed by the **DL algorithm**, previously trained using a cohort of Spanish neonatal patients, and a threshold of ≥30 WBC/µL to define meningitis cases.

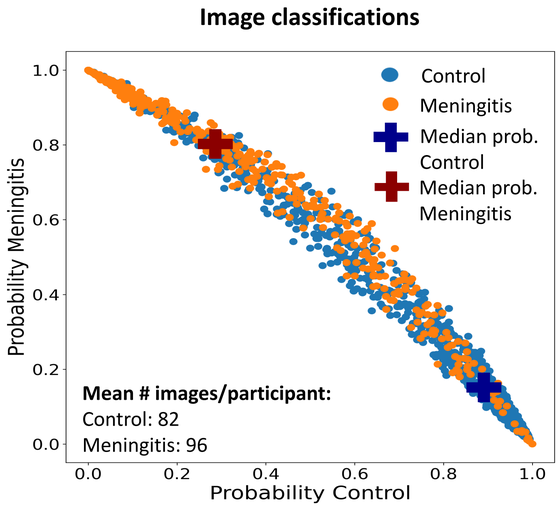


Results

- **Interim results** analysis for 68 participants recruited from March 2021-June 2023 was performed.



- Exclusion of 2 participants diagnosed with hydrocephalus, 12 with inadequate image acquisitions (incorrect imaging location, excessive movement, overlying blood vessels, or poor coupling), 11 without CSF results and 24 with sub-optimal acquisitions (due to signal attenuation), **19 (27.9%) participants with 20 paired CSF WBC count/HFUS were included** (one participant with a repeat LP during treatment).
- The DL algorithm correctly identified 5/5 meningitis cases (**100% sensitivity**) and 13/15 controls (**86.6% specificity**).



Patient Group	WBC number (cells/µl)	Classification Probability (median)
Control	0-25 (median: 0)	0.85
Meningitis	175-19200 (median: 380)	0.88

Conclusions

- **HFUS+DL** show promise as a **non-invasive, quick screening tool for CSF pleocytosis** suggestive of meningitis in neonates and infants.
- Efforts are underway to **improve HFUS image quality and penetration** by using methods for improved coupling for patients with dense/curly hair or thicker fontanelles, higher voltage, increased pulse frequency, and refined DL models.
- Follow-up images will be analyzed to assess the use of **HFUS+DL to measure treatment response**.

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