MENINGITIS SCREENING IN YOUNG INFANTS BASED ON A NOVEL, NON-INVASIVE, TRANSFONTANELLAR ULTRASOUND DEVICE: A PROOF-OF-CONCEPT STUDY

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Background:

Meningitis is a potentially life-threatening disease if not promptly diagnosed and treated. Clinical presentation is often unspecific, especially among young infants and newborns, justifying the need to perform lumbar punctures (LP) to obtain cerebrospinal fluid (CSF) for a laboratory-based confirmation. In high-income settings, LPs are often part of the protocolized systematic approach to screen for meningitis, but as a result, and given the relatively low incidence of meningitis, most are not confirmatory. Additionally, nearly half of LPs cause small bleeding in the puncture zone, hindering the interpretation of cellularity evaluation. The aim of this study was to validate a novel transfontanellar ultrasound-based technique to screen for meningitis, designed to non-invasively identify ranges of white blood cells(WBC) in CSF, to be used on patients with criteria for a LP.

Methods:

Study design:

- Prospective recruitment
- N: 6 cases & 10 controls.
- Three Spanish Hospitals
- Recruitment: 2021-2023

Inclusion criteria:

- Patients under 1 year
- Suspected meningitis
- Permeable fontanel
- LP performed within 24h before enrolment.

Image acquisition, deep learning and prediction:

- Customized high-resolution ultrasonic probe
- Images of the backscatter pattern from CSF
- Deep-learning model trained to classify patterns according to LP WBC values.
- Threshold: 30cells/mm3 (cases vs. controls)

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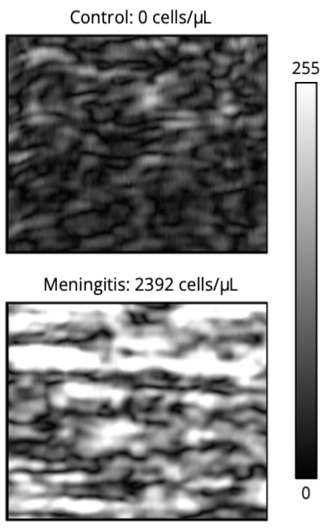

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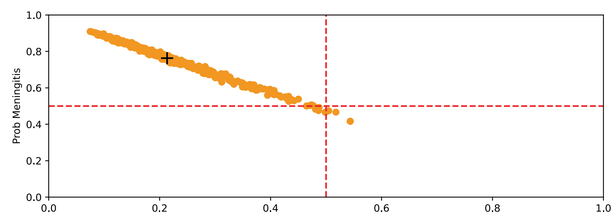

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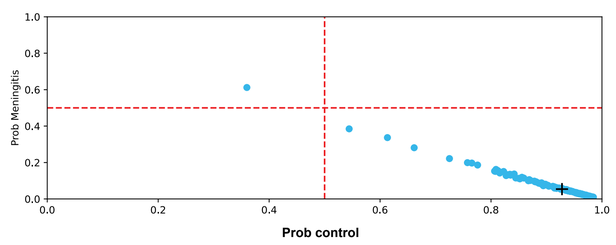

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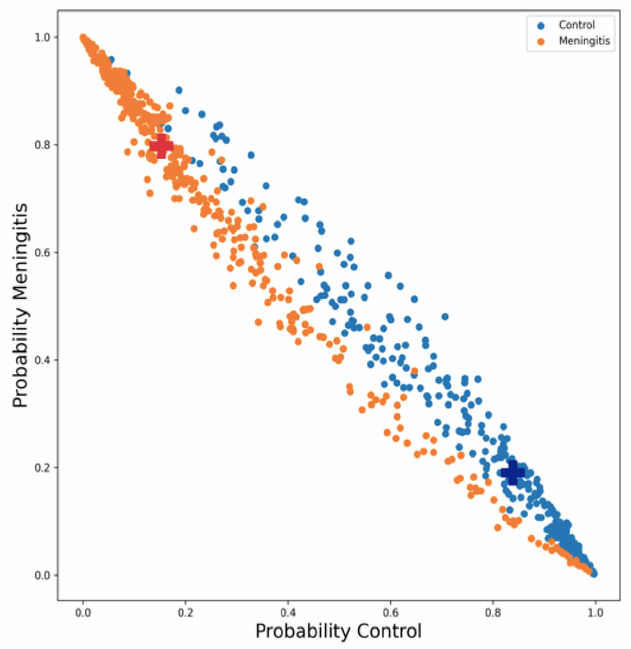

Fig 1: Image of the device positioned on the fontanelle of a neonate. **Fig 2**:Representative examples of the CSF backscatters from a control patient and a patient with confirmed meningitis with high cellularity in CSF. **Figs 3-4**: Individual probabilities of "having meningitis" vs. "not having meningitis" for a patient with meningitis (3) and a control (4). **Fig 5:** cummulative probabilities of "having meningitis" vs. "not having meningitis" across all participants..

Results:

Twenty-five patients were enrolled in the study until we reached the predefined targeted N with good quality images for DL analysis.
Among 16 targeted and recruited patients, 17 LPs were performed, confirming 6 meningitis cases (one patient had a second LP to verify response to treatment) and 10 negative controls.
The final prediction on a patient level relies on a global analysis of all the acquired HR frames.
The device showed a sensitivity of 100% and a specificity of 90%, with one control misclassified.

Participant number	Age (days)	Weight (grams)	Sex	WBC in CSF	% N	CSF micro	Blood culture	Clinical final classification	HR result
1	4	2,035	f	53	66	Negative	***S. hominis***	Not microbiologically confirmed meningitis	case
2	63	5,000	f	85	42	Negative	***S. agalactiae***	Not microbiologically confirmed meningitis	case
3	9	3,900	f	520	3	**Enterovirus**	Negative	Confirmed meningitis	case
4	22	3,370	m	2,400	90	***Klebsiella***	Negative	Confirmed meningitis	case
5	93	4,900	m	300	62	***S. agalactiae***	***S. agalactiae***	Confirmed meningitis	case
6	32	3,600	m	430	41	***S. agalactiae***	Negative	Confirmed meningitis	case
6 (*)				169	29		-		case
median (IQR)	**27** (IQR 15.5-78)	**3,900** (IQR 3,485 - 4,950)		**300** (IQR 85-520)					
7	64	4,420	f	7	-	Negative	Negative	No meningitis	control
8	3	3,290	f	3	-	Negative	Negative	No meningitis	case
9	29	3,000	m	5	-	Negative	Negative	No meningitis	control
10	17	2,965	m	15	-	Negative	Negative	No meningitis	control
11	4	3,890	f	5	-	Negative	Negative	No meningitis	control
12	5	2,690	f	9	0	Negative	Negative	No meningitis	control
13	32	4,000	m	18	16	Negative	Negative	No meningitis	control
14	61	4,150	m	0	-	Negative	Negative	No meningitis	control
15	337	3,600	m	11	-	Negative	Negative	No meningitis	control
16	23	4,220	f	0	-	Negative	Negative	No meningitis	control
median (IQR)	**26** (IQR 5-64)	**3,495** (IQR 3,290 - 4,220)		**6** (IQR 3-11)					

Conclusions:

Our non-invasive ultrasound-based technique, utilizing DL models to determine WBC in CSF, shows great promise in screening for meningitis in neonates and infants with a permeable fontanel. This technique has the potential to aid clinicians in modulating meningitis suspicion, particularly in patients with nonspecific clinical presentations. The use of our device could ultimately lead to a more agile meningitis confirmation, and a reduction in LPs and empirical antimicrobial prescriptions. This will allow a more efficient use of resources and improve patient outcomes at both the individual and public health levels. Studies with larger number of participants are currently ongoing to help us validate these promising results.

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Funding:
Neotec funded by CDTI and supported by the Spanish Ministry of Economy.
SNEO-20161336

Acknowledgements: