Therapeutic Hypothermia for Neonatal Encephalopathy in Indian Neonatal Units: A Survey of National Practices

This cross-sectional web-based survey suggests that cooling therapy is offered as standard of care for babies with neonatal encephalopathy in 10/25 (40%) of public and 37/68 (51%) of private level 2 or 3 neonatal units in India. 25 (53%) used locally improvised cooling methods, and the cooling practices differed from established protocols in high-income countries.

Key words: *Asphyxia, Hypoxic ischemic encephalopathy, Practices, Treatment, low- and middle-income countries*

Therapeutic hypothermia is now the standard of care treatment for neonatal encephalopathy in high-income countries [1]. Although all major cooling trials so far have been conducted in such settings, anecdotal evidence suggests that therapeutic hypothermia is increasingly used in many low- and middle-income countries (LMIC), despite a lack of adequate safety and efficacy data [2]. The dangers of clinical adoption without robust local evidence have been recently highlighted with several therapeutic interventions such as antenatal corticosteroids [3, 4], and fluid bolus for septic shock, where a standard of care therapy in high-income countries was shown to be harmful in LMIC settings [4]. We wanted to examine if therapeutic hypothermia was being offered as a standard of care in Indian neonatal units, and if so, whether the established cooling protocols from high-income countries were being adhered to.

We identified potential participants using the online listing of all level 2 (a and b) and 3 neonatal intensive care units in hospitals across India on the National Neonatology Forum database [5]. We formulated a 10-part questionnaire using multiple choice or dichotomous questions (*www.surveymonkey.com*), and e-mailed an individualized link to the survey to the lead clinicians of the eligible centers, in May 2015. We contacted the lead clinician over telephone if there was no response to multiple e-mail reminders. We exported the responses to Microsoft Excel, and calculated the frequencies and percentages for all categorical responses. We clarified any data queries over telephone with the participants.

We contacted a total of 120 neonatal units, of which 93 (78%) responded. The majority (91%) of respondents were of consultant grade. Of those who responded, 68 (73%) units were in the private or semi-private sector (where patients had to pay full or partial treatment costs), and 25 (27%) were in the public sector (offering free health care to patients). Annual median neonatal encephalopathy admissions in public and private sector hospitals were 250 and 31, respectively.

Forty-seven (51%) units offered cooling therapy in clinical practice, and all of these units were located in areas of low infant mortality (***Web Fig.* 1**). A further 41 (44%) hospitals wanted to offer cooling therapy, but were unable to, due to a lack of cooling devices and trained staff. Although five (5.4%) wanted to see more rigorous research data from clinical trials before routine clinical use, none of the responders felt that cooling therapy was unsafe or ineffective (***Table* I**).

TABLE I PRACTICE OF COOLING THERAPY IN SELECTED TERTIARY AND SECONDARY CARE INDIAN NEONATAL UNITS

	Public (n=10)	*Private (n=37)*
	No (%)	*No (%)*
Criteria for cooling		
Clinical	8 (80)	22 (60)
Clinical and aEEG	0	1 (3)
Clinical and blood gas	2 (20)	12 (32)
Clinical, blood gas and aEEG	0	2 (5)
Cooling devices		
Approved*	9 (90)	13 (35)
Indigenous**	1 (10)	24 (65)
Initiation of cooling#		
Within 6 hours	10 (100)	28 (76)
Upto 12 hours	0	7 (19)
Upto 24 hours	0	2 (5)
Sedation during cooling		
Intravenous	6 (60)	20 (54)
Oral	2 (20)	2 (5)
None	2 (20)	15 (41)
Neuroimaging		
Cranial ultrasound	8 (80)	28 (76)
Computerized tomography	1 (10)	2 (5)
Magnetic resonance imaging	8 (80)	32 (86)

Tecotherm or Blanketrol® ;Phase change material, ice, water bottles, saline bottles and air conditioning: #after birth.*

Our survey suggests that despite a lack of local evidence [2], cooling therapy is now widely used both in public and private sector hospitals in all major Indian cities. However, the cooling practices varied widely from high-income country guidelines [1], particularly in private sector hospitals. As with any survey, the data presented here is subject to recall bias of the respondents as there are no prospective cooling registries in India. Hence, we made no attempt to collect mortality or morbidity data.

Many of these current cooling practices (lack of sedation, delayed cooling therapy beyond 6 hours of age), and locally improvised cooling methods without reliable core temperature control, may be ineffective, and potentially harmful [4]. Extreme cooling methods using ice and frozen gel packs may result in marked fluctuations in core temperature without close nursing monitoring. On the other hand, milder cooling methods using phase change materials, fans, water bottles, or air-conditioning may not result in adequate hypothermia [4]. Furthermore, lower thresholds of inclusion criteria may unnecessarily expose babies without encephalopathy or with mild encephalopathy to cooling therapy.

Deviation from the evidence base established by rigorous randomized controlled trials is not uncommon when a new therapy is introduced into clinical practice, with clinicians becoming increasingly comfortable with the new therapy. A recent Australian survey reported almost half of the cooling in babies in New South Wales deviated from accepted protocols [6]. However, clinicians in LMIC need to recognize that the evidence base for the routine use of cooling therapy in these settings is not yet available, and further research is required to establish this. The success of the cooling story appears to be so overwhelming that none of the neonatal centers in India expressed concerns about safety or ineffectiveness, despite a lack of any published long-term outcome studies of cooling therapy from low- and middle-income countries.

Whilst more research data are awaited from rigorous randomized controlled trials of cooling therapy in LMIC, it may be prudent to develop national guidelines and training programs on cooling therapy for routine clinical practice in these countries.

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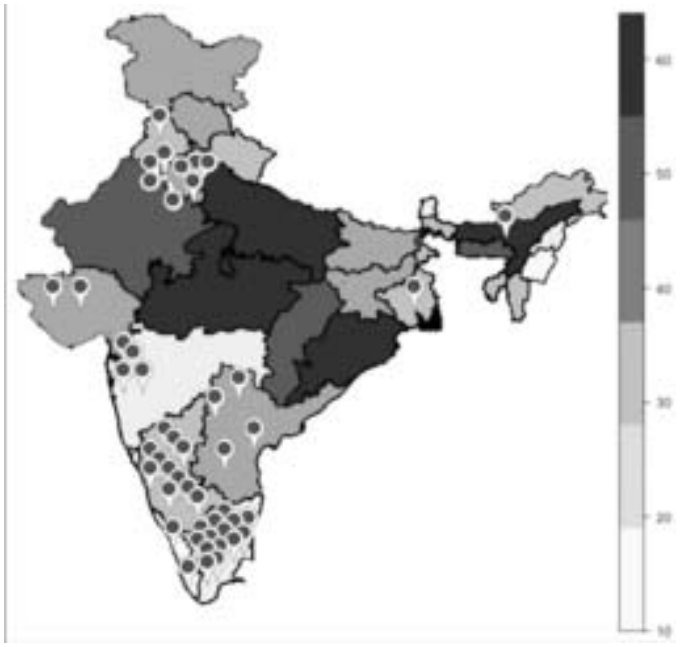

WEB FIG. 1 *Distribution of the hospitals offering cooling therapy (blue circle), superimposed on a heat map of infant mortality rates.*