

The assessment of general movements in term and late-preterm infants diagnosed with neonatal encephalopathy, as a predictive tool of cerebral palsy by two years of age - A scoping review.

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Research

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Abstract

BACKGROUND The General Movements Assessment is a non-invasive and cost-effective tool with demonstrated reliability for identifying infants at risk for cerebral palsy. Early detection of cerebral palsy allows for implementation of early intervention, and is associated with better functional outcomes. No review to date has summarized the utility of the General Movements Assessment to predict cerebral palsy in term and late-preterm infants diagnosed with neonatal encephalopathy.

METHODS We conducted a scoping review involving infants born greater than or equal to 34 weeks gestational age to identify all available evidence and delineate research gaps. We extracted data on sensitivity, specificity, positive and negative predictive value and described the strengths and limitations of the results. We searched five databases (MEDLINE, Embase, PsychINFO, Scopus and CINAHL). Two reviewers conducted all screening and data extraction independently. The articles were categorized according to key findings and a critical appraisal performed.

RESULTS From the electronic database search, only two studies, case series, met all of the inclusion criteria. The total number of participants were 60. Neither of the final eligible studies included late-preterm neonates. Both studies reported on sensitivity, specificity, positive predictive and negative predictive value. The newer study reported that in the time period between term and 4-5 months post-term, that any cramped synchronized movements in this time period had results of 100% sensitivity and variable results for specificity, positive predictive value and negative predictive value. Neither of the studies had infants that received therapeutic hypothermia for Neonatal Encephalopathy.

CONCLUSIONS The finding of cramped synchronized General Movements is a strong predictor for the diagnosis of cerebral palsy by two years of age in the term population with neonatal encephalopathy. The deficit of high quality research limits the applicability and so the general movements assessment should not be used in isolation when assessing this population.

Systematic review registration

Title registration with Joanna Briggs Institute. URL: http://joannabriggswebdev.org/research/registered_titles.aspx

Background

Prediction of long-term neurodevelopmental outcomes remains an elusive goal for neonatology. Clinical and socioeconomic markers have not proven to be as reliable as we have hoped^{1,2}. The limitation in prognostication is particularly challenging for those term and late-preterm infants born with neonatal encephalopathy (NE).

NE describes those infants born with an atypical neurological exam and is by definition heterogeneous in etiology³. The specific etiology may not be clear for months to years later but the presentation is characterized by central nervous system disruption⁴ and is associated with an increased risk for long-term neurodevelopmental challenges including cerebral palsy (CP). Infants presenting with NE are managed now with therapeutic hypothermia as the standard of care; this is presumptive management, and is time sensitive should the etiology be hypoxia/ischemia (Hypoxic Ischemic Encephalopathy (HIE)), in term and late-preterm infants^{4,5}. Therapeutic hypothermia reduces the likelihood of challenging outcomes by containing any potential ongoing neurological injury. It does not, however, completely eradicate the possibility of long-term neurodevelopmental disability⁶.

For parents of infants affected by NE, the desire for accurate prognostication is of tantamount importance^{6,7}. This information can guide decisions around early intervention and, in severe cases, withdrawal of care for those infants with severe involvement. For those infants that survive NE and are at increased risk for CP, recent international recommendations now call for early detection and intervention of CP in order to improve functional outcomes^{1,8,9}. These recommendations are based on mounting evidence for better detection tools as well as the benefits of early intervention.

Historically, clinical and radiological predictors of neurological outcomes were used to classify the degree of NE. Severity scoring systems include the classical grading by Sarnat and Sarnat¹⁰ in 1976, to the newer scores by Miller et al.¹¹ in 2004, with added parameters such as oral feeding difficulties and the presence of seizures. Radiologically, specific findings of diffusion restriction on magnetic resonance imaging (MRI) have been linked to later development of CP⁴. These predictors, however, were not sufficiently accurate^{1,2} and the high costs of imaging as well as shortages in access further restricts the utility. Neurological examinations have historically been limited in predictive value but recent emerging evidence with an observational tool, the General Movements Assessment (GMA) developed by Dr. Heinz Prechtl has demonstrated strong predictive value^{12,13}.

The GMA is a non-invasive, cost-effective tool with demonstrated reliability for identifying infants at risk for neuromotor impairment¹⁴. General movements (GMs) are complex, highly variable, whole-body movements which emerge in the fetus and progress through an age-specific developmental trajectory, dissipating by the end of the first four to five months of life¹³. Developmental progression and variety, or lack thereof, are indicators of nervous system integrity and can reflect neurodevelopmental outcomes¹⁵. Cramped synchronized (CS) and absent fidgety movements are considered abnormal GMAs, demonstrating developmental stereotypy¹³. Additionally, the Motor Optimality Score (MOS) represents a more detailed quantitative analysis of the general movements motor repertoire of infants between 11 and 17 weeks post-term. The MOS has been shown to be predictive of the severity and type of Cerebral Palsy^{16,17}.

Several researchers have looked at the GMA from different aspects. We were interested in term and late-term preterm infants with NE and how the GMA may be useful in predicting CP. A preliminary search of PROSPERO, MEDLINE, the Cochrane Database of Systematic Reviews and the Joanna Briggs Institute (JBI) Database of Systematic Reviews and Implementation Reports was conducted to assess this research. There were two current systematic reviews on GMA, one in 2018¹⁸ and the other in 2017⁹. In addition, eight older reviews were identified: seven systematic reviews^{13,19-24} and one literature review²⁵ done between 2001 to 2013. The search also revealed three pending reviews identified around the topic of the predictive value of GMA²⁶⁻²⁸. These pending reviews were all systematic reviews.

The key characteristics and main findings of the above reviews on GMA are detailed in the protocol for this systematic review²⁹ and is included in Table 1, Additional file 1. The two latest reviews were by Kwong et al. 2018¹⁸ and Novak et al. 2017⁹. In general, these reviews did not look specifically at the population we were interested in for this scoping review, that is, term and late-preterm infants with NE. Additionally, the other systematic reviews and literature review were all more than five years ago with the latest in 2013¹³. Thus, a gap exists in the literature to clearly identify the evidence for our population of interest.

The objective of this review is therefore, to identify the scope of the research with regards to the GMA and its ability to predict CP, in term and late-preterm infants with a diagnosis of NE, and to identify the gaps in the literature.

Objectives

The primary research question for this review is: What is the published data on the predictive value of the GMA for the diagnosis of CP by two years of age in infants born at term or late-preterm presenting with NE?

The secondary research question is: What is the gap in the literature when the GMA is used to predict CP by two years of age in infants born at term or late-preterm presenting with NE?

Methods

Study Design

A scoping method was chosen for this type of review to fulfil our objective which requires searching and assessing a wide range of research methodologies involving the use of the GMA in CP prediction. A scoping review captured all types of relevant research on the topic in a systematic, transparent, rigorous and reproducible manner. This scoping review was conducted in accordance with the JBI methodology for scoping reviews⁴⁰. The objectives, inclusion criteria and methods for this scoping review were detailed in advance and documented in a proposal (included as Additional file 2). The title of our review was registered with JBI. The protocol was published prior to this review³⁹ (Additional file 1).

Inherent in the nature of the scoping review is the inclusiveness of a wide range of literature, and so we anticipated differences in the data quality. Critical appraisal and data synthesis therefore were challenging in terms of conclusive evidence as opposed to that from a systematic review. The scoping review methodology was however especially advantageous to our question as these types of reviews target areas that have not been comprehensively assessed before.

Eligibility Criteria

The participant, concept, context (PCC) framework for scoping reviews was used to define the review focus and is summarized in Table 2 below.(see Additional file 1).

Table 2

Inclusion and exclusion criteria for the prediction of CP by the GMA in late-preterm and term infants with NE		
	Inclusion criteria	Exclusion criteria
Participants	Studies with infants who were: <ul style="list-style-type: none"> - ≥ 34 0/7 wks GA - diagnosis of NE - had a GMA done between birth up to six months of life - had an assessment for CP by at least two years of age 	Studies with infants born with: <ul style="list-style-type: none"> life threatening congenital abnormalities, congenital viral infections, an abnormal karyotype, and metabolic disorders
Concept	GMA as a predictor of CP by two years of age is the main concept	
Context	Studies that reported on: <ul style="list-style-type: none"> - Infants with NE managed in hospitals and diagnosed by the standard of care (neurological history and examination) - Studies from all countries that have outcomes reported in the acute neonatal and in the follow-up period by two years of age - Studies in the English language only 	

Note. CP = cerebral palsy, GA = gestational age, GMA = general movements assessment, NE = neonatal encephalopathy, wks = weeks

Participants

Our chosen population encompasses an age group ≥ 34 0/7 weeks GA as the option in this group exists for medical management for NE that significantly impacts neurological outcomes, specifically therapeutic hypothermia²⁰. Current eligibility criteria for therapeutic hypothermia has been determined by randomized controlled trials, supporting intervention in infants ≥ 35 weeks GA⁴¹. There are variations in practice with consideration for extension of treatment to younger gestational ages⁴². We therefore chose this GA to ensure we captured all the relevant literature.

Concept

The GMA is a non-invasive tool that has been shown to have predictive validity for CP⁶. Traditionally, CP has been diagnosed by 12 to 24 months^{11,43}. We considered a diagnosis by two years as by this time the majority of diagnoses should be made⁶.

For the GMA to be used as a predictive tool for CP we considered studies with the statistical tests named in Table 2 above, as these would provide the best guidance for this clinical application⁴⁴. Detailed definitions of concepts can be found in Table 3 (Additional file 1).

Context

Management affects outcome and so to potentially avoid having results that were vastly different due to non-hospital based management, we restricted our search to studies with in-hospital care in the acute period. We also considered the variability in the diagnosis of NE and so chose a baseline of at least a history and neurological examination for the diagnosis. We chose to look at all countries to be able to be as exhaustive as possible in our search.

Studies in the English language only were considered as there is no team member with adequate language skills to translate from any other language.

Search strategy and databases searched

A range of electronic databases were searched to include medicine, nursing, allied health professions, sociology, psychology, education and social work. This scoping review considered both experimental and quasi-experimental study designs including randomized controlled trials, non-randomized controlled trials, before and after studies and interrupted time-series studies. Case reports, case series, case control and cross-sectional studies and systematic reviews that met the inclusion criteria were included. Text and opinion papers were not considered for inclusion in this scoping review as this is a highly specific and medical topic. Animal studies were not included. Studies published from at least 1970 were included. Prechtl first described GM in 1979 and so we chose this date to ensure all the related research would be captured^{1,28}. The reference lists of articles were scanned and experts in the infant developmental field were consulted to identify studies relevant to our topic.

The search strategy was phased, firstly created in Ovid Medline using a combination of index terms and keywords around general movements, Prechtl, brain disease, HIE and perinatal asphyxia. An initial limited search of Ovid Medline, Embase and PsychINFO was undertaken to identify articles on the topic (See Additional file 3). There were no previous similar reviews. The text words contained in the titles and abstracts of relevant articles, and the index terms used to describe the articles from this limited search were then used to develop a more refined full search strategy in the second phase, for MEDLINE, Embase, PsychINFO, Scopus and CINAHL (Additional file 4). The search strategy, including all identified keywords and index terms, were adapted for each included information source.

Study selection

EndNote X9 was used for citation collation. Duplicates were removed manually. Covidence was used for screening by two independent reviewers (JS and ML). Disagreements were resolved through a third reviewer (RB). The results of the search were reported in a Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping reviews⁵¹.

Ethical approval was not required as this was a scoping review and did not contain information directly identifying patients or content requiring patient consent. We conducted our bibliographic database searches between April 30, 2019 and March 30, 2020. The reference lists of all full-text relevant studies that were identified were hand-searched for additional relevant studies. Citations were identified, duplicates removed and screened by two independent reviewers (JS, ML). Relevant studies were identified for full text review and searched for via Google Scholar, institutional journal access, e-Resources and databases sites. Any disagreements that arose between the reviewers at each stage of the study selection process was resolved through discussion. A third reviewer (RB), was the final arbitrator for any unresolved disagreements.

From the full texts, articles were selected for further review that met most of the inclusion and exclusion criteria. From these, articles were identified that fully met all the criteria. The results of the search were reported in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA-ScR) flow diagram⁵². Each article was independently reviewed and assessed by two of the authors (JS, ML). The data was extracted from articles using a data extraction tool developed by the reviewers. The format for the data extraction tool was modeled after that used by Kwong et al. in their 2018 review²⁷. This decision was taken as that review aligned well with our study in describing the predictive ability of GM for later CP, although not specifically to our population.

The distribution of the studies was determined by year of publication, as well as country of origin. These were important contextual factors as the older studies and the physical and human resources of each country may have posed limiting factors. A major consideration could have been the ability to obtain a representative portion of the population which affects the generalizability of the results. The study characteristics included information such as gender, GA, birth weight, numbers of term and late-preterm neonates in the sample as well as the overall sample size, number of neonates diagnosed with NE and the number of cases of CP.

Results

Following the searches, 883 citations were identified. The results of the search were reported here in a flow diagram (Figure 1), adapted from the PRISMA-ScR⁵² structure.

There were 19 studies^{5,9,10, 53, 54, 57, 60, 62, 64, 66, 67, 69, 70, 72, 73, 75,77, 79, 80} that included late-preterm and term infants but did not delineate them as a specific group as it relates to their diagnosis of NE and their CP outcomes and when using GMA as a predictive tool. Table 4 (Additional file 4) presents the summary of the characteristics of the excluded studies. There was a wide variety in their key characteristics. We summarized these characteristics here. These studies had a wide date range from 1997 to 2019. They were mainly prospective studies (14 of the 19) and the majority used clinical assessments only to identify infants at high risk (10 of the 19). With regards to the assessment tools used, of the 19 studies, 18 used the GMA by Prechtl. For the age at which CP was diagnosed, 12 of the excluded studies used the same criteria as we did in this study, that is, CP diagnosis by at least 2 years. For the method of CP diagnosis, a variety of standardized assessments were used, with the most frequent being by Amiel-Tison and Grenier⁵⁸.

Eight studies either used non-standardized methods or did not clearly state their method.

Table 5 (Additional file 4) presents the summary of the key findings of these excluded studies and reasons for their exclusion. These findings showed that in high-risk infants, including those with NE, GMA is a strong predictor of CP⁵³, especially when used in the fidgety period period^{10,54, 67,69,75,79}. In 1997 Prechtl et al.⁵ demonstrated that movement quality was important. Abnormal quality and absent fidgety movements, in a mixed group of preterm and term infants, predicted neurological abnormalities with a sensitivity of 96%. The majority of these were diagnosed as CP. We see in our results, that over time this result has been repeatedly duplicated showing that CS⁶⁰ and absent fidgety⁷⁰ GM are highly predictive of CP. The trajectory of the GMA is more important as a predictor of CP⁵⁴.

The GMA is more sensitive than the traditional neurological examination^{55,60,64} and the sensitivity increases with combined use of other modalities such as electroencephalogram (EEG)⁶⁴, neuroimaging⁷⁷, Hammersmith Infant Neurological Examination (HINE) and neuroimaging⁷⁰.

For these excluded studies, sensitivity values were as high as 100%^{53,54,60,66,69} and specificity similar close to^{53,70} or at 100%⁷⁵. We contacted the authors of the study closest to our inclusion criteria, Solemani et al.⁷⁵, as they delineated their populations by NE and by GA but their outcome was reported as “neurodevelopmental outcomes” and not CP. They reported to us that they did not specifically report CP and so could not be included for us. PPV and NPV was reported for eight of the excluded studies^{5,64,46,67,70,73,75,77} with some studies reporting PPV as high as 98% when used in combination with HINE and neuroimaging⁷⁰ and NPV as high as 100%⁶⁶. Themes for the limitations identified by the authors can be summarized as limited external validity due to small population size,^{60,62,70,79,80} selection bias related to recruitment from high-risk populations^{5,9,70}, and practice

variation between sites^{53,66,69}. The most common reasons for exclusion of these studies were failure to delineate their participants for the diagnosis of NE, most quoting their participants as high-risk infants, or not delineating their GA into the groups relevant to our questions (late-preterm and term).

Only two articles therefore, one by Ferrari et al.⁸¹ and the other by Prechtl et al.⁸², were identified as meeting selection criteria and were included in the final review. The results of the search were reported here in a flow diagram (Figure 1)⁵². The final two studies included were case series^{81,82} from Italy. The total number of participants were only 60 term neonates (34 and 26 participants respectively); neither included late-preterm neonates. NE was reported as a single group by Ferrari et al.⁸¹ but divided into mild-moderate and severe by Prechtl et al.⁸². The high-risk groups in both studies were identified by history only. The GMA used by both studies was Prechtl. Table 6 (Additional file 4) presents the characteristics of these two studies. Both were published more than five years ago and reported on sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

A variety of standardized tools were used for CP diagnosis between the two studies. Table 7 (Additional file 4) details the key findings and the outcomes evaluated, with the limitations identified by the authors. In the more recent study, Ferrari et al.⁸¹ reported that the presence of any CS movements between term and four to five months post-term had a sensitivity of 100%, specificity of 68.7%, with a PPV 100% and a NPV of 78.3% for predicting CP. In the older study by Prechtl et al.⁸², the predictive ability in terms of the timing of the GMA was determined, that is, if done early, in the first two weeks of life versus late assessments between 15-22 weeks of life. Their findings were: sensitivity 100%, specificity 46.2%, with PPV 65.0% and NPV 100% for the early assessments, compared to late assessments with 84.6% across the board for sensitivity, specificity, PPV and NPV. Neither of the studies included infants receiving therapeutic hypothermia for NE which was not yet the standard of care. Ferrari et al.⁸¹ identified selection bias as a limitation, where mild HIE as a contributor to NE may have been underrepresented due to these infants not being referred for evaluation. Prechtl et al.⁸² did not state their limitations.

Risk of Bias

Even though this was a scoping review and did not require the critical appraisal of the two included articles, the critical appraisal tool for JBI⁸³ helped to identify differences and similarities between these two case studies. These main points are summarized here and details are presented in Table 8 (Additional file 5).

The quality of evidence derived from a review is largely dependent on the quality of the studies included. Neither study scored 100% on all ten questions. The two studies scored 100% for six of the ten questions on the checklist. These questions assess the two included studies as being moderate quality case series as there were limitations. They had good scores for using valid methods for identification of the condition for all participants, having clear reporting of the demographics of the participants in the study, as well as, having clear clinical information of the participants. The outcomes of the cases were clearly reported for both studies. They also had clear reporting of the presenting sites demographic information and used appropriate statistical analysis.

According to the JBI method, for the study participants, the authors should provide clear and exclusion criteria. These inclusion and exclusion criteria should be specified with sufficient detail and all the necessary information critical to the study. While Ferrari et al.⁸¹ did fulfil this criteria, of note, Prechtl et al.⁸² did not state their exclusion criteria and so this may limit the generalizability of the results. For good quality case series, the study should clearly describe the method of measurement of the condition. This should be done in a standard (i.e. same way for all patients) and reliable (i.e. repeatable and reproducible results) way. The clinical condition for our study is NE. Both studies listed a number of criteria for possible inclusion for NE but did not state the number or combination of these criteria required for the diagnosis and so scored 0.0% for this question. They did use a standard, albeit different, method for NE severity, with Ferrari et al.⁸¹ use the Sarnat staging²² while Prechtl et al.⁸² used the Levene method⁸⁴. With regards to consecutive inclusion, studies that indicate a consecutive inclusion are more reliable than those that do not. Neither of our included studies stated clearly if they did consecutive inclusion of every neonate meeting the inclusion criteria, at their institutions, during the identified periods. Thus they both scored 0.0% for this. Along a similar vein, the completeness of a case series contributes to its reliability. Studies that indicate a complete inclusion are more reliable than those that do not. Neither Ferrari et al.⁸¹ nor Prechtl et al.⁸² clearly stated that they included all the patients in their studies and scored 0.0% for this question.

The biases include selection, information and sampling variation. Selection bias is typical of case series as it is a choice of a series of patients with a particular illness (NE), and a suspected linked outcome (CP)⁸⁵. Selection bias limits the generalizability of results. Information bias is less in retrospectively collected data as it is determined by what is already documented in the medical chart. These two studies both were prospectively collected data making them susceptible to information bias. With regards to sampling variation, the precise determination of the rate of a disease, other than by chance, requires a large sample size. Both studies can be described as employing small sample sizes, Ferrari et al.⁸¹ had 34 cases and Prechtl et al.⁸² had 26 cases with a follow up period of over three to four years. Sample size may have been limited by the collection method as neither study stated if they were inclusive of every neonate meeting the inclusion criteria, at their institutions, during the identified periods.

Discussion

The scoping review methodology provided valuable insight to the current limited state of knowledge on the use of the GMA in the term neonate diagnosed with NE to predict CP by the age of 2 years. In fact, in the late preterm infant with NE there was no evidence that met our inclusion criteria.

Furthermore, the evidence was derived from case studies which does not constitute a level of evidence on which we can base definite recommendations. Our scoping review results highlights the need for more specific, higher quality research in this area.

From the review we were able to glean some important insights for the use of the GMA in our population. In both studies the presence of the CS movement pattern of the GMA does correlate with the prediction of CP by two years of age. Prechtl et al.⁸² noted that NE has an effect on spontaneous movements in term neonates, be it transient or persistent. Early assessments may be unable to differentiate between abnormal spontaneous movements that may be transient from those that will persist and eventually be associated with CP. Early assessments do not give as good predictive values as later assessments therefore the trajectory of the GMA may be a more significant indicator of outcomes than a solitary assessment^{54,82}.

Limitations of the included studies

Our findings support the role of the GMA as a good tool for prediction of CP for those infants born at term with NE. There are however limitations to consider including: both publications were case series, the variability in the NE definitions, the date of the publications identified and neither study contained neonates treated with the now standard of care, therapeutic hypothermia. Another important limitation is the low number of studies meeting our inclusion criteria.

Firstly, internal validity is likely to be low, as occurs in case series, since there are no comparator groups exposed to a similar array of variables. External validity would similarly be limited. Since this scoping review only represents Level IV evidence⁸⁶ it reveals the need for future research in this area since it suggests that neonates with NE, at least those at term may benefit from follow-up assessments with the GMA to help earlier identification of CP.

Secondly, in terms of the definition of NE, for the study by Ferrari et al.⁸¹ there were some differences in the way NE was defined. In general, the standard accepted criteria that defines NE was used, but they stated that study participants had different combinations of the NE criteria. Evidence shows that the etiology^{23,27} of encephalopathy as well as its severity²³ may influence outcomes. Although the severity of NE (that is, mild, moderate or severe reflected by the Sarnat stage) was assessed in the study, no further differentiation of severity as it related to the predictive ability for CP was done. This may have been due to the small sample size of the study (n=34) and the inevitable decreased power that would have resulted from subdivisions. Prechtl⁸² also subdivided the NE diagnosis into mild to moderate (n=13) and severe (n=13) NE. Similar to Ferrari⁸¹, outcomes were not reported according to these NE subdivisions.

Thirdly, in terms of the timing of the publications, both were more than five years old. Management has changed over time and updated data in this evolving area would be beneficial. It is however interesting that the older study by Prechtl et al.⁸² in 1993 supports the same later findings of the Ferrari et al.⁸¹ study in 2011 with respect to the predictive ability of the GMA. This lends support to the reliable role of the GMA in the identification of those children born at term with NE who are at risk for CP.

Fourthly, neither of the studies seemed to have been done in neonates treated with therapeutic hypothermia, which is the current standard of care^{18,19}. We are therefore uncertain if therapeutic hypothermia changes the quality of the GM and if it does change, how long might this persist. Information like this is important to inform the timing of the early GMA- post therapeutic hypothermia intervention. Similar consideration had to be done for identifying the optimal window for cranial MRI in neonates treated with therapeutic hypothermia⁸⁷. This lends credence to the gap in research in this area of NE and its association with CP.

Strengths and Limitations of this review

The strength of our review primarily lies in the Scoping review methodology that we chose. This method was advantageous as it facilitated an exhaustive search of the literature to define the current extent of knowledge and so allowed the research gaps to be identified.

We appreciated that there were several limitations. Firstly, we excluded studies that were not in English. This may be significant as there were only two studies identified in the review that met the established inclusion criteria. Therefore with this limited number any additional studies may have impacted our results. Secondly, the ages of the studies are of concern. The study that was published in 2011 by Ferrari⁸¹, recruited participants between 2003 and 2006. The cohort of the Prechtl study was recruited between 1985 and 1989. Medical management has evolved since then to include strategies such as therapeutic hypothermia^{18,19}. The impact of this on our results is unknown. Lastly, we recognize that using a cut off of CP diagnosis by two years of age constitutes a limitation as milder forms of CP may not be identified by this age.

Suggestions for further research

This review elucidates multiple potential areas for research.

Quantitative research:

Meta-analysis - A meta-analysis of the data was not possible due to the minimal number of studies available. As more data becomes available more accurate suggestions, for the use of the GMA in our population, can be made.

Prospective study - To provide higher quality evidence, a prospective study looking at the use of the GMA with the MOS in our population of term and late-preterm infants diagnosed with NE is needed. Medical management has changed since the era of the cohorts included in this review. The link of the GMA with respect to NE severity, etiology and contemporary management would be of benefit.

Predictive ability of GMA in CP severity in our population – Determination of the predictive ability of the GMA, including the MOS, for the degree of functionality in CP, such as that determined by the Gross Motor Function Classification System (GMFCS)⁶³ scoring system would be beneficial for implementation of early intervention strategies.

Optimal timing of an early assessment - Since the trajectory of the GM may provide significant clues to neurodevelopmental outcomes more research is needed in this area. Transient effects on the GM may result from medical management such as therapeutic hypothermia and medications including sedatives and anticonvulsants. Optimal timing of the first assessment in this population requires further elucidation.

Qualitative research:

Parental counseling and anticipatory intervention – Parental perspectives on the use of the GMA as a predictor of neurodevelopmental outcomes in our population would be desirable for future research. This would influence counseling by the medical teams with regards to reassurance or the need for early intervention and extent of neurodevelopmental follow-up.

Conclusion

The finding of CS GM is a predictor for the diagnosis of CP by two years of age in the term population with NE. In term infants with encephalopathy the predictive ability of the GMA is not as reliable when performed early versus later (at 15-22 weeks of age). Additionally, there are no existing studies specific to the application of the GMA in late-preterm infants with NE.

The deficit of high quality research limits the applicability and so the GMA should not be used in isolation when assessing these populations. The evidence for this is limited by few studies and a lack of high quality research. The evidence is lacking for the utilization of the GMA in these populations treated with therapeutic hypothermia. Furthermore, of possibly greater potential applicability is the inclusion of the MOS as a predictor of CP^{7,8} in term and late preterm infants with NE when treated with therapeutic hypothermia.

List Of Abbreviations

BW, birth weight; CI, confidence interval; CP, cerebral palsy; CS, cramped synchronized; EEG, electroencephalogram; ELBW, extremely low birth weight; FM, fidgety movements; GA, gestational age; GM, general movements; GMA, general movements assessment; GMFCS, Gross Motor Function Classification System; HIE, hypoxic ischemic encephalopathy; HINE, Hammersmith Infant Neurological Examination; JBI, Joanna Briggs Institute; LR, likelihood ratio; LBW, low birth weight; MOS Motor Optimality Score; MRI, magnetic resonance imaging; NAPI, Neurobehavioral Assessment of the Preterm Infant; NBW, normal birth weight; NE, Neonatal encephalopathy; NPV, negative predictive value; n.s., not stated; PCC, participant, concept, context; PMA, postmenstrual age; PR, poor repertoire; PPV, positive predictive value; PRISMA-ScR, Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping review; TIMP, Test of infant motor performance, SD, standard deviation; US, ultrasound; VLBW, very low birth weight; wks, weeks.

Declarations

Ethics approval and consent to participate

Ethical approval was not required as this is a scoping review of the literature and did not contain information directly identifying patients or content requiring patient consent.

Consent for publication

Not applicable

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study. Materials during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

First author: Judy Seesahai

Contributions: Substantial contributions to research design, acquisition, analysis and interpretation of data as well as drafting the paper.

Second author: Thomas Rotter

Contributions: Substantial contributions to research design and reviewing of the paper.

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Contributions: Contribution to acquisition, analysis and interpretation of data as well as involved in revisions to the paper.

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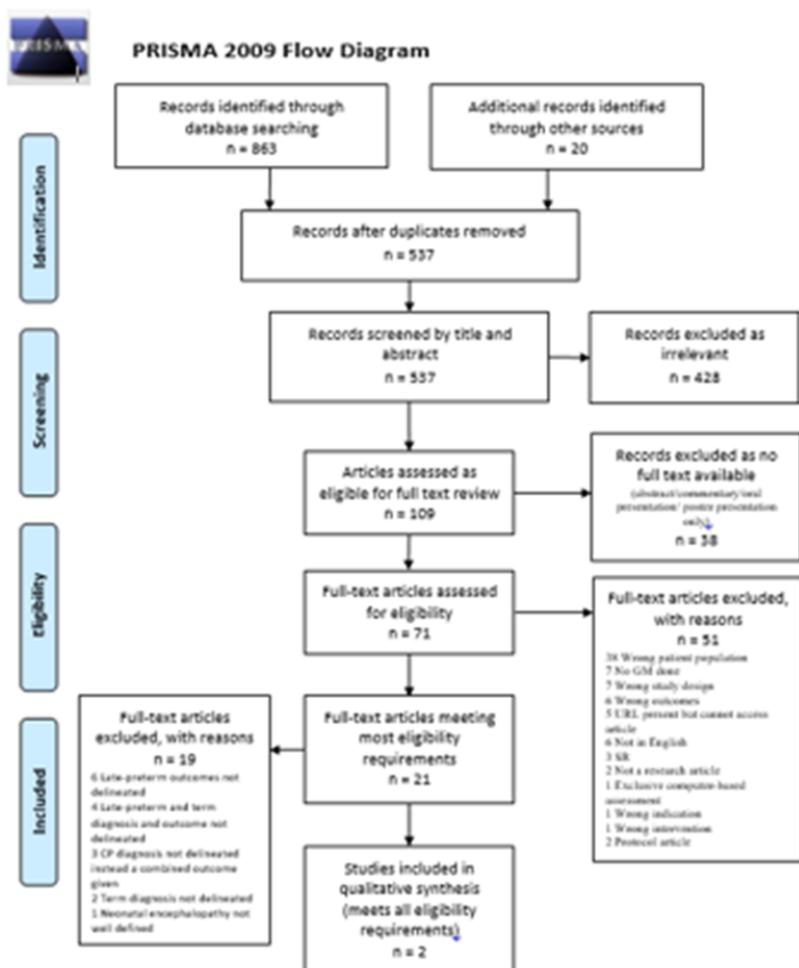
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Figures



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Figure 1

Flow chart for the selection of articles at different phases of the scoping review

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