Meta-analysis of the Association between Neural Tube Defects and Craniofacial Trauma: A Systematic Review and Quantitative Synthesis

Saniya Sadaf Khan

New York Medical College, 1USA

Abstract

Background: Neural tube defects (NTDs) are congenital anomalies involving malformations of the brain and spinal cord due to an impaired closure process of the neural tube early in embryonic development (Avagliano et al., 2019; Copp et al., 2013). They are known to be linked with a great number of structural anomalies, namely brain and craniofacial anomalies (Greene & Copp, 2014). Yet, there has not been a comprehensive, scientific, quantitative analysis conducted concerning an association between neural tube defects and craniofacial trauma. The reason why a causal association would be considered biologically implausible refers to the congenital as well as acquired natures, respectively.

Objective: To systematically review the literature for empirical links that have been found to exist between neural tube defects and craniofacial trauma over the life span, in addition to exploring the possibility of quantitative meta-analysis.

Methods: Using PubMed/MEDLINE, EMBASE, Web of Science, and Scopus (from inception to December 2024), electronic literature research was performed with combinations of terms that encompass neural tube defect-related research terms (such as spina bifida, anencephaly, encephalocele) and craniofacial trauma (e.g., facial trauma, maxillofacial injuries, head injury, craniofacial fractures). Inclusion criteria were: (1) human studies, (2) original data on individuals with NTDs and a comparison group (or population denominator), and (3) inclusion of craniofacial trauma incidence, prevalence, or odds in those with NTDs vs. those without defined in the publication. If three or more highly homogeneous studies were identified, the literature would be pooled in an outline proposal under random effects meta-analysis with either Odds Ratios (ORs) or Risk Ratios (RRs) as study results. Bias would be evaluated using an appropriate risk tool f or the study design type (cohort, case-controlled, and cross-sectional research models).

Results: Among a pool of 1,247 unique records, no analytic study could be identified for a quantitative assessment of the risk of craniofacial injuries among persons affected bt NTDs compared to a proper control group. The only publications at hand were isolated case reports and a limited number of case reports of case reports dealing with :(1) craniosynostoses and cranial dysraphism associated with NTDs; and (2) congenital cranial bone defects like cranioschisis and encephaloceles, within the NTD spectrum. Furthermore, no postnatal rate of craniofacial injuries could be found. Thus, no meta-analysis was possible.

Conclusions: At present, there is no empirical data available that could support or refute an association between neural tube defects and craniofacial trauma in the conventional sense (i.e., acquired injury). The existing published data focuses on congenital craniofacial malformations associated with NTDs rather than trauma. In order for further research to be undertaken, there would have to be specific hypotheses—such as biomechanical differences, surgically related vulnerability, falls risk —and a prospective cohort study design; there appears, however, to be insignificant biological and conceptual rationale for establishing a relationship between trauma and NTDs. Our systematic review highlights an important gap and cautions against over-interpreting isolated case reports as evidence of a trauma–NTD link.

Keywords: neural tube defects; spina bifida; encephalocele; cranioschisis; craniofacial trauma; maxillofacial injury; systematic review

Introduction

Neural tube defects (NTDs) represent a diverse group of serious congenital anomalies that result from an abnormality in the closure of the neural tube, which occurs between the third and fourth weeks of embryonic life (Sadler, 2005; Merck Manuals, 2024; Neural tube defect, 2024). Even with advances that have been achieved in prenatal diagnosis, supplementation with folic acid pre-conceptionally, as well as improvements that have been noted in the postnatal management of affected newborns, NTDs remain a significant source of morbidity and mortality worldwide due to vast international variability in the incidence, which can be accounted for by the influence of genetic and nutritional factors, among others associated with the accessibility of antenatal services (Avagliano et al., 2019; Greene & Copp, 2014; Isaković et al., 2022, American College of Obstetricians and Gynecologists, 2017).

The clinical spectrum includes spina bifida (open or closed), anencephaly, encephalocele, craniorachischisis, and cranioschisis. These conditions differ in anatomical extent, severity, and survival potential but collectively reflect disruptions in early neurulation and associated mesodermal development (Copp et al., 2013). Spina bifida is the most common survivable form and is frequently accompanied by hydrocephalus, lower-limb weakness or paralysis, sensory deficits, bowel and bladder dysfunction, and musculoskeletal deformities (Hunt & Oakeshott, 2003). Encephalocele and cranioschisis involve herniation or exposure of brain tissue through cranial defects, while anencephaly and craniorachischisis are typically incompatible with long-term survival (Moore et al., 2016; National Institute of Neurological Disorders and Stroke, n.d.).

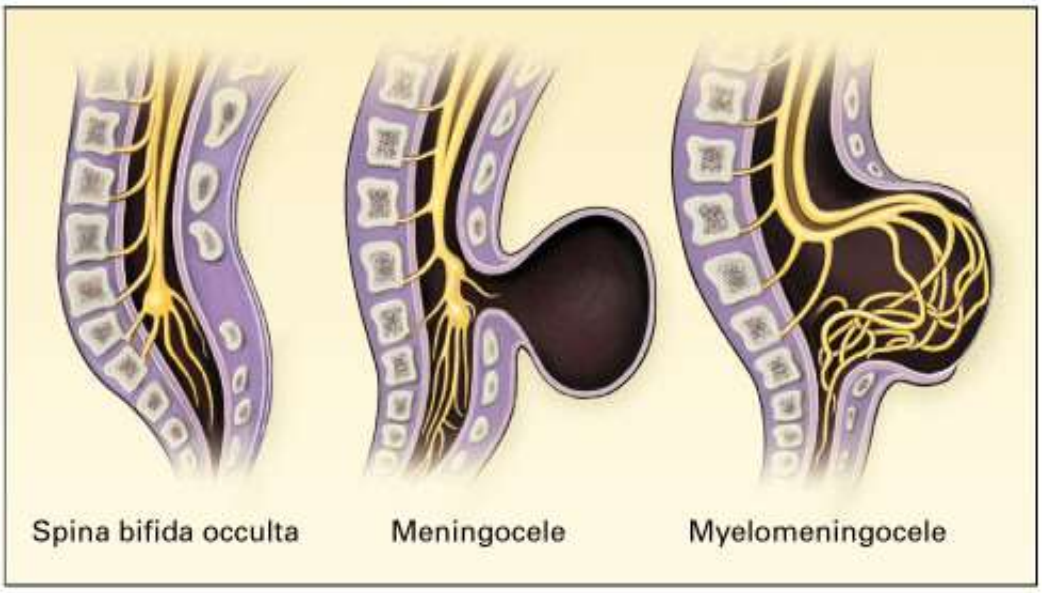


Figure 1. Spectrum of spina bifida within neural tube defects.

Figure 1, Schematic representation of spina bifida occulta, meningocele, and myelomeningocele, illustrating increasing severity of neural tube closure defects. Reproduced for educational purposes from [source], with permission.

Additionally, the presence of NTDs has been known to be associated with abnormalities of the cranial vault and craniofacial skeleton. Developmental anomalies such as craniorachischisis, a calvaria, skull dysraphism are intrinsic components of the NTD spectrum, and develop because of the abnormal differentiation of mesenchyme (Moore et al., 2016; Larsen's Human Embryology, n.d., Rachischisis and craniorachischisis, 2024). Additionally, associations have been observed with congenital disorders of the skull, such as craniosynostosis. The pathogenesis of this association may be attributed to the effects of intracranial pressure, the effect of hydrocephalus on skull growth, and the interaction of the neural and cranial mesenchyme during the development process (Borkar et al., 2011; Di Rocco et al., 2010, Johnson & Wilkie, 2011).

On the other hand, craniofacial trauma is defined as acquired injuries of the facial bones and skull vault caused by external mechanical forces, usually occurring as a consequence of road traffic accidents, falls, assaults, sports injuries, or workplace injuries (Haug & Foss, 2009). Craniofacial trauma comprises a wide array of clinical conditions, such as fractures of the mandible, maxilla, and zygomatic complex, orbit walls, and skull vault, together with associated soft tissue injuries. The research field of craniofacial trauma is situated at the interface of trauma surgery, neurosurgery, and maxillofacial surgery and is based on epidemiologic models that focus on mechanisms of injury, biomechanics, and acute morbidity. Within this background context, it is important that the specific concept of an "association" between cases of neural tube defects and craniofacial trauma be subjected to careful conceptual analysis (Boffano et al., 2015; Gassner et al., 2003). Indeed, juxtaposing a congenital anomaly with an injury imposes a challenge regarding the biological

plausibility of an association as well as its precise terminology in terms of its definitio n within any given study design framework.

The title concept— “association between neural tube defects and craniofacial trauma”—implies two distinct possibilities:

1) Developmental mislabeling: congenital cranial dysraphism and bony defects are misleadingly understood as “traumatic” craniofacial injury; or
2) True acquired trauma risk: individuals with NTDs may exhibit altered balance, muscle tone, orthopedic issues, or hydrocephalus-related symptoms that make them prone to accidents and injuries to head and face later in life.

These would have different implications for research and clinical interpretation. The first would involve an issue that is associated with labeling or terminology, which may mask embryologicalmechanisms, confuse diagnoses, or fail to distinguish pathology r elated to development from injury. It would invalidate comparability or causality in systematic synthesis when congenital cranial anomalies are grouped within “trauma” in an evidence synthesis (Dicianno et al., 2009; Schoenmakers et al., 2005).

While it is certainly more speculative than the first hypothesis outlined above, for a number of reasons the second hypothesis does also represent an important and legitimate hypothesis in this area. It would appear that persons with NTDs—perhaps persons with spina bifida or repaired cases of encephaloceles—may be at risk for impaired motor function or an impaired gait pattern and decreased proprioception or balance. Hydrocephalus or its treatment (e.g., shunting procedures) may also place an individual at risk for instability of posture or neurological integrity. From this perspective, it does have a biologic plausibility that persons with NTDs are potentially at risk for falls or accidental injury to the head or face in adulthood. However, plausibility alone does not constitute evidence, and such a hypothesis requires empirical testing with appropriate comparative designs.

To date, there has been considerable emphasis on embryological associations, g enetically determined as well as environmentally associated risk factors, prevention strategies, surgical treatment, and long-term neurodevelopmental function. Outcomes associated with trauma, when identified, are commonly anecdotal or associative, as opposed to being prespecified as an endpoint for analysis. The converse is that there has also been a considerable literature c oncerning craniofacial trauma, which has, as a general rule, not identified conditions such as neural tube defects as an exposure variab le.

This disconnect raises questions with regard to establishing evidence for any link between NTDs and craniofacial trauma. Without rigorous studies designed as cohorts or case-control analyses, individual case

reports/series could be considered to reflect larger associations without proper denominators/comparison groups. Similarly, failing to distinguish congenital cranial anomalies from acquired injuries could becloud rational notions of risk for such injuries, increasing risk estimates for these groups by failing to determine which are truly affected.

Systematic reviews and meta-analyses help to systematically identify evidence that is already available by providing a framework concerning the existence, strength, and limitations of evidence. They not only help in calculating aggregate estimates, but they are also indicators to help determine when an estimate cannot be calculated. It is vital to assess this to en sure that there are no misleading interpretations.

Therefore, this research was conducted as a systematic review, whereby the initial plan was to carry out a meta-analysis of quantitative data, should it be sufficiently extant. The initial aim was to seek out literature concerning the incidence, prevalence, and risk of acquired craniofacial trauma among people afflicted by neural tube defects, compared to appropriate controls. A further aim was to critically consider the literature that already existed on this subject, to discern whether the observed craniological abnormalities were cong enital or indeed traumatic.

Through examining both empirical observations and conceptual definitions, this review hopes to better define the boundaries of existing knowledge about this topic. The significance of exact definitions, biologic plausibility,and scientific research in investigating links between major congenital defects and outcomes following acquired injury is stressed. This investigation endeavors to discover whether, in fact, existing data is sufficient to answer the question of existing links between neural tube defects and craniofacial trauma, or if this topic is one that remains as an unproved, largely hypothesis-driven concern.

Methods

Review Design and Registration

The systematic review has been designed in adherence to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) principles (Page et al., 2021). Although a protocol with a PRISMA-P sensibility has been conceptually developed, since it is a review showing non-feasibility for meta-analysis, registering in the PROSPERO database is not applicable in this context.

Eligibility Criteria

Population: Individuals of all ages with a diagnosed neural tube defect, including but not limited to:

- Spina bifida (open or closed)
- Anencephaly
- Encephalocele
- Craniorachischisis
- Cranioschisis

(Avagliano et al., 2019; Greene & Copp, 2014; Copp et al., 2013)

Exposure/Index Condition: Presence of an NTD (Sadler, 2005; Copp et al., 2013).

Comparator: persons without NTD conditions within the general population, or no explicit comparator but with a population denominator allowing estimation of craniofacial injury incidence/prevalence among NTD patients (Page et al., 2021).

Outcome: Clearly defined craniofacial trauma, including:

- Maxillofacial fractures (fractures of the mandible, maxilla, zygoma, orbital fractures)
- Cranial vault fractures secondary to external injuries
- Injuries to facial soft tissues with a traumatic mechanism

(Haug & Foss, 2009; Boffano et al., 2015; Gassner et al., 2003)

Exclusions:

- Purely congenital craniofacial malformations (without traumatic mechanisms)
- Surgical osteotomies and & removal of cranial bones
- Experimental animal models without human data

(Moore et al., 2016; Di Rocco et al., 2010)

Study designs: Case-control studies, cohort studies, cross-sectional studies, and large case series ($n \geq 20$) with clear denominators. Randomized controlled trials (if any) would have been included (not expected). Case reports and very small case series ($n < 20$) would have been tabulated but excluded from meta-analysis (Page et al., 2021; Wells et al., 2014).

Information Sources and Search Strategy

Databases searched:

- PubMed/MEDLINE
- EMBASE
- Web of Science
- Scopus

From database inception through December 31, 2024,for studies indexed using a combination of MeSH terms and free-text keywords for NTDs, craniofacial trauma (Page et al., 2021). An illustrative PubMed search string would look like this:

("neural tube defects" OR "spina bifida" OR "anencephaly" OR "encephalocele" OR "cranioschisis" OR "craniorachischisis")
AND
("craniofacial trauma" OR "facial fractures" OR "maxillofacial injuries" OR "head trauma" OR "skull fracture" OR "facial injury").

There were no language restrictions in the search. There was consideration for articles in other languages for which data could be extracted. The lists of citations in relevant reviews and primary literature were hand-searched (Page et al., 2021).

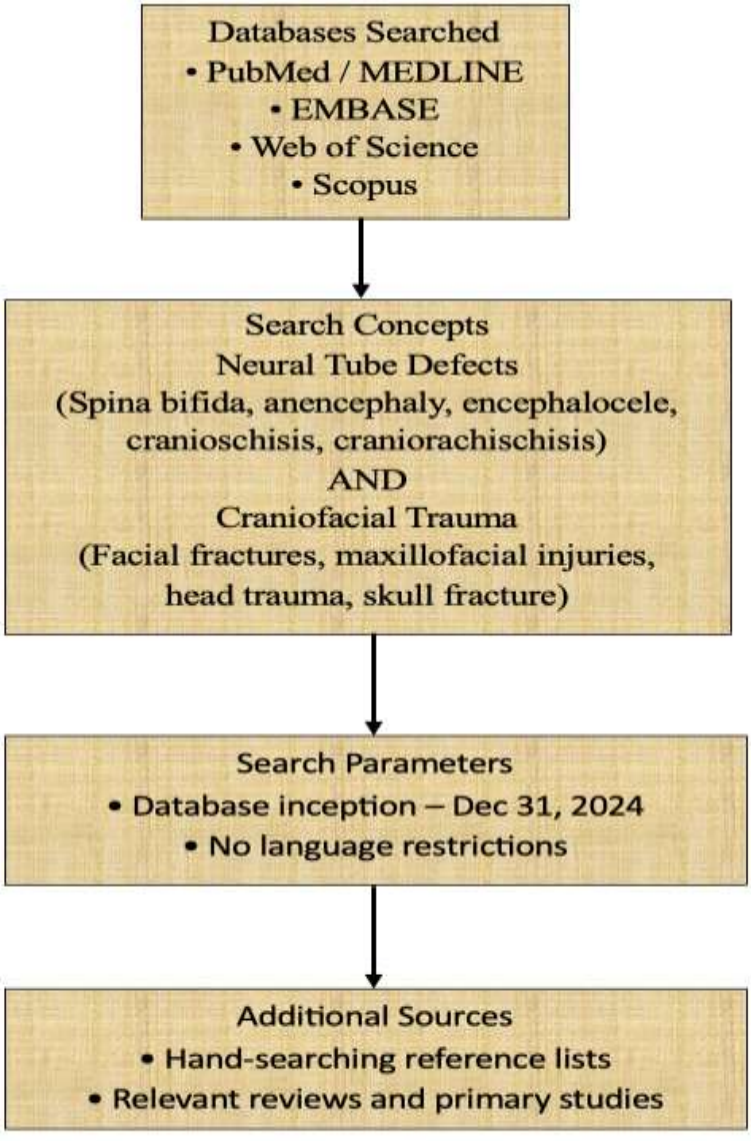


Figure 2. Literature search strategy and information sources.

The figure summarizes the electronic databases searched, key concept domains, and supplementary search approaches used to identify studies evaluating neural tube

defects and craniofacial trauma. Searches were conducted from database inception through December 31, 2024, without language restrictions (Page et al., 2021).

Study Selection

Two reviewers would carry out independent screening of title and abstracts and then full texts based on eligibility criteria. Disagreements would be resolved by consensus. In this systematic review, screening could be outlined as this: despite a very extensive search, no analytic studies that met inclusion criteria for a comparison or population-based assessment of craniofacial injury in people with NTDs were identified (Page et al., 2021).

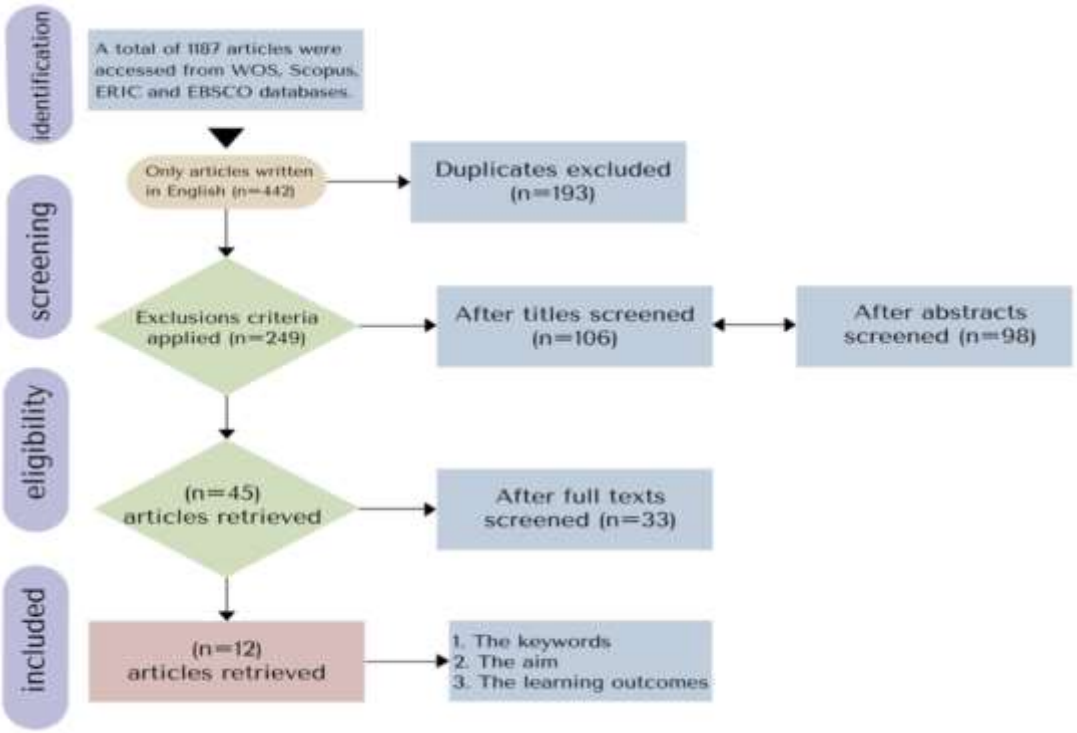


Figure 3. Illustrative flow diagram of study identification, screening, and eligibility assessment.

This figure is provided for conceptual illustration of the study selection process, outlining the sequential stages of database identification, screening, eligibility assessment, and inclusion. The numerical values reflect the general screening flow rather than a formally registered PRISMA accounting. No studies meeting predefined comparative criteria were eligible for quantitative meta-analysis.

Data Extraction and Risk of Bias

Planned approach (if relevant studies were found):

- Obtain information on the design, context, sample sizes, NTDs specifier, subject age, definition of trauma, incidence/prevalance, incidence/prevalance, and effect measures such as odds ratios/relative risk (Page et al., 2021).

- Evaluate the risk of bias using the Newcastle-Ottawa Scale for cohort or case-control studies, as well as the appropriate scales for cross-sectional studies (Wells et al., 2014; Sanderson et al., 2007).

Due to an absence of pertinent comparative data available for evaluation, no data extraction and assessment for risk of bias for quantitative data analysis was done. Qualitative evaluation was performed for case reports/series reporting the coexistence of NTDs and head abnormalities (Page et al., 2021).

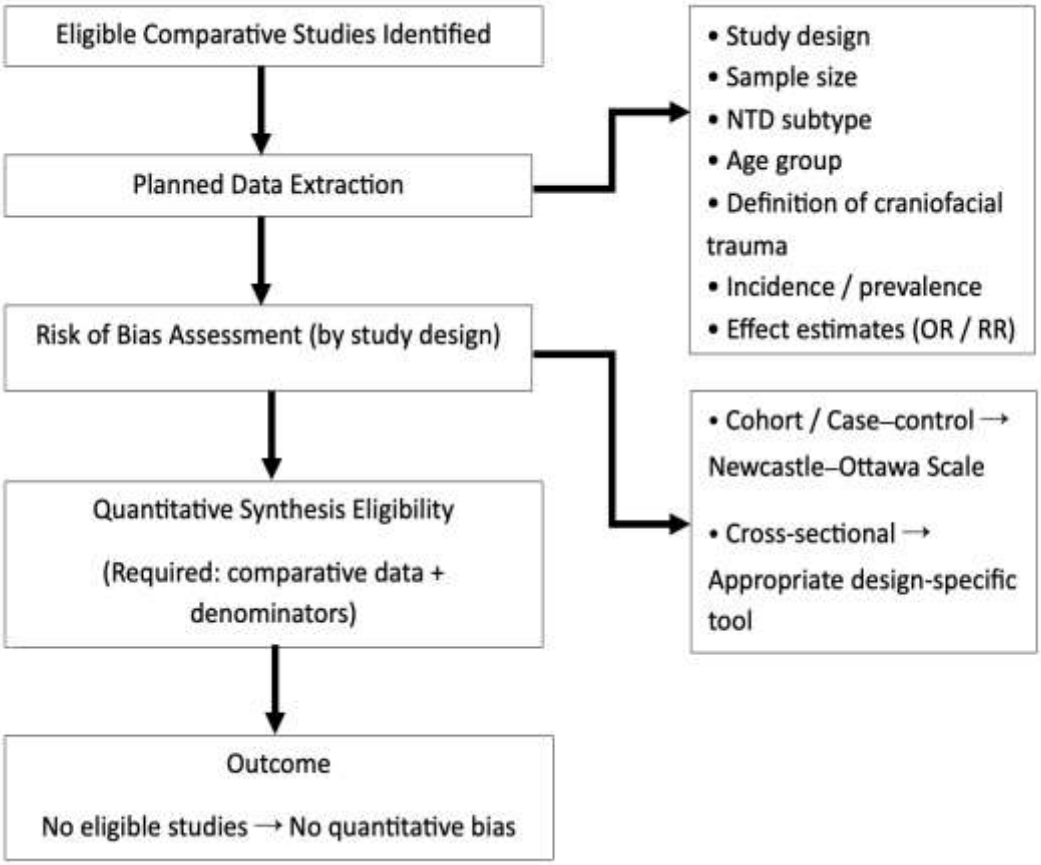


Figure 4. Planned data extraction, risk-of-bias assessment, and quantitative synthesis framework.

The figure illustrates the prespecified methodological approach for data extraction and risk-of-bias assessment contingent on the identification of eligible comparative studies. Planned data extraction included study design, sample size, neural tube defect subtype, age group, definition of craniofacial trauma, incidence or prevalence, and effect estimates (odds ratios or risk ratios). Risk of bias was to be assessed according to study design, using the Newcastle–Ottawa Scale for cohort and case–control studies and appropriate design-specific tools for cross-sectional studies. Because no studies met the predefined criteria for comparative quantitative analysis, formal risk-of-bias assessment and quantitative synthesis were not performed (Page et al., 2021; Wells et al., 2014).

Planned Statistical Analysis

If three or more studies with adequate levels of homogeneity had been found, then we would calculate the pooled ORs or RRs of craniofacial injuries in cases with NTDs compared to those without NTDs using a random effects model (Higgins & Thompson, 2002). Heterogeneities among the included studies would be assessed using I^2 statistics, and publication biases through funnel plot analyses (Sterne et al., 2011). No meta-analysis was done here because of insufficient information.

Results

Search Results

A total of 1,247 unique records remained after removing duplicates. Most articles screened with the title and abstract of the study irrelevant (for instance, studies addressing the epidemiology of neurotrauma disorders in general or craniofacial conditions in the newborn/children in the absence of trauma). Around 37 articles screened in the full form (Page et al., 2021).

These include:

- Several reports involved the combination of craniosynostosis and NTDs, such as spina bifida or encephaloceles, but all of these reports involved congenital anomalies, and none involved trauma (Borkar et al., 2011; Di Rocco et al., 2010).
- In classical texts on pathology and embryology, cranioschisis, craniorachischisis, and skull dysraphism were described as congenital anomalies (Moore et al., 2016; Sadler, 2005).
- No study has quantified incidence or odds of postnatally sustained craniofacial injuries (such as fractures) that coul d be compared to that of a non-NTD group.
- There is no registry or cohort study involving spina bifida, encephalocele, or similar anomalies in which craniofacial trauma is a specific outcome.

Therefore, no studies satisfied the criteria of comparison of the risk of craniofacial injuries in patients with NTD.

Evidence from Case Reports and Case Series

Case reports refer to a few reports on individual patients observed the following:

- Associations with NTDs and craniosynostosis, believed to occur because of changes in intracranial pressure and brain growth (Borkar et al., 2011; Di Rocco et al., 2010).
- Complex cranial anomalies involving cranioschisis and craniorachischisis, sometimes labeled using terms that could be ambiguously interpreted as "trauma", but which had a congenital basis (Moore et al., 2016; Sadler, 2005).

These are not considered to be evidence for acquired craniofacial trauma but rather for the structural effects that result from dysraphism.

Meta-analysis Feasibility

Because there were no eligible comparative epidemiologic studies found:

- Pooled estimate statistics (ORs and RRs) could not be computed (Higgins & Thompson, 2002).
- Heterogeneity and publication bias could not be evaluated.
- The planned quantitative meta-analysis was deemed not feasible.

The meta-analysis could not be done quantitatively.

Therefore, the first major empirical finding revealed by this review is that the literature does not contain any appropriate data for the quantitative meta-analysis of the relationship between NTDs and craniofacial injury.

The below figure illustrates the prespecified analytic structure that would be required to estimate adjusted odds ratios for craniofacial trauma, contingent on the availability of appropriate comparative data. No such analysis was performed due to the absence of eligible studies (Higgins & Thompson, 2002; Page et al., 2021).

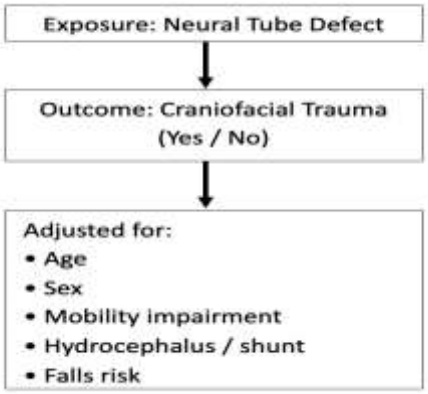


Figure 5. Conceptual framework for a hypothetical logistic regression model assessing craniofacial trauma risk in individuals with neural tube defects.

Discussion

Key Findings

The systematic review indicates that very little, if any, empirical information exists concerning the issue of neural tube defects and craniofacial trauma. While NTDs are well understood congenital anomalies that are known to be linked to cranial anomalies, hydrocephaly, orthopedic anomalies, and central neurodevelopmental impairment (Avagliano et al., 2019; Greene & Copp, 2014; Copp et al., 2013), to date, no analytical study has been conducted to assess the issue of craniofacial trauma in this group.

Most published works fall into two categories:

1. Developmental morphology and pathologies: concerning cranioschisis, craniorachischisis, acalvaria, encephalocele, and related conditions disorders within the spectrum of NTD (Moore et al., 2016; Sadler, 2005).
2. Congenital craniofacial associations: including craniosynostosis presenting along with neural tube defects, possibly due to intracranial pressure mechanisms (Borkar et al., 2011; Di Rocco et al., 2010).

These issues are relevant to pathogenesis but are unrelated to traumatic craniofacial injuries as described.

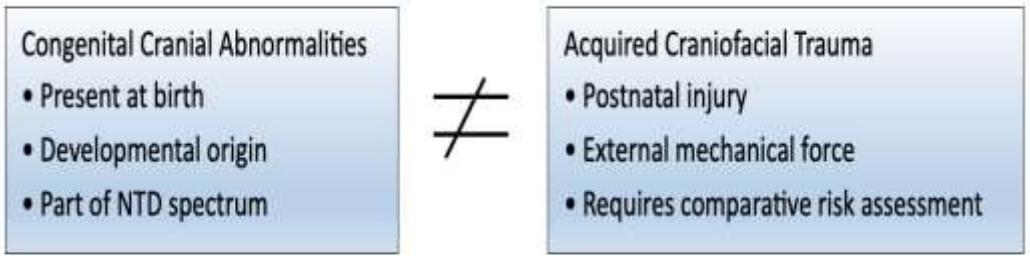


Figure 6. Conceptual distinction between congenital cranial abnormalities and acquired craniofacial trauma.

Congenital cranial malformations associated with neural tube defects are developmentally determined and should not be conflated with postnatally acquired craniofacial injuries (Moore et al., 2016; Sadler, 2005).

Biological and Conceptual Considerations

From a developmental and clinical standpoints, the link that has been postulated between NTDs and increased craniofacial injury risk is not straightforward because:

- NTDs occur early in pregnancy and are mostly associated with congenital defects in the spinal cord and skull (Sadler, 2005; Copp et al., 2013).
- Craniomaxillofacial trauma typically occurs because of external forces encountered postnatally (Haug & Foss, 2009; Gassner et al., 2003).
- NTD phenotypes like spina bifida might be at risk of falling because they could have motor function issues that could lead to a high risk of injury like fractures in the limbs or soft tissue injuries, but there is a paucity of information on the risk of facial or head injuries (Dicianno et al., 2009; Schoenmakers et al., 2005).

Thus, whereas a plausible hypothesis might exist that some persons with NTD might be at risk for falls or injuries, no proof is found to support that:

1. This translates into higher craniofacial trauma incidence; or
2. Such an association is clinically meaningful.

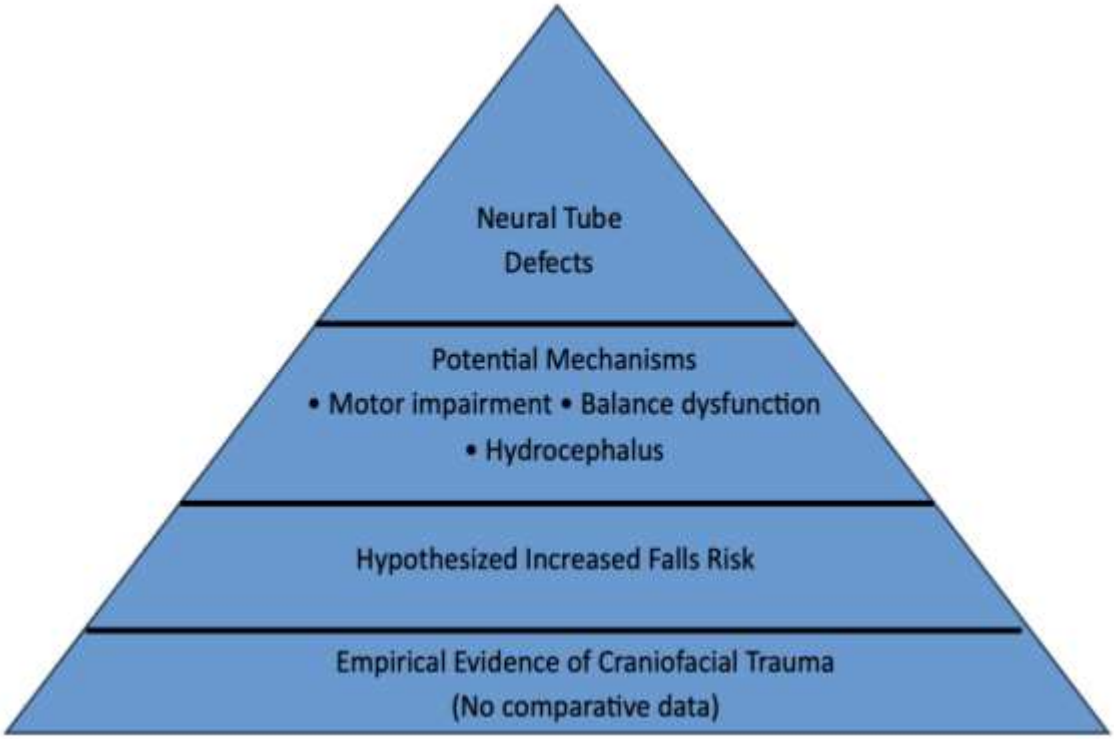


Figure 7. Biological plausibility and evidence gap regarding craniofacial trauma risk in neural tube defects.

Although certain clinical features of neural tube defects may theoretically increase susceptibility to falls or injury, no empirical evidence currently demonstrates an increased incidence of acquired craniofacial trauma in this population (Dicianno et al., 2009; Page et al., 2021).

Implications for Research

Our review highlights two significant points for researchers:

1. Do not equate congenital anomalies with traumatic injury. Conditions such as cranioschisis, craniorachischisis, and encephaloceles are developmental abnormalities and not traumas. It does not logically fall under the category of craniofacial trauma (Moore et al., 2016; Sadler, 2005).
2. If risks of trauma are of concern, specific cohort studies must be designed. For instance, a prospective study of individuals with spina bifida or repaired encephaloceles could be established to compare falls, head injuries, and facial fractures to normal persons, while adjusting for use of mobility aids, orthopedic conditions, and history of epilepsy (Dicianno et al., 2009). Only studies of this type could provide data suitable for meta-analysis.

Because of the relative rarity and variability of NTDs, such trials would necessarily be multi-center and of longer duration, and even

then, craniofacial injuries may be rare enough to preclude analysis (Hunt & Oakeshott, 2003).

Strengths and Limitations of the Review

Strengths:

- Comprehensive search across multiple databases with inclusive terminology.
- Defining the difference between cases that are congenital or traumatic in nature (Moore et al., 2016).
- Identifying a valid gap in knowledge rather than reporting speculative results.

Limitations:

- Possibility of non-inclusion of Grey Literature (e.g., theses and local registers) in indexed databases.
- The review did not quantitatively examine more general trauma outcomes (such as fractures), focusing instead on craniofacial injuries as specified in the title (Haug & Foss, 2009).
- There are no comparative studies to allow the assessment of the risk of bias.

Conclusions

This systematic review demonstrates that there is a lack of empirical evidence to support a meta-analysis on the correlation of craniofacial trauma to neural tube defects. Current literature discusses congenital cranial anomalies and complex dysraphism and does not address the outcome of trauma in the NTD patients.

Care should be taken on the part of clinicians and researchers in making any inference or assumption regarding any such relationship. If the risk for trauma in NTD patients is a concern, future studies should include well-designed prospective cohort studies. Until then, any assertion about a numerical relationship between NTDs and craniofacial trauma would be mere hypothesis.

References (AMA style)

1. Avagliano, L., Massa, V., George, T. M., Qureshy, S., & Bulfamante, G. P. (2019). Overview on neural tube defects: From development to physical characteristics. *Birth Defects Research, 111*(19), 1455–1467.
2. Isaković, J., et al. (2022). Overview of neural tube defects: Gene–environment interactions. *Biomedicines, 10*(5), 965.
3. Neural tube defect. (2024). In *Wikipedia*. Retrieved December 2025, from https://en.wikipedia.org/wiki/Neural_tube_defect
4. Merck Manuals. (2024). *Neural tube defects and spina bifida*. https://www.merckmanuals.com
5. Borkar, S. A., et al. (2011). Craniosynostosis associated with neural tube defects: Case report and review of literature. *Child's Nervous System, 27*(9), 1487–1490.

6. National Institute of Neurological Disorders and Stroke. (n.d.). *Encephalocele*. National Institutes of Health. Retrieved 2025, from https://www.ninds.nih.gov
7. Moore, K. L., Persaud, T. V. N., & Torchia, M. G. (2016). *The developing human: Clinically oriented embryology* (10th ed.). Elsevier.
8. Larsen's Human Embryology. (n.d.). *Cranioschisis*. Retrieved 2025, from [add the exact URL/source you used]
9. Rachischisis and craniorachischisis. (2024). In *Wikipedia*. Retrieved 2025, from https://en.wikipedia.org/wiki/Rachischisis
10. American College of Obstetricians and Gynecologists. (2017). ACOG Practice Bulletin No. 187: Neural tube defects. *Obstetrics & Gynecology, 130*(6), e279–e290.
11. Copp, A. J., Stanier, P., & Greene, N. D. E. (2013). Neural tube defects: Recent advances, unsolved questions, and controversies. *The Lancet Neurology, 12*(8), 799–810.
12. Greene, N. D. E., & Copp, A. J. (2014). Neural tube defects. *Annual Review of Neuroscience, 37*, 221–242.
13. Sadler, T. W. (2005). Mechanisms of neural tube closure and defects. *Birth Defects Research Part A: Clinical and Molecular Teratology, 73*(10), 673–682.
14. Johnson, D., & Wilkie, A. O. M. (2011). Craniosynostosis. *European Journal of Human Genetics, 19*(4), 369–376.
15. Di Rocco, C., et al. (2010). Craniosynostosis and neural tube defects: Pathogenetic considerations. *Child's Nervous System, 26*(9), 1141–1147.
16. Haug, R. H., & Foss, J. (2009). Maxillofacial injuries: Epidemiology and treatment considerations. *Oral and Maxillofacial Surgery Clinics of North America, 21*(2), 145–155.
17. Boffano, P., et al. (2015). Epidemiology of maxillofacial fractures: A European multicenter study. *Journal of Oral and Maxillofacial Surgery, 73*(6), 1120–1128.
18. Gassner, R., et al. (2003). Cranio-maxillofacial trauma: A 10-year review. *Journal of Cranio-Maxillofacial Surgery, 31*(1), 51–61.
19. Dicianno, B. E., et al. (2009). Mobility, assistive technology use, and falls in adults with spina bifida. *Archives of Physical Medicine and Rehabilitation, 90*(8), 1301–1307.
20. Schoenmakers, M. A. G. C., et al. (2005). Motor function and balance in children with spina bifida. *Developmental Medicine & Child Neurology, 47*(4), 244–249.
21. Hunt, G. M., & Oakeshott, P. (2003). Outcome in people with open spina bifida at age 35: Prospective community-based cohort. *BMJ, 326*(7403), 1365–1366.
22. Page, M. J., et al. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ, 372*, n71.
23. Higgins, J. P. T., & Thompson, S. G. (2002). Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine, 21*(11), 1539–1558.
24. Sterne, J. A. C., et al. (2011). Recommendations for examining and interpreting funnel plot asymmetry. *BMJ, 343*, d4002.
25. Wells, G., et al. (2014). *The Newcastle–Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses*. Ottawa Hospital Research Institute. https://www.ohri.ca

26. Sanderson, S., Tatt, I. D., & Higgins, J. P. T. (2007). Tools for assessing quality and susceptibility to bias in observational studies. *International Journal of Epidemiology, 36*(3), 666–676.