



Review Article

## Epidemiology and determinant factors of neural tube defect: Narrative review

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### ABSTRACT

**Background:** The epidemiology of neural tube defect (NTD) is face ignorance from the global community. However, the problem is complex and it is a cause for child mortality and morbidity. We provide the latest insights with respect to determinant factors of NTD.

**Methods:** Google Scholar and PubMed were systematically searched to identify potential research articles concerning the epidemiology and its determinant factors of NTD.

**Results:** The epidemiology of Neural tube defects increased in some countries. The epidemiology and determinant factors were varies across countries, geographical regions and socioeconomic status of the populations. In general, the determinant factors of NTD were summarized as behavioral, nutrition-related, environmental, medical illness, and health service-related factors.

**Conclusion:** Birth defect is fatal which affects the new generation; specifically, NTD is the problem of middle- and low-income countries. It is a direct cause for neonatal and perinatal mortality rate globally. Even if little factors identified, yet conducting experimental and clinical trial researches are a better approach to slow down the progress.

**Keywords:** Determinant factors, Epidemiology, Neural tube defect

### BACKGROUND

Neural tube defects (NTDs), including spinal bifida, anencephaly, and encephalocele, occur when part of the neural tube, which forms the spine, spinal cord, skull, and brain, fails to close between 21 and 28 days after conception – before the women realize that they are pregnant.<sup>[1]</sup> The physiological development of central nervous system (CNS) develops from ectoderm by folding it to form a tube. The tube has two ends caudally develop to spinal cord and rostral part develop to CNS (forebrain, midbrain, and hindbrain).<sup>[13]</sup>

Basically, the exact cause of birth defect is unknown, but nowadays, it is recognized partially, broadly the cause is classified into two that is genetic (preconception) and partially genetic causes (postconception).<sup>[1]</sup>

The most common form of NTD is spinal bifida which results functional disabilities, that is, loss to control the bladder and bowel and paralysis of the legs.<sup>[9]</sup> Fortification of staple diet and supplementation of folic acid for the women facilitates closure of NTD early.<sup>[2,3,14]</sup> On

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the contrary, excess intake of folate increases incidence of twin pregnancy and cancer as explained in systemic review done in Sweden.<sup>[9]</sup> Fortified flour consumption lowers the occurrence of NTD as explored from the experimental study in Zhongyang county, serum folate level among intervention group is higher than in control group.<sup>[2]</sup>

At population level, all women of child-bearing age who are capable of becoming pregnant should consume 400 (0.4 mg) g of folic acid daily to facilitate NTD closure as per the WHO recommendation, this might be not applicable at individual level.<sup>[5]</sup>

Worldwide 2 billion people were deficient from micronutrients which hamper their physical growth and mental performance. The worst affected countries include Afghanistan, Pakistan, Cambodia, Ethiopia, and West and Central African nations.<sup>[29]</sup>

## METHOD

Google Scholar and PubMed were systematically searched to identify potential research articles concerning the Epidemiology and its determinant factors of Neural Tube defects. Additionally, by retrieving references from a list of eligible studies was conducted to be confident about the search strategy. We apply Boolean operator that is “AND”, “NOT” and “OR”. Through consideration of the Boolean operator we searched as follows: ((Neural tube defect OR Epidemiology of Neural tube defect) AND (Determinant Factors))

## EPIDEMIOLOGY OF NTD

Birth defects means any type of anomaly which occurred congenitally, worldwide 3% of neonates suffered from this defect from all births or 1 in every 33 baby born which is a cause for perinatal and infant mortality in developing and developed countries.<sup>[6]</sup>

NTDs cause death, paralysis, or life-long disability – but many consequences of it is preventable. Each year spinal bifida and anencephaly, the two most common forms of neural tube defects, occur in an estimated 3,00,000 newborns worldwide.<sup>[8]</sup>

The overall burden of NTD based on live births was 1.67/1000 (IQR = 0.98–3.49) for total NTD burden according to a systemic review conducted elsewhere.<sup>[10]</sup> NTD prevalence is higher in Argentina among all congenital anomalies (spinal bifida: 5%, anencephaly: 3%, and encephalocele: 1.4%)<sup>[11]</sup> and 1.58/1000 births in bantia.<sup>[12]</sup>

The prevalence of spinal bifida 4.5 in India,<sup>[33]</sup> 15.1% in Zhengzhou City, China<sup>[36]</sup> and a trend analysis done in China 2006–2015 showed that the prevalence of NTD was decreasing<sup>[15]</sup> and similarly decreases in Kenya.<sup>[16]</sup> The prevalence of NTD in Sudan was 2.8%.<sup>[17]</sup> The prevalence of birth defect in central and northwest of Ethiopia is 30.8% and 22.5% in the Amhara region.<sup>[18]</sup>

Another finding which is done in Mekelle Ayder Hospital Ethiopia identifies CNS malformation was the most common one with a prevalence of 1.5%;<sup>[19]</sup> additionally, a retrospective finding which is done in Addis Ababa referral hospitals identified that spinal bifida and hydrocephalus are a main cause of childhood mortality in the area.<sup>[7]</sup> A retrospective descriptive study conducted among Central and Northwest Ethiopia revealed that the prevalence of NTD is 30.8%.<sup>[18]</sup>

Almost all states plan Sustainable Development Goal 3 that is building good health and well-being in all community, but such type of international consensus may be affected through unrecognizable hidden and preventable problems.<sup>[20]</sup>

## DETERMINANT FACTORS OF NTD

In general, the determinant factors of NTD were summarized as behavioral, nutrition-related, environmental, medical illness, and health service-related factors.

Women who have exposure to second-hand smoking have strong positive association to NTD.<sup>[21]</sup> Taking foliate tablet increases serum level of folic acid.<sup>[2,22]</sup> In contrary, taking excessive amount of folic acid hampers brain development and change child behavior.<sup>[25]</sup> The use of trimethoprim, a folic acid antagonist, at the preconception period increased the risk of exencephaly in the mouse. A study conducted in primate animals (mouse) showed that; the use of trimethoprim, a folic acid antagonist, at the preconception period increased the risk of exencephaly.<sup>[23]</sup>

Fever, hyperthermia in early pregnancy,<sup>[4]</sup> certain medications (e.g., valproic acid), alcohol, tobacco, certain chronic diseases (e.g., diabetes and obesity), iodine, iron, and vitamin B12 deficiency have an association with NTDs.<sup>[24,26,27]</sup>

People living near to industry, especially in coal mine, living near to main road, production of fruit, maternal occupational exposure, distance to factories, living in higher altitude, soil type, number of doctors, use of chemical fertilizers,<sup>[28,30,31]</sup> per capita income, and living in faults were correlated with NTD as reported study conducted in China.<sup>[32]</sup> A case–control study in Iran revealed that maternal history of abortion and obesity<sup>[26]</sup> has a significant association with NTD.<sup>[34]</sup> The occurrence of NTD affected by biological differences; high in female as compared to male.<sup>[35]</sup>

In general, NTD has a high correlation with, prenatal screening, nutritional, environmental, occupational exposure, and genetic factors.<sup>[37]</sup>

## CONCLUSION

Birth defect is fatal which affects the new generation; specifically, NTD is the problem of middle- and low-income countries. It is a direct cause for neonatal and perinatal

mortality rate globally. Even if little factors identified, yet conducting experimental and clinical trial researches are a better approach to slow down the progress.

### Declaration of patient consent

Patient's consent not required as there are no patient's in this study.

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### Conflicts of interest

There are no conflicts of interest.

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