J Afric Neonatal 2023;4: 114 – 119

REVIEW

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Prevalence of neural tube defects and uptake of the folic acid program in antenatal clinics in Tanzania: A systematic review

Received: 31t July 2023
Accepted: 6th October 2023

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Abstract*:* Neural tube defects are birth deformities of the brain, spine, or spinal cord which occurs when the neural tube does not close properly. Significant link between dietary folic acid deficiency during pregnancy and the development of neural tube defects has been found, hence emphasis of nutritional supplements for women in reproductive age for almost half a century.
Google scholar, PubMed, PubMed Central were systematically searched for relevant community-based and hospital-based studies up to 30th April 2023. Search terms used were “neural tube defects”, “folic acid program”, “Tanzania”, “antenatal care”.
The literature search yielded eight eligible studies and three surveys done in few regions of Tanzania. A prevalence estimate ranging from 9.9 to 30.2 per 10 000 was demonstrated. In the studies included, the largest sample size was 28 217 participants, and lowest 445 participants.
With the folic acid program, 0.7% of women of reproductive age were aware that folic acid intake during pregnancy can prevent NTDs. About28.5% of women 15-49 years of age with children under five years of age took an iron-folic acid supplementation during 90 days or longer during pregnancy for past birth, which was much lower in Zanzibar (12.8%).
Limited available data on NTD inform the need for additional primary, wide scope research that would expose the true burden of the defects and facilitate preventive policies on preventive factors. Efforts to increase intake of folic acid supplements and fortified flour among women of reproductive age and the general community are needed to reduce occurrence of NTDs.

Keywords: Neural tube defects, Spina bifida, Anencephaly, Encephalocele, Birth prevalence, Antenatal care, Folic acid supplementation, Food fortification, Tanzania

Résumé: Les anomalies du tube neural sont des malformations congénitales du cerveau, de la colonne vertébrale ou de la moelle épinière qui surviennent lorsque le tube neural ne se ferme pas correctement. Un lien significatif entre une carence alimentaire en acide folique pendant la grossesse et le développement d'anomalies du tube neural a été découvert, d'où l'accent mis sur les suppléments nutritionnels destinés aux femmes en âge de procréer depuis près d'un demi-siècle.
Jusqu'au 30 avril 2023, Google Scholar, PubMed et PubMed Central ont fait l'objet d'une recherche systématique d'études communautaires et hospitalières pertinentes. Les termes de recherche utilisés étaient « anomalies du tube neural », « programme d'acide folique », « Tanzanie », « soins prénatals ». .
La recherche documentaire a donné lieu à huit études éligibles et trois enquêtes réalisées dans quelques régions de Tanzanie. Une estimation de prévalence allant de 9,9 à 30,2 pour 10 000 a été démontrée. Dans les études incluses, la plus grande taille d’échantillon était de 28 217 participants et la plus petite, de 445 participants.
Grâce au programme d'acide folique, 0,7 % des femmes en âge de procréer savaient que la consommation d'acide folique pendant la

grossesse pouvait prévenir les malsdie de tube neural (MTN). Environ 28,5 % des femmes âgées de 15 à 49 ans ayant des enfants de moins de cinq ans ont pris une supplémentation en fer et en acide folique pendant 90 jours ou plus pendant leur grossesse pour un accouchement antérieur, ce qui était beaucoup plus faible à Zanzibar (12,8 %).
Les données limitées disponibles sur les MTN soulignent la nécessité de mener des recherches primaires supplémentaires a grande echelles qui exposeraient le véritable fardeau des défauts et faciliteraient les politiques préventives sur les facteurs préventifs. Des efforts visant à augmenter la consommation de suppléments d'acide folique et de farine enrichie chez les femmes en âge de procréer et dans la communauté en général sont nécessaires pour réduire l'apparition des MTN.

Mots clés: Anomalies du tube neural, Spina bifida, Anencéphalie, Encéphalocèle, Prévalence des naissances, Soins prénatals, Supplémentation en acide folique, Enrichissement des aliments, Tanzanie

Introduction

Neural tube defects (NTD) are birth deformities of the brain, spine, or spinal cord which occurs when the neural tube does not close properly. They arise from a flaw in the embryonic phase of neurulation that normally takes place in the 3rd and 4th weeks of gestation. Since rostral and caudal neuropore closure is the last phase of neurulation, they are particularly vulnerable to defects.[1]
Anencephaly, encephalocele, craniorachischisis totalis, and congenital dermal sinus are a few examples of cranial forms of neural tube defects. Spinal form of neural tube defects includes; Spina bifida, split-cord malformations, Diastematomyelia, Diplomyelia, Caudal agenesis and lipomyelomeningocele.

Several randomized controlled trials have revealed a highly significant link between dietary folic acid deficiency during pregnancy and the development of neural tube abnormalities. Thus, the value of nutritional supplements for women who are in reproductive age has been emphasized for almost half a century.[2,3]
Other factors causing neural tube defects are genetic, environmental and certain drugs or substance use during pregnancy (e.g., valproic acid, if given during first four weeks development as the neural folds are fusing) as well as presence of chronic disease during pregnancy. [4]
Neural tube disorders further raise health care expenses for survivors and significantly contribute to disability-adjusted life years (DALYs), apart from causing stillbirths, neonatal, infant, and under-five mortality.[5]
Globally, it is estimated that approximately 400,000 babies are born each year with neural tube defects and contribute about 10% of total neonatal mortality.[6,7]
Among those born with NTDs, mortality is over 75% before five years.[8]
Both the birth and total prevalence of NTD have declined during the past three decades among high income countries.[8] Evidence suggests that the reduction in number is largely due to improvements in folic acid supplementation and food fortification programmes. Additionally, it has been contributed by termination of pregnancy after the introduction of routine serum alpha-fetoprotein measurements and advances in ultrasonography resolution for in utero early detection. [2,4]
In Africa, neural tube defects are the most prevalent birth disorders as it has been reported to affects about 1-3/1000 babies each year.[9]
The pooled period prevalence of all neural tube defect events in Eastern Africa was 33.30 per 10,000 observations, which is nearly five times that of the United States.[10] Ethiopia, followed by Eritrea, showed the highest birth frequency of NTDs, at 59.74. Malawi had the lowest rate at 4.69.[10]
Tanzania is an east African low-income country with a current population of approximately 64 million people.
We aimed to estimate the prevalence of NTD and assess implementation of the folic acid program in antenatal care (ANC) in Tanzania including challenges hindering its effectiveness.

Methodology

We sought to include as many available data sources as possible.

Review outcomes

The first outcome is the pooled birth prevalence of neural tube defects, defined as the number of neural tube defect cases of live births and/or stillbirths at birth from the total number of births during the study period.
The second outcome is the status of the implementation of the folic acid program in antenatal clinics

Study eligibility criteria

The inclusion criteria for this review were published and unpublished studies in any period, with no restriction. Surveys and reports from Ministry of Health of Tanzania were also included. Case reports, editorials, anonymous reports and conferences were excluded.

Searching strategies and information sources

Google scholar, PubMed, PubMed Central were systematically searched for relevant studies, both community-based and hospital-based, up to 30th April 2023. Search terms used were "neural tube defects", "folic acid program", "Tanzania", "antenatal care"

Study selection

After identification of studies through database searching, they were screened by title and abstract. Irrelevant studies that lacked outcome of interest were excluded. Full texts for eligible studies were retrieved, and in-

cluded in the systematic review.

Results

The literature search in this systematic review yielded eight studies that met the inclusion criteria and were done in few regions of the country (Mwanza, Dar es Salaam, Arusha, Kilimanjaro, Morogoro and Kigoma). All studies were cross-sectional studies, except one cohort study[11] done in Dar es Salaam in 2017. All of the studies except one that was done by Kinasha et al,[12] were done in health facilities. A total of 3 surveys/ guidelines were included, which were Tanzania National Fortification Assessment Coverage Tool (FACT) Survey in Tanzania (2015),[13]Tanzania National Nutrition Survey (2018) [14] and National Biofortification guidelines (2020). [15]

Prevalence of neural tube defect in Tanzania

Great variability of prevalence estimate was demonstrated, ranging from 9.9 to 30.2 per 10 000. The largest sample size was from a study done in 2015 in Dar es Salaam, with 28 217 participants, and the lowest from a study conducted in Mwanza in 2014, with 445 participants. Prevalence of neural tube defect was not stated in some of the studies.

Table 1: Characteristics of the studies included in the systematic review

First author	Region	Year of publication	Study design	Sample size	Duration/ months	Prevalence per 10 000 livebirths
Mashuda et al [16]	Mwanza	2014	Cross-sectional	445	4	-
Kishimba et al [17]	Dar es Salaam	2015	Cross-sectional	28 217	5	9.9
Kinasha et al [12]	Dar es Salaam	2003	Cross-sectional	11 500	24	30.2
Magwesela et al [18]	Arusha	2022	Cross-sectional	822	120	-

Folic acid program in Tanzania

In the Tanzania National Nutrition Survey (2018), 28.5% of pregnant women 15-49 years of age with children under five years of age took iron-folic acid supplementation for 90 days or longer after the preceding birth. The rate was much lower in Zanzibar, at 12.8%.

Different uptake rates of the folic acid program were observed. The largest sample size was observed in a study done by Ogundipe et al[19] with a sample size of 21 889 which showed a prenatal folic intake of 17.2%. Awareness that folic acid intake during pregnancy can prevent NTDs among women of reproductive age was 0.7%, as observed by Mwandelile et al.[20]

Table 2: Outcome of implementation of the folic acid program

First author	Region	Year of publication	Study design	Sample size	Duration/ months	Outcome
Ogundipe et al [19]	Kilimanjaro	2012	Cross-sectional	21 889	120	Prenatal folic acid intake – 17.2%
Mwandelile et al [20]	Morogoro	2019	Cross-sectional	698	1	Folic acid fortified flour consumption – 63.3% Awareness of folic acid fortified flour – 6.9%
Lyoba et al[21]	Kigoma	2020	Cross-sectional	320	1	Adherence to Iron/Folic acid supplementation – 20.3%
Noor et al [11]	Dar es Salaam	2017	Cohort	600	12	Mean plasma folate concentration doubled 6 months after fortification

Discussion

Studies showing the overall prevalence and pattern of distribution of NTDs in Tanzania remains scarce in the literature. Prevalence rates ranging from 9.9 to 30.2 per 10 000 live births were noted in this systematic review. Iron and folic acid supplementation has been instituted as a key component of antenatal services since the establishment of maternal and child health services in the 1960s [15] Tanzania passed a policy for mandatory fortification of commercial wheat and maize flour with micronutrients, including folic acid in 2011.[13] To our knowledge, this is the first systematic review that explored the prevalence and implementation of the folic acid program in Tanzania.

The two studies that reported NTD prevalence in our systematic review were done in the same region but different levels of hospitals, more than ten years apart. The prevalence of 30.2 per 10 000 live births was reported from a single tertiary hospital, which receives referrals from the whole country hence having a higher pooled prevalence as compared to the other study. Prevalence rates of NTDs seen in developed countries ranging from 2.2 to 6.9 per 10 000 live births are far lower than found in the current review.[22,23,24,25] These variations might be explained by the influence of racial, geographical, nutritional, socioeconomic and biological differences. Elec-

tive termination of pregnancy after prenatal NTDs diagnosis in the developed countries may also have affected the prevalence.

Tanzania adopted the WHO recommendation requiring all pregnant women to take 400 micrograms of folic acid daily starting early at first antenatal visit. Since adoption, the Ministry of Health has worked closely with important stakeholders to make sure that the folic acid supplementation program is sustained in all health facilities, both in urban and rural areas. Folic acid supplementation is also reflected in the current national antenatal care guideline, in support of sustainability plan, and is offered for free as part of the antenatal package in combination with Iron.[26] According to the 2018 Tanzania National Nutrition Survey (TNNS)[14], the proportion of pregnant women taking iron-folic acid supplements had increased over time form 3.5% in Tanzania Demographic Health Survey (TDHS) 2010 to 17.5% in the TNNS 2014, to 21.4% in the TDHS 2015-16, and further to 28.5% in 2018. This proportion was however not stated in the TDHS 2022 key indicators report.[27]

Mandatory fortification policy of commercial wheat and maize flour with folic acid was passed in Tanzania in 2011.[13] In developed countries, folic acid fortification of staple foods has been in place for over two decades after several studies demonstrated that it can help to prevent neural tube defects.[7] Risk of NTDs is high during the first few weeks post conception during embryology. In our setting, most often pregnancies are unplanned thus missed in the early stages, hindering target interventions to prevent this risk, especially during peri-conception period. Fortification of staple foods with folic acid allows all women to access this nutrient throughout their reproductive years and thus reduce the risk of NTDs without active behavioral change.[7]

Challenges with micronutrient supplementation such as folic acid in Tanzania has been linked to unsustainable supply of commodities due to dependence on donor funds.[15] Another challenge identified by Mwandelile et al[20] was the low awareness of the preventive role of folic acid among women of reproductive age. The observed awareness rate of 0.7% was far lower than 16.3%, 17%, and 24% reported from Nepal, Europe and USA, respectively.[28,29,30] The reason for this disparity could be due to the fact that during antenatal clinic visits, folic acid is provided in combination with iron in a formulation known as FEFO with health education on prevention of anaemia alone, therefore awareness of folic acid in the formulation prevents NTDs remains poor. Challenges to sustain food fortification include dependence on imported food fortifiers, high price of fortified food and underutilization of fortified food especially in the rural areas where locally made food is preferred.[15]

The results of this systematic review contribute to literature and necessitate call for action to reduce the burden of NTDs in Tanzania. Public health interventions can be conceptualized to increase awareness in the community and among health care providers at the antenatal clinic. Internationally recommended daily intake of 400 micrograms folic acid for primary prevention among low-risk women preconceptionally should be advocated.[31] Interventions for fortifying dietary foods with folic acid in local-level context should be sought, matching the universal iodization experience which has now proven to be efficient and successful to prevent acquired cause of intellectual disability.[32]

The main limitation of this review is the limited number of published studies. We did not find data from all the regions of the country, and no availability of sources of nationwide data showing the burden of NTDs. Most studies looked at the prevalence of birth defects as a whole, not showing the prevalence of NTDs. Most studies obtained were done in health facilities, not capturing community involvement which may lead to an underestimation of the burden of neural tube defects due to underreporting (home births). The TDHS 2022 key indicators report[27] showed that 81% of live births and 93% of still births in the two years preceding the survey were born in a health facility. These high percentages imply that institutional data may reflect population figures because most of the NTDs can still be picked in health facilities. Estimation of the prevalence may also be affected by miscarried pregnancies due to NTDs.

Conclusion

Although few studies have been conducted to determine the prevalence of NTD in Tanzania, the reported prevalence is noted to be high compared to other countries. Also, the use of folic acid supplementation for pregnant women is low and does not meet WHO recommendations for the prevention of NTD and anaemia during pregnancy. Low awareness of existence of fortified flour underscores the efforts and importance of mandatory fortification.

Therefore, to reduce the burden of NTD and to prevent folic acid deficiency, government should strengthen the folic acid program to create community awareness, health promotion and counseling; education programs among health care providers and pregnant women at ANC. Moreover, efforts to increase intake of folic acid-fortified flour among women and the general community are needed. We recommend ensuring availability of folic acid fortified flour by scaling up fortification programs to all selected food vehicles especially maize flour fortification including small-scale mills in our settings.

Limited available data on neural tube defects inform the need for additional primary, wide scope research that would improve the true burden of the defects and facilitate preventive policies on preventive factors. This can be achieved by establishing a population-based birth defects surveillance program, and large community-based studies in different geographical, environmental

and socio-economic settings should be conducted to provide accurate and reliable estimates of the prevalence and risk factors for NTDs in Tanzania.

Acknowledgements

We would like to express our deep sense of gratitude to all the authors of this systematic review.

Authors' contributions
HKM and PC designed the review. HKM prepared the draft of the manuscript. KM, senior supervisor, conceived the review, and finalized the manuscript. Final version of the manuscript was approved by all the authors.
Conflict of Interest: None
Funding: None

References

1. Egbe A, Uppu S, Lee S, Stroustrup A, Ho D, Srivastava S. Congenital malformations in the newborn population: A population study and analysis of the effect of sex and prematurity. Pediatr Neonatol. 2015;
2. Kondo A, Morota N, Date H, Yoshifuji K, Morishima T, Miyazato M, et al. Awareness of folic acid use increases its consumption, and reduces the risk of spina bifida. *Br J Nutr. 2015;114(1):84–90.*
3. Young N, Bowman A, Swedin K, Collins J, Blair-Stahn ND, Lindstedt PA, et al. Cost-effectiveness of antenatal multiple micronutrients and balanced energy protein supplementation compared to iron and folic acid supplementation in India, Pakistan, Mali, and Tanzania: A dynamic microsimulation study. *PLoS Med [Internet]. 2022;19(2):1–22. Available from: http://dx.doi.org/10.1371/journal.pmed.1003902*
4. Corona-Rivera JR, Olvera-Molina S, Pérez-Molina JJ, Aranda-Sánchez CI, Bobadilla-Morales L, Corona-Rivera A, et al. Prevalence of open neural tube defects and risk factors related to isolated anencephaly and spina bifida in live births from the "Dr. Juan I. Menchaca" Civil Hospital of Guadalajara (Jalisco, Mexico). *Congenit Anom (Kyoto). 2021;61(2):46–54.*
5. Githuku JN, Azofeifa A, Valencia D, Ao T, Hamner H, Amwayi S, et al. Assessing the prevalence of spina bifida and encephalocele in a Kenyan hospital from 2005-2010: implications for a neural tube defects surveillance system. *Pan Afr Med J. 2014;18:60.*
6. Liu L, Johnson HL, Cousens S, Perin J, Scott S, Lawn JE, et al. Global, regional, and national causes of child mortality: An updated systematic analysis for 2010 with time trends since 2000. *Lancet [Internet]. 2012;379 (9832):2151–61. Available from: http://dx.doi.org/10.1016/S0140-6736(12)60560-1*
7. Christianson A, Howson C, Modell B. March of Dimes. Global report on birth defect. The hidden toll of dying and disabled children. New York. 2006;
8. Blencowe H, Kancherla V, Moorthie S, Darlison MW, Modell B. Estimates of global and regional prevalence of neural tube defects for 2015: a systematic analysis. *Ann N Y Acad Sci. 2018;1414(1):31–46.*
9. Oumer M, Tazebew A, Silamsaw M. Birth prevalence of neural tube defects and associated risk factors in Africa: a systematic review and meta-analysis. *BMC Pediatr. 2021;21(1):1–13.*
10. Ssentongo P, Heilbrunn ES, Ssentongo AE, Ssenyonga LVN, Lekoubou A. Birth prevalence of neural tube defects in eastern Africa: a systematic review and meta-analysis. *BMC Neurol [Internet]. 2022;22(1):1–11. Available from: https://doi.org/10.1186/s12883-022-02697-z*
11. Noor RA, Abioye AI, Ulenga N, Msham S, Kaishozi G, Gunaratna NS, Mwiru R, Smith E, Dhillon CN, Spiegelman D, Fawzi W. Large–scale wheat flour folic acid fortification program increases plasma folate levels among women of reproductive age in urban Tanzania. *PloS one. 2017 Aug 10;12(8):e0182099.*
12. Kinasha ADA, Manji K. The incidence and Pattern of Neural Tube Defects in Dar es Salaam, Tanzania. *Eur J Pediatr Surg 2002; 12: S25-S52.*
13. Tanzania National Bureau of Statistics. National Fortification Assessment Coverage Tool (FACT) Survey in Tanzania, 2015. 2016.
14. Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC) [Tanzania Mainland], Ministry of Health (MoH) [Zanzibar], Tanzania Food and Nutrition Centre (TFNC), National Bureau of Statistics (NBS), Office of the Chief Government Statistician (OCGS) [Zanzibar] and UNICEF. 2018. Tanzania National Nutrition Survey using SMART Methodology (TNNS) 2018. Dar es Salaam, Tanzania.

15. United Republic of Tanzania (2020), National Biofortification Guidelines. Ministry of Agriculture, May 2020.
16. Mashuda F, Zuechner A, Chalya PL, Kidenya BR, Manyama M. Pattern and factors associated with congenital anomalies among young infants admitted at Bugando medical centre, Mwanza, Tanzania. *BMC research notes. 2014 Dec;7(1):1-7.*
17. Kishimba RS, Mpembeni R, Mghamba JM, Goodman D, Valencia D. Birth prevalence of selected external structural birth defects at four hospitals in Dar es Salaam, *Tanzania, 2011–2012. J. global health. 2015 Dec;5(2).*
18. Magwesela FM, Rabiel H, Mung'ong'o CM. Pattern of congenital anomalies among pediatric surgical patients in a tertiary care hospital in northern Tanzania. *World Jnl Ped Surgery 2022;5:e00410.doi:10.1136/wjps-2021-000410.*
19. Ogundipe O, Hoyo C, Østbye T, Oneko O, Manongi R, Lie RT, Daltveit AK. Factors associated with prenatal folic acid and iron supplementation among 21,889 pregnant women in Northern Tanzania: a cross-sectional hospital-based study. *BMC public health. 2012 Dec;12:1-10.*
20. Mwandelile IF, Mpembeni R, Abade A, Rumisha SF, Massaga JJ, Kishimba R. Awareness and factors associated with reported intake of folic acid-fortified flour among women of reproductive age in Ifakara, Morogoro region, Tanzania: a cross-sectional study. *BMC nutrition. 2019 Dec;5:1-7.*
21. Lyoba WB, Mwakatoga JD, Festo C, Mrema J, Elisaria E. Adherence to iron-folic acid supplementation and associated factors among pregnant women in Kasulu communities in north-western Tanzania. *International J. Reproductive Medicine. 2020 Jun 4;2020.*
22. Shechter-Maor G, Czuzoj-Shulman N, Spence AR, Abenhaim HA. The effect of assisted reproductive technology on the incidence of birth defects among livebirths. *Arch Gynecol Obstet. 2018;297:1397-1403.*
23. Liu S, Evans J, MacFarlane AJ, Ananth CV, Little J, Kramer MS, Joseph KS. Association of maternal risk factors with the recent rise of neural tube defects in Canada. *Paediatric and Perinatal Epidemiology. 2019 Mar;33(2):145-53.*
24. Gildestad T, Øyen N, Klungsøyr K, Nilsen RM, Daltveit AK, Vollset SE. Maternal use of folic acid supplements and infant risk of neural tube defects in Norway 1999-2013. *Scand J Public Health. 2016;44:619-626.*
25. Nishigori H, Obara T, Nishigori T, Ishikuro M, Sakurai K, Hoshiai T, Saito M, Fujiwara I, Arima T, Nakai K, Kuriyama S. Preconception folic acid supplementation use and the occurrence of neural tube defects in Japan: A nationwide birth cohort study of the Japan Environment and Children's Study. *Congenital Anomalies. 2019 Jul;59(4):110-7.*
26. Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC). Antenatal Care Guidelines November 2018. Dar es Salaam Tanzania.
27. Ministry of Health (MoH) [Tanzania Mainland], Ministry of Health (MoH) [Zanzibar], National Bureau ofStatistics (NBS), Office of the Chief Government Statistician (OCGS), and ICF. 2023 Tanzania Demographicand Health Survey and Malaria Indicator Survey 2022 Key Indicators-Report. Dodoma, Tanzania, and Rockville,Maryland, USA: MoH, NBS, OCGS, andICF.
28. Paudel P, Wing K, Silpakar SK. Awareness of periconceptional folic acid supplementation among Nepalese women of childbearing age: a cross-sectional study. *Prev Med. 2012 Nov;55(5):511-3. doi:10.1016/j.ypmed.2012.09.001. Epub 2012 Sep 10.*
29. Bitzer J, von Stenglin A, Bannemerschult R. Women's awareness and periconceptional use of folic acid: data from a large European survey. *Int J Womens Health. 2013 Apr 26;5:201-13. doi: 10.2147/IJWH.S40149.*
30. Folic acid and the prevention of birth defects. National Survey of Pre-Pregnancy Awareness and Behavior Among Women of Childbearing Age 1995-2004. The Gallup Organization for March of Dimes Birth Defects Foundation. 2004. 31-1897-04. p. 3.
31. World Health Organization. Periconceptional folic acid supplementation to prevent neural tube defects. In: WHO-e-library of evidence for nutrition action. (eLENA). Geneva;2017.
32. Pandav C, Viswanathan H, Haxton D. Sustaining elimination of iodine deficiency disorders. In. 1995.