Neurosurgical Forum LETTERS TO THE EDITOR

Family history of neural tube defects

TO THE EDITOR: We read with great interest the recent article by Dupépe et al.⁴ (Dupépe EB, Patel DM, Rocque BG, et al: Surveillance survey of family history in children with neural tube defects. *J Neurosurg Pediatr* 19:690–695, June 2017). Regarding this survey of 254 patients, the authors state that the overall prevalence of family history of neural tube defects (NTDs) in children with an NTD was 16.9%, of which 3.1% occurred in first-degree relatives. The findings reported by these authors also interestingly reveal that in patients with myelomeningocele, as many as 17.7% had a positive family history for NTDs, with up to 3.8% of cases occurring in first-degree relatives. These figures appear to be remarkably much higher than the rates previously documented for positive family history in patients with NTDs, as shown in Table 5 of the article by Dupépe et al.⁴

However, we observed that the cited literature on previously documented findings shown in Table 5 of the authors' discussion includes no established statistics from an African setting. Therefore, we present a few available statistics on this etiological aspect of NTDs in Table 1 of this letter.^{1,3,6} Of particular interest to note is the same marked contrast of our local observations in Africa with the previously published statistics presented by Dupépe et al. The established prevalence of family history of NTDs at our center in Nigeria is in fact 0.9%¹ (Table 1), though we have not noticed any significant change in positive family history from unpublished data of our more recent research. Furthermore, we also observed that the most recent among all the cited literature in Table 5 of the discussion by Dupépe et al. was published in 1995 (Partington and McLone). So, as Dupépe et al. rightly mentioned, virtually

all the cited literature in Table 5 contains data obtained during the pre-folate fortification era when the associated risk from folate deficiency was far higher than it is presently, whereas now more emphasis is placed on the risk from other causative factors. While all these publications from Africa include data obtained after the era of folate fortification, Uganda had the highest rate (7.8%)³ and is one of the few countries with a policy for folate fortification, which may explain their having a relatively higher rate of family history of NTDs compared to most other African countries that do not have such a program. Hence, the finding by Dupépe et al. of such a high prevalence of 16.9% for positive family history raises concerns regarding a probable rise in genetic problems as an underlying cause of NTDs.

Dupépe et al. suggest other possible reasons such as regional and geographic differences, as well as the reduced risk of folate deficiency which now highlights other risk factors.⁴ We suggest that one possible reason for the comparatively low values from Africa as shown in Table 1 is the decrease in available data to work with due to lingering and persisting difficulties with collating and managing data in various data registries in several African countries. In addition, the prevalence of most NTDs is likely to be grossly underestimated in most developing areas, particularly in Africa, as a result of irregularities in referral patterns and health care access.^{1,5} Some mothers deliver their babies at home or in unregistered maternity facilities while others may simply hide information on positive family history of NTDs out of shame, ignorance, or superstitious beliefs. Furthermore, in spite of extensive research, current knowledge of the genetic and epigenetic basis of NTDs in humans is still limited.²

Truly, the role of family history in the development of NTDs still needs to be fully investigated on a much

TABLE 1. Africa-based studies showing positive family history in patients with NTDs

Authors & Year (location of study)	No. of Pts	Sex Ratio (M/F)	Type of NTD studied	Prevalence of Positive Family History Established
Alatise et al., 2005 (Ife-Ijesa, Nigeria)	106	1.1:1	Spina bifida (myelomeningocele in 86.8%; meningocele in 10.4%; lipomeningocele in 1.9%; myelocele in 0.9%)	0.9%
Byabato et al., 2012 (Kampala, Uganda)	51	1.2:1	Spina bifida (myelomeningocele in 98%; meningocele in 2%)	7.8%
Kheir & Eisa, 2015 (Khartoum, Sudan)	91	5:8	NS	1.1% (1/91)

NS = not specified; pts = patients.

larger scale, particularly in this era when the burden of the problem globally still remains quite significant despite better folate levels in the diet. NTDs recur within families, with first-degree relatives of an NTD patient possessing a 3%–5% risk of having offspring with an NTD and second-degree relatives a 1%–2% risk.² The need for further reduction of the burden of NTDs, in view of the limited genetic management options currently available, highlights the importance of adequate history-taking of all NTD patients. Obtaining information on any positive family history should be included as a routine part of the standard management of NTDs in order to better monitor and identify those whose family members are at risk of transferring the problem to their own offspring. Health campaigns to involve community participation for public awareness may also be beneficial in this regard. All these measures might help to increase opportunities for genetic testing in such individuals for a better understanding of the genetics of this condition with the aim of providing new treatment options.

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Disclosures

The authors report no conflict of interest.

Response

We appreciate Dr. Komolafe and colleagues' interest in our article and their comments. In addition, we appreciate the discussion of the prevalence of family history of NTDs among children with NTDs in Africa. These data certainly contribute to the knowledge base.

We agree with Dr. Komolafe et al. that the study of family history is challenging, as it often relies on patient or parent reports. As such, it is subject to a substantial recall bias. Undoubtedly, these challenges are as great or greater in low- and middle-income countries, and the authors point out cultural challenges that may make this type of research even more difficult in the African setting.

Finally, we agree that the genetics of NTDs requires more rigorous investigation. The tools of modern genetics have yet to be applied to spina bifida on a large scale. It is estimated that in the United States, folate acid fortification of wheat has prevented up to 89% of folic-preventable spina bifida and anencephaly cases.¹ Therefore, it may be hypothesized that genetics plays a larger role in the modern incidence of spina bifida than it has historically. Like the authors, we are hopeful that better understanding of the genetics of this condition will lead to new treatment and prevention options.

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