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Research Article

Neural Tube Defect in Kinshasa: Socio-Demographic, Epidemiological and Clinical Aspects

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Abstract

Background: Neural Tube Defect (NTD) has a variable incidence in Word but data for these pathologies are fragmentary in Sub-Saharan Africa.

Aim: The aim of study was to identify the socio-demographic and epidemiological aspects of patients with NTD.

Methods: This is a cases series study of 82 children with NTD transferred to University Clinics of Kinshasa by peripheral maternity hospitals in the city of Kinshasa and two neighboring countries (Republics of Congo and Angola), during the period from January 2014 to December 2018. The socio-demographic and clinical data of parents and children were studied.

Results: For a period of 5 years, we received 82 patients with an average of 17 cases per year. Among these patients, 81.7% were transferred from maternities of Kinshasa city; 12.2% came from other regions of the country and 6.1% were nationals of two neighboring countries. There were 71.9% boys and 25.6% girls (sex ratio M/F: 2.8). Two children (2.5%) presented a disorder sexual development. Among the NTDs encountered, there was a predominance of children with myelomeningocele (80.5%), 47.6% of NTD were isolated, 13% of children died awaiting surgery. The treatment accessibility rate was 39%.

Conclusion: NTD exist in our environment, affecting boys more. Almost all cases were diagnosed at birth. Myelomeiningoceles were the most common form. The rate of accessibility to surgical treatment has been low.

Keywords: NTD; Epidemiology; Clinic; Accessibility to care; Surgery

Introduction

Neural Tube Defects (NTD) represents all congenital malformations resulting from a failure to close the neural tube during fourth week of embryonic development [1,2]. They are usually divided into cephalic forms (anencephalia, exencephalia, encephalomeningocele, meningocele) and spinal forms (meningocele, myelomeningocele). NTD are estimated to affect around 250,000 pregnancies worldwide [3]. The global incidence of NTD is variable and varies between 3 and 40 per 10,000 births [4-6]. These variations could be explained, among other things, by the increase in the termination of pregnancies. Indeed, the medical termination of pregnancy is most often decided in some countries because of the severity of the prognosis [7-11]. In anencephaly or exencephaly, survival ranges from a few hours to a few days. As for the meningoencephaloceles, they leave neurological sequelae of varying severity while the myelomeningoceles are responsible for a more or less severe handicap including a sensitivomotor deficit of lower limbs, sphincter disorders and impact of frequent hydrocephalus.

The administration of folic acid during periconceptional period shows good results in the prevention of NTD. Research suggests that disorders of folate metabolism during the embryonic period, particularly through polymorphisms in genes such as that of Methyl Tetrahydrofolate Reductase (MTHFR), may contribute to the development of NTD [1,6]. However, studies on the distribution of these polymorphisms show contradictory results. As an illustration, a study conducted in Constantine in Algeria for gene did not show a significant association between the C677T mutation and NTD, although the mothers of children with NTD showed elevation homocysteine level, which was partly related to mutation [4].

In Democratic Republic of Congo (DRC), incidence of NTD has not yet been determined. A few studies on congenital malformations in DRC report a predominance of NTD over other types of malformation [12-14]. In the service of Pediatric Surgery of the University Clinics of Kinshasa, annual frequency of NTD seems to be increasing (two patients in 2007, four patients in 2008, two patients in 2009, six patients in 2010, four patients in 2011, fourteen patients in 2012 and twelve patients in 2013). This tendency to the progressive growth of NTD in our consultations motivated us to initiate this study which had as objectives to note the socio-demographic and epidemiological

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aspects of patients with NTD, describe clinical aspects of NTD and determine rate of access to care for children with NTD at University Clinics of Kinshasa.

Material and Methods

We conducted a cases series study from January 2014 to December 2018 in the service of pediatric surgery, Department of Surgery, University Clinics of Kinshasa. It involved patients with an abnormal neural tube closure, whether isolated or associated with other apparent birth defects. Patients were transferred from maternity hospitals in Kinshasa city (capital of Democratic Republic of Congo), other regions of DRC and two countries bordering DRC (Republic of Congo and Republic of Angola).

The parameters of interest were:

- For both parents: age, education level, profession, family urinary incontinence, history family of of NTD.
- For the mother: the concept of diabetes mellitus, convulsion or fever in first trimester of pregnancy, drugs taken in first trimester, spontaneous abortion or stillbirth history, carrying out ultrasound on the third trimester of pregnancy, antenatal diagnosis.
- For the child: age at admission, sex, rank in siblings, birth weight, location and condition of integuments of lesion suggesting malformation, other associated apparent congenital malformations, surgery delay from admission.

NTD have been categorized into two forms: the cephalic form including Anencephaly (AC), Encephalomeningoceles (EMC), Cranial Meningoceles (CM); and the spinal form including Myelomeningoceles (MMC).

Statistical analysis

Data was entered into Excel 2013 software and exported to IBM SPSS for Windows version 22 (IC Chicago) software for analysis. Results are expressed as means plus standard deviation for data with Gaussian distribution, medians with Interquartile Space (EIQ) for data with non-Gaussian distribution and absolute or relative frequency for categorical data. Fisher's chi-square or exact test was used to compare the proportions. We also used Student's t-test to compare the means and Man Whitney's test to compare medians. The statistical significance threshold was set at 5%.

Results

For a period of five years, we received 82 patients with, an average hospital frequency of 17 cases per year. Among these patients, sixty-seven (81.7%) were transferred from maternity hospitals in Kinshasa, 10 (12.2%) were from other provinces of country and 5 (6.1%) were nationals of two neighboring countries. Figure 1 shows the frequency of types NTD observed. There was a predominance of children with myelomeningocele (80.5%). There were 59 boys (71.9%) *vs.* 21 girls (25.6%), sex ratio M/F: 2.8. Two children's (2.5%) had a disorder sexual development. Fifty-two percent of children transferred from Kinshasa maternity hospitals arrived more than two days after their birth. The frequency of NTD was inversely proportional to the birth order in the siblings (p<0.001).

The socio-demographic characteristics of children are illustrated in Table 1. We have not seen a history of urinary incontinence in the family or diabetes mellitus in mother. No history of NTD has been reported in family member of our patients. No mother took folic acid during periconceptional period. However, drugs taken during first trimester of pregnancy were antimalarials (alpha-beta arteether, manalaria, and quinine), nonsteroidal anti-inflammatory drugs (paracetamol, ibuprofen, diclofenac) and antibiotics (ampicillin, ciprofloxacin).

The clinical characteristics of children by type of NTD are presented in Table 2. Thirty-nine cases of NTD (47.6%) were isolated. The apparent malformations associated with NTD are listed in Table 3. Nine cases (13%) died for sepsis or respiratory distress while awaiting surgery. The rate of accessibility to surgical treatment as well as operating time is presented in Table 4.

Table 1: Socio-demographic characteristics of children according to type of NTD.

Variables	Over all n=82 (%)	Spinal form n=66 (%)	Cephalic form n=16 (%)	P
Age (days)	2.0(2.0-6.0)	2.0(2.0-6.0)	2.5(1.0-18.0)	0.009
Sex				
Male	58(72.5)	48(75.0)	10(62.5)	0.241
Female	22(27.5)	16(25.0)	6(37.5)	
Sibling rank				
1st rank	24(29.3)	21(31.8)	3(18.8)	0.599
2nd rank	19(23.2)	15(22.7)	4(25.0)	
3rd rank	14(17.1)	11(16.7)	3(18.8)	
4th rank	11(13.4)	8(12.1)	3(18.8)	
5th rank	5(6.1)	4(6.1)	1(6.3)	
6th rank	7(8.5)	6(9.1)	1(6.3)	
7th rank	1(1.2)	0(0.0)	1(6.3)	
8th rank	1(1.2)	1(1.5)	0(0.0)	
Father's age (years)	36.3 ± 8.2	37.3 ± 7.8	31.9 ± 9.0	0.024
Monthr's age (years)	27.8 ± 6.6	28.2 ± 6.4	26.2 ± 7.3	0.267
p-value	<0.001	<0.001	0.001	
Father's level of education				
Unknown	14(17.1)	8(12.1)	6(37.5)	0.043
Secondary	40(48.8)	33(50.0)	7(43.8)	
University	28(34.1)	25(37.9)	3(18.8)	
Mother's level of education				
Unknown	7(8.5)	4(6.1)	3(18.8)	0.274
Secondary	61(74.4)	50(75.8)	11(68.8)	
University	14(17.1)	12(18.2)	2(12.5)	
Father's profession				
No occupation	24(29.3)	19(28.8)	5(31.3)	0.212
Officiel	27(32.9)	25(37.9)	2(12.5)	
Liberal	27(32.9)	19(28.8)	8(50.0)	
Student	4(4.9)	3(4.5)	1(6.3)	
Mother's profession				
Household	57(69.5)	42(63.6)	15(93.8)	0.118
Officiel	6(7.3)	6(9.1)	0(0.0)	
Liberal	17(20.7)	16(24.2)	1(6.3)	
Student	2(2.4)	2(3.0)	0(0.0)	

Discussion

Eighty-two cases of NTD made up our study series. Antenatal diagnosis was only made in four children (4.9%) while 42 mothers (51.2%) had an ultrasound in the third trimester. Ulcerated myelomeningoceles made up the majority of our sample. Our hospital frequency was 17 cases per year while in the seven years prior to our study it was 6 Cases. This increase in hospital frequency is largely due to the prospective nature of the study. As hospital data is not yet computerized, recording and storing data on survey form appears to compensate the frequent loss of records which underestimates the hospital frequency. This increase would also be linked to the improvement of the referral network by raising awareness among doctors working in the maternity hospitals. Our hospital frequency is the same as that found at reference center for neonatology and

Table 2: Clinical characteristics of children according to NTD.

Variables	Over all n=82 (%)	Spinal form n=66 (%)	Cephalic form n=16 (%)	P
Diabete millitus family father	5(6.1)	4(6.1)	1(6.3)	0.672
Mother's diabete millitus	11(13.4)	10(15.2)	1(6.3)	0.318
Convulsion in 1st Trimester	2(2.4)	2(3.0)	0(0.0)	-
Fiever in 1st Trimester	29(35.4)	24(36.4)	5(31.3)	0.47
Medication in 1st Trimester	19(23.2)	16(24.2)	3(18.8)	0.461
spontaneous abortion	14(17.1)	14(21.2)	0(0.0)	-
Stillborn	2(2.4)	2(3.0)	0(0.0)	-
Ultrasound in 3rd Trimester	42(51.2)	37(56.1)	5(31.3)	0.047
Antenatal diagnosis	4(4.9)	3(4.5)	1(6.3)	0.588
Birth weight (g)	3150.0 ± 686.5	3138.6 ± 701.0	3196.9 ± 642.5	0.763
Category				
≤ 2500	16(19.5)	15(22.7)	1(6.3)	0.355
2600-3900	51(62.2)	39(59.1)	12(75.0)	
≥ 4000	15(18.3)	12(18.2)	3(18.8)	
NTD integuments				
Intact	21(25.6)	11(16.6)	10(62.5)	0.001
Ulcerated	55(67.1)	50(75.8)	5(31.3)	
Ulcerated and Ruptured	6(7.3)	5(7.6)	1(6.3)	
Head circumference (cm)	36.3 ± 5.7	37.0 ± 5.2	31.3 ± 6.5	0.005

Table 3: Malformations associated with NTD.

Malformations apparentes associées	Spinal form n=66 (%)	Cephalic form n=16 (%)	Over all n=82 (%)
Associated malformation			
No	27(40,9)	12(75,0)	39(47,6)
Yes	39(59,1)	4(25,0)	43(52,4)
Isolated clubfoot	30	0	30
Clubfoot and knee valgum	1	0	1
Clubfoot and low ears inserted	1	1	2
Clubfoot and craniostenosis	0	1	1
Clubfoot, bilateral 2nd and 3rd toe syndactyly and hypertelorism	0	1	1
Supernumerary finger	1	0	1
Parasitic twin (a lower limb with slender handles in the lumbar region)	1	0	1
Microcrania and bladder exstrophy	1	0	1
Sexual ambiguity	1	0	1
Sexual ambiguity, omphalocele and bladder exstrophy	1	0	1
Omphalocele, bladder extrophy and anorectal malformation	1	0	1
Bilateral cleft palate, exophthalmos with bilateral extropion, hypertelorism and lower ears inserted	0	1	1
Anorectal malformation	1	0	1

Table 4: Accessibility to surgical treatment and operating time.

Variables	Over all n=82 (%)	Spinal form n=66 (%)	Cephalic form n=16 (%)	p
Surgery				0.523
No accessibility to treatment	50(61.0)	39(59.1)	11(68.8)	0.942
Acces to treatment	32(39.0)	27(40.9)	5(31.3)	
Follow up time operating (days)	38.0(30.0-62.0)	38.0(20.0-64.0)	49.0(30.0-74.0)	
1-5 (days)	3(9.4)	3(11.1)	0(0.0)	
6-10 (days)	2(6.3)	2(7.4)	0(0.0)	
11-20 (days)	4(12.5)	4(14.8)	0(0.0)	
21-30 (days)	6(18.8)	4(14.8)	2(40.0)	
>30 (days)	17(53.1)	14(51.9)	3(60.0)	

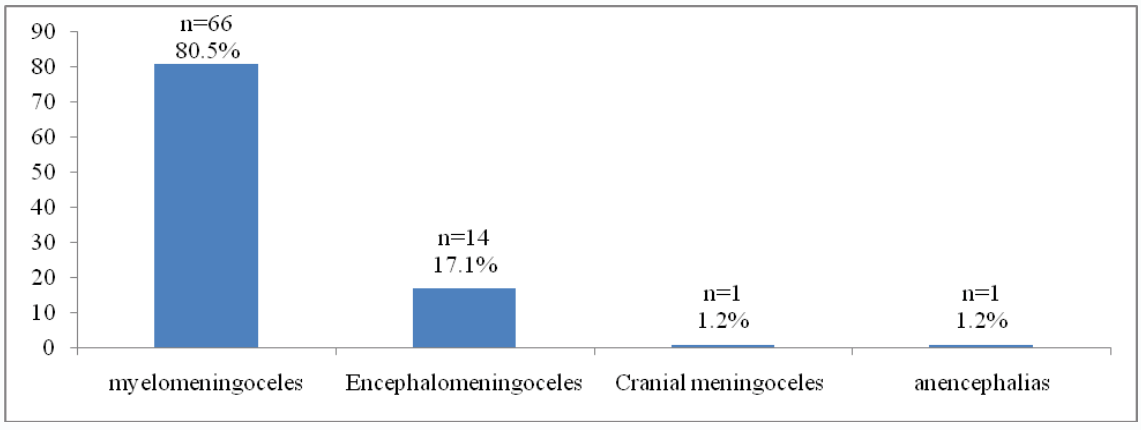

Figure 1: Frequency of type neuronal tube defect.

nutrition at Rabat children's hospital by Radouani et al. [6]. This annual frequency is higher than that of 15 cases found by Owen et al. [15] in Australia that of 13.5 cases found in province of Kenitra in Morocco by Daoudi et al. [16] and that of 11 cases found in Iraq by Al-Ani et al. [17].

Although transfer was decided immediately after birth for almost all newborns, more than 50% of our patients arrived in hospital beyond second day after their birth. The late arrival was explained by the fact that parents had to not only overcome the fear of the surgical intervention that was looming for the first days of their child's life but also have financial means for this intervention. With 68.3% of ulcerated lesions at birth, this late arrival raised the risk of meningitis for children who must be operated within the first 72 hours. While most authors in the literature have found a female predominance, our sample consisted mainly of male newborns [6,18-22].

Like Teckie et al. [22] and Sanoussi et al. [23], we noted a progressive decrease in the frequency of NTD with the increase in the rank of the newborn in his siblings. Owen et al. [15], Omer et al. [20], Chuckwunyere and Singh [21] found an increase in the frequency of NTD in multiparous women. The relatively low frequency in multiparous women in our series could be linked to folic acid supplementation during previous pregnancies. It is also necessary to point out the role that the stress could play in occurrence of malformations in primiparas sometimes carrying unwanted pregnancies. The mothers of our patients were aged 19 to 44 with an average of 27.8 years. This average age is close to that found by Radouani et al. [6], Al-Ani et al. [17], Mohammed et al. [19], chuckwunyere and singh [21] (respectively 29.3; 31.7; 29.85; 27.3).

No case of NTD has been reported in the family of our patients. Studies by Toriello et al. [24], Baraitser et al. [25] and Kenefick [26] have reported familial cases of NTD. A recurring genetic cause has been suspected or identified in several cases. For our study, genetic analyzes were not performed to rule out recurring genetic abnormalities. We noted a low rate of completion of obstetric ultrasound (only 51.2% in the third trimester) and antenatal diagnosis (4.9%). Mohammed et al. [19] noted 85% of prenatal diagnosis. Chuckwunyere and Singh [21], Forrester and Merz [28] and Van Allen et al. [29] reported 74%, 86% and 50% respectively. Our low prenatal diagnosis rate has resulted in a delay in the care of our patients. Their parents were neither psychologically nor financially prepared for emergency surgery.

Eighty percent of our patients had a myelomeningocele. Radouani et al. [6] found 32% myelomeningocele, 2% meningoencephalocele and 66% anencephaly. Mohamed et al. [19] reported 50% myelomenigocele, 28% anencephaly, 17% encephalocele and 2% meningocele. Omer et al. [20] reported 47% myelomeningocele, 18% anencephaly, 14% encephalocele, 7% meningocele. Li Z [8] reported 48% anencephaly, 42% spina bifida and 10% encephalo-meningocele. We recorded a case of anencephaly. It can be explained by the fact that the patients were all transferred to us. The anencephali living a few hours to a few days, they would die before or during their transfer to our hospital.

Only 39% of our patients had surgery, after 30 days of admission in the service for 53.1% of them. The lack of antenatal diagnosis, absence of mutual health insurance that can facilitate treatment, lack of allowance for our hospital are all factors behind this low rate of accessibility to care.

Conclusion

NTD is a frequent pathology in our environment. They most affected male newborn babies. Almost half of the mothers performed an obstetric ultrasound even in the third trimester. Almost all cases were diagnosed at birth. Ulcerated myelomeningoceles made up the majority of our cases. The rate of accessibility to surgical treatment has been low.

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