ISSN: 1813-1638

The Medical Journal of Tikrit University

Available online at: www.mjotu.com

العراقية
المجلات الاكاديمية العلمية
IRAQI
Academic Scientific Journals

Neural tube defects: Incidence and types

Saad .M .H. Alshahwani (1)

Samira .A-H. Abdullah *(2)

(1) Department of Anatomy
College of Medicine
Almustansyriah University
Baghdad
Iraq

(2) Department of Anatomy
College of Medicine
Tikrit University
Salahaldeen
Iraq

***Keywords*:**

Neural tube defects
Anencephaly,
Encephalocele,
Spina bifida,
Folic acid defect

ARTICLE INFO

Article history:

Received 15 Sep 2018
Accepted 01 Dec 2018
Available online 01 June 2019

ABSTRACT:

Background Neural tube defects (NTDs) are a group of severe congenital abnormalities resulting from the failure of closure of neural tube .It is result from a combination of genetic and environmental factors and therefore are classified as having a multifactorial etiology. Aim: to identify the incidence of neural tube defects through the following objectives to :Determine the frequency of NTD, , determine the types of NTDs, Compare the gender differences, and Study the histological appearance of the brain tissue in case of NTDs.

Patients & Methods: Routine antenatal trans-abdominal ultrasound examination was made for 6720 outpatients' women with missed period of 12-36 week ,for two years duration from september 2010 to october 2012. Thirty two patients were diagnosed as NTDs sonographically. The frequency of which was 0.47% of the total, which is higher than previous studies in other countries.

The Results: The majority of cases was anencephaly (17 cases 53%) followed by encephalocele (8 cases 25 %) while spina bifida cystica was found in 7 cases (22 %); five cases were myelomeningocele and two cases were meningocele. The higher maternal age group affected with NTDs was the group 20- 24 years

Anencephaly and encephalocele were most common defects among maternal age groups 20-24years and 15-19years, the frequency was higher in rural area than urban 21(65.6%) and 11(34.4%) respectively. NTDs are more common among female than male fetuses. The commonest type of NTD was anencephaly .

Normal cerebral cortex with less gyri and sulci was clear in all cases of encephalocele, while in cases of anencephaly about 8(47%) cases had normal brain tissue .Absent brain tissue were seen 9(52.9%),12(70%) had hemorrhage within the Brain tissue, while 11(64.7%) had necrosis with brain tissue **Conclusions:** The rickets is an important disease to be studied in this country account about nearly half of cases of preterm babies and about 10% of term babies .Breast feeding is a risk factor of the disease .Alkaline phosphatase activity and radiological feature are important for screening.

DOI: http://dx.doi.org/10.25130/mjotu.25.01.10

*Corresponding author E mail : drsamira2018r@gmail.com

Introduction

Neural tube defects (NTDs) are one of the most common birth defects, occurring in approximately one in 1,000 live births in the United States(1). An NTDs are an opening in the spinal cord or brain that occurs very early in human development (2, 3). There are two types of NTDs, open and closed. The open is more common, this is occur when the brain and/or spinal cord are exposed at birth through a defect in the skull or vertebrae ,While the closed is a rare type , it occurs when the spinal defect is covered by skin(4,5.(

Open NTDs include many types as anencephaly (6), encephalocele (i.e, primary and secondary (7), spina bifida (i,e cystica and occulta) (8,9), Iniencephaly (10), Hydranencephaly (11) and Schizencephaly (12).

Neural tube defects result from a combination of genetic and environmental factors and therefore are classified as having a multifactorial etiology Studies show that a woman who has had one child with a neural tube defect such as anencephaly has about a 3% risk of having another child with a neural tube defect (13).It is known that women taking certain medications for epilepsy and women with insulin-dependent diabetes have a higher risk of having a child with a neural tube defect (14).

Anencephaly and other physical and mental deformities have also been blamed on exposure to high heat (such as a fever or use of a sauna) in early pregnancy, In addition, high exposure to toxins as lead, chromium, mercury, and nickel may result in same defect (15, 16, 17).

Aim And Objectives:

The present study aimed to identify the incidence of neural tube defects through the following objectives to

1. Determine the frequency of NTDs.
2. Determine the types of NTDs.
3. Compare the gender differences.
4. Study the histological apperance of the the brian tissue in case of NTDs.

Patients and methods:

Prospective study was carried out on 6720 pregnant women consulting a private ultrasonographic clinic.The study was conducted over about two year duration started from september 2010 to october 2012.

Ultrasonographic examination, Using color Doppler ultrasound equipment type Sonoscop/Chines made model 2010/SSI-6000 was used. Inclusion and exclusion criteria were also applied.

Inclusion criteria's included all pregnant women who consulted the

clinic with 12- 36 weeks missed periods only. Pregnant women with <12 weeks or >36 weeks gestational were excluded from the study.

Calculation of the gestational age depends on the history of LMP confirmed by U/S measurements .

After the diagnosis of NTDs, the woman referred to obstetrician for further management which is termination of pregnancy ؛

The terminations were either by using cytotic drugs, or caesarean section depending on the obstetrician`s opinion. The caesarean section is done either in Tikrit teaching hospital or in private hospital.

The fetus was examined clinically after termination to determine the type of anomaly then a picture was taken in the theater (after taking the permission of the parent) to document the diagnosis and the type of NTDs. Biopsy was taken from the brain tissue in case of anencephaly and encephalocele; slides were prepared for examination for further histological study .

Results:

Out of the 6720 outpatients' women of 12-36 weeks of pregnancy .32 patients of them were diagnosed as having opened NTDs sonographically. Another 10 patients with hydrocephalus and one with iniencephaly were diagnosed but excluded from the study because the skull is completely formed and the brain is covered by skull vault and skin.

The frequency of NTDs was 0.47%, the majority of cases was anencephaly (17 cases 53%) followed by encephalocele (8 cases 25 %) while spina bifida cystic was (7 cases 22 %) out of which 5/7 cases were myelomeningocele and 2/7 cases were meningocele .

The incidence of NTDs was related to the maternal age as it is clear in the results of the present work (table 1). Wrist X-ray was don using X-ray device .

Patient were divided according to maturity into full term(>37 completed weeks of gestation) and preterm(<37 completed weeks of gestation),200 cases were studied ,of them 150 case full term and 50 case preterm , 19 cases were diagnosed as rickets in preterm and 15 cases in term children.

Table 1: The incidence of NTDs in relation to maternal age.

Maternal age	Total	NTDs	Percentage %
15-19	1398	8	25%
20-24	1720	12	37.5%
25-29	1730	7	21.8%
30-34	1272	3	9.3%
35-39	600	2	6.2%
Total	6720	32	100

The maternal ages ranged between 15- 39 years .The highest incidence of open NTDs was among maternal age group 20- 24 years which was 12 (37.5%) , 8 cases were between 15-19 years (25 %) , 7 cases ranged between 25-29 years 21.8 % , 3 cases were 30-34 years of age(9.3.%), 2 Cases between 35-39 year(6.25%);

Twenty one cases were terminated after 20 weeks of gestation. (Table 2) shows the types of NTDs related to time of termination. All anencephalic cases were terminated, 7(87.5%) of encephalocele cases were terminated except one case refused and continued to term when born alive and died two months later, Cases of spina bifida were 5(71.4%) terminated because of its association with severe hydrocephalus and very thin or absence of brain tissue, while 2(28.6%) cases continue to terms because they were only meningocele without hydrocephalus and were surgically correctable.

Table 2: Type of NTDs related to time of termination.

NTDS	No.	Percentage	Early termination < 20 weeks	Late termination > 20 week
Anencephaly	17	53.1	5	12
Encephalocele	8	25	3	4*
Spina bifida	7	21.9	-	5**
Total	32	100	8	21

P-value=0.253

- *One case refuse termination
- ** two cases correctable so continued to term.

The frequency was higher in rural area 21(65.6%) compared to the urban which was 11 cases and formed (34.4%) NTDs were, generally, more common among female than male fetuses with a ratio of 3:1; Table (3) show these results. Moreover the ratio was highest in case of anencephaly to reach about 5:1.

Table 3: Type of NTDs related to gender

NTDs	Male %	Female %	Total
Anencephaly	3 (9.3%)	14 (43.7%)	17(53.1%)
Encephalocele	2 (6.2%)	6 (18.7%)	8(25%)
Spina bifida	3 (9.3%)	4 (12.5%)	7(21.9%)
Total	8(25%)	24(75%)	32(100)

P-value =0.432

Histological appearance of NTDs:

Histological processing was made for all cases of anencephaly and encephalocele .Normal cerebral cortex with less gyri and sulci are seen histologically in all slide of encephalocele, About 8(47%) cases of anencephaly had normal brain tissue .Absent brain tissue is seen 9(52.9%),12(70%) had haemorrhage within the Brain tissue, while 11(64.7%) had necrosis with brain tissue .Figure 1 shows normal brain tissue in normal fetus, Figure 2 shows normal brain tissue in fetus with encephalocele. The meninges with pia mater (Blue arrow).The external molecular layer(red arrow). External granular layer (yellow arrow). External pyramidal layer (Black arrow). Figure 3 revel multiple area of hemorrhage is seen as a collection blood cells.

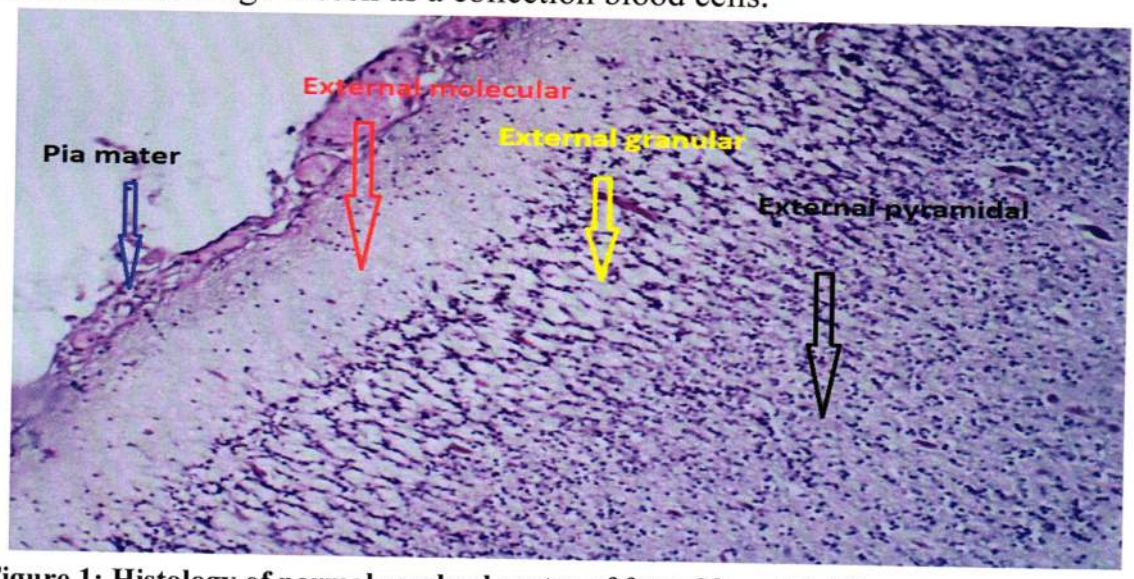

Figure 1: Histology of normal cerebral cortex of fetus 28 week(x10).

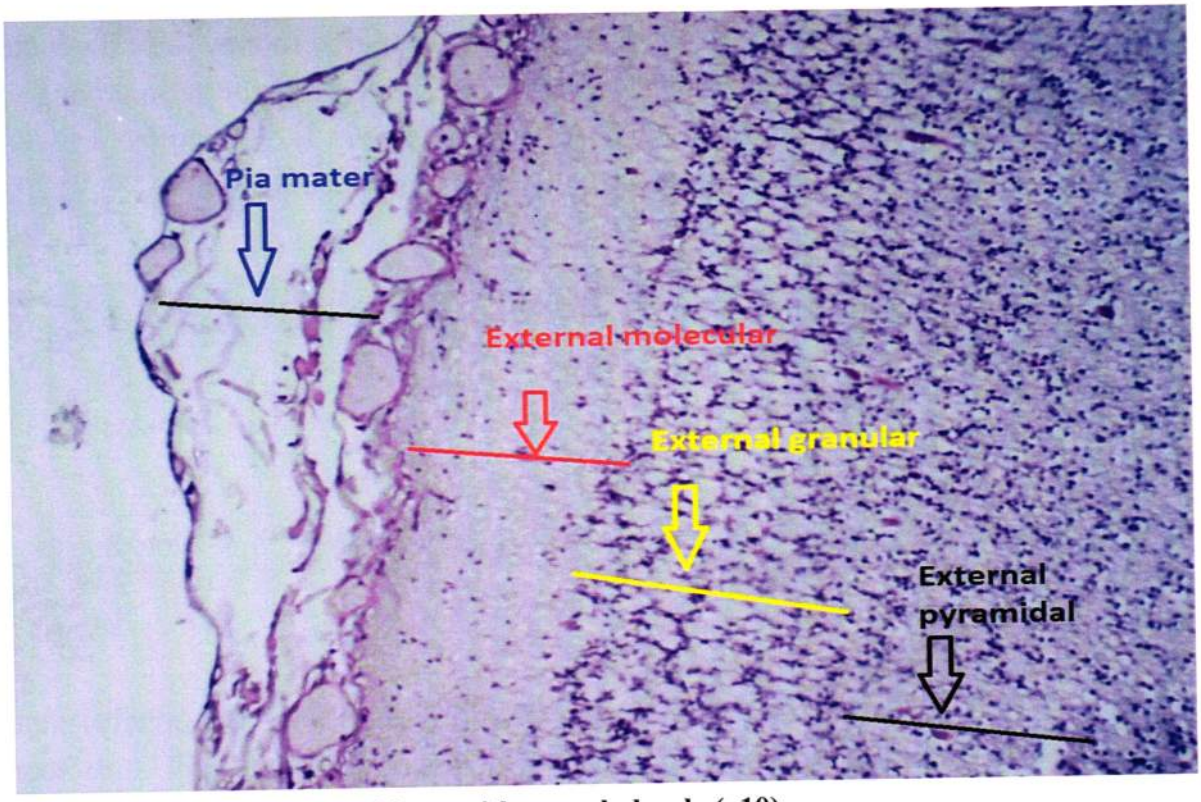

Figure 2: cerebral cortex of fetus with encephalocele (x10).

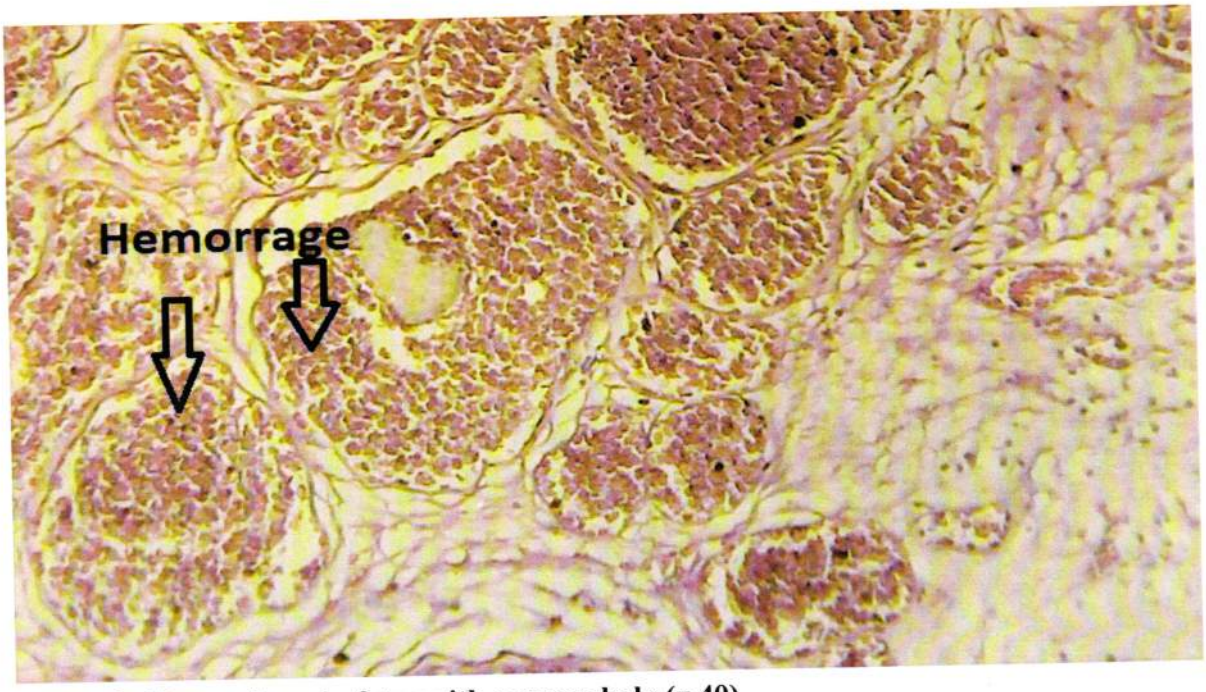

Figure 3: Hemorrhage in fetus with anencephaly (x 40).

Discussion

The incidence of NTDs in present study was 0.47% which is approximately similar to other studies performed in different countries (18).

Anencephaly , encephalocele and myelomeningocele, are the most common type of NTDs(19) so as the present study revealed that anencephaly was the most common type of NTDs (53%), its incidence in USA was approximately 1/1000 deliveries(20). The incidence of both anencephaly and spina bifida accounted for up to 95% of all NTDs (21), in comparison to the present study; spina bifida encountered in isolated manner i.e. not associated with other NTDs with a frequency (21.9%). Most recent studies indicate towards 1500 babies (1 out of every 2,800) are born with spina bifida each year in the United States(22).The prevalence at birth was 0.52/1000 births for anencephaly, 0.51/1000 for spina bifida, and 0.08/1000 for encephalocele. The ratio considered to be low for a predominantly white population.

In Los Angeles, an epidemiological study was carried out where they compared NTDs with high-prevalence populations. The results did not support a major etiologic role for environmental factors: (1) no significant differences were found between rates by month of birth or conception; (2) no significant association with maternal age or parity for anencephaly; for spina bifida a significant maternal age effect ($P < 0.01$) and for encephalocele a parity effect ($P < 0.02$); and (3) no significant relationship with father's occupational class for either anencephaly or encephalocele but a marginally significant ($P < 0.05$) inverse association was found for spina bifida when a statistic based on ordinal relationships was used, and their findings were in conjunction with those from other areas and times of low prevalence suggest that environmental factors play a relatively insignificant role in the etiology of NTDs in such populations(23)..

The NTDs, among females were more than males in a ratio of 3:1.The ratio of female to male in the anencephaly was nearly 5:1, 3:1 for encephalocele and approximate 1.3: 1 for spina bifida respectively. This result is comparable with other studies, where they found significant differences between females (58.6%) and male (40.9%) Also they found significant differences between the types of NTD among female to male sex ratio. The female ratio was significantly higher for anencephalic (1.76) and spina bifida and anencephalic (4.0) compared with spina bifida (1.1) (24) while in another study the Girls are three times

more likely than boys to have anencephaly(25).

Histological appearance of NTDs:

The encephalocele appeared as a hemorrhagic mass, protruding from the forehead to cover the right eye. Histologic examination of the encephalocele revealed extramedullar hemopoiesis(EMH) both within and adjacent to malformed cerebral cortex, with a tendency for the hematopoietic cells to line up in columns within malformed cerebral cortex. The propose that a single event during the fourth week of gestation could both interrupt closure of the neural tube, giving rise to the encephalocele, and impair migration of the neural crest, leading to holoprosencephaly secondary to failure of neural crest derivatives to induce basomedial telencephalic differentiation. EMH may have been induced from hematopoietic stem cells in the richly vascular meningeal component of the encephalocele, in response to anemia and hypoxia (26).

In other studies they found (68 %) of the cases with no recognizable anatomic structures. And the present tissue was sometime disorganized mass of nonspecific cell types, or the so-called "area cerebrovasculosa," a mass of thin-walled vascular channels distended with blood (27)

In the present study (52%) was absent brain tissue, in (70%) hemorrhage with brain tissue and in (64.7%) showed necrotic tissue with or without brain tissue, necrotic tissue .The necrotic tissue which is known as cerbrovasculosa of non-organized tissue.

Conclusions

1- NTDs is a common condition in our community (0.47%) with higher incidence than previous studies in other countries
2- The commonest type of NTDs was anencephaly
3- Women with low socioeconomic status be at highest risk ,
4- women aged between 20-24 years being the most vulnerable group
5- In 6 cases the neural tube defects extend below the cervical region and extend to the lumber region while the distal part of the neural tube is closed so the fusion of neural tube extend from distal or caudal neuropore toword cranial neuropore in such cases
6- Encephalocele is considered as an open NTDs ,in current study in all cases of encephalocele the brain is covered by skin in certain stage of development but due to growth and increase in size of herniated part of brain; it results in perforation of the skin covering the brain
7- In most of the research the major part of cerebral hemisphere is

absent in anencephaly, in current study in 50 % there is brain tissue of cerebral hemisphere with or without hemorrhage and necrosis.

8- Ultrasound is the method of choice in diagnosis of NTD

9- NTDs is more common in female than male in ratio of 3:1 in case of encephalocele while it is about 5:1 in case of anencephaly.

References

1- Bentley TG, Willett WC, Weinstein MC and Kuntz KM. neural tube defects Population-level changes in folate intake by age, gender, and race/ethnicity after folic acid fortification. Am J Public Health 2006; 96:2040-7.

2- Dias MS, and Li V. Pediatric neurosurgical disease. Pediatr Clin North Am. Dec 1998; 45(6):1539-78,

3- Dirks PB, and Rutka JT. The neurogenetic basis of pediatric neurosurgical conditions. In: Albright L, Pollack I, Adelson D, eds. Principles and Practice of Neurosurgery. New York: Thieme Medical Publishers; 1999: 23-4.

4- Saladin, Kenneth. Neural tube defect. Anatomy. USA: The McGraw-Hill Companies, Inc. 2010; 485-92.

5- Pittman, T. "Spina bifida occulta. Journal of neurosurgery. 2008:1; (2): 113

6- Badano, Jose L.; Norimasa Mitsuma, Phil L. Beales, and Nicholas Katsanis. "The Ciliopathies: An Emerging Class of Human Genetic Disorders". Annual Review of Genomics and Human Genetic 2006; 7,125–148.

7- Albert L Jr,and DeMattia JA. Cocaine-induced encephalocele: case report and literaturereview. Neurosurgery 2011; 68:E263.

8- Juranek, J; and Salman MS. "Anomalous development of brain structure and function in spina bifida myelomeningocele". Developmental Disabilities. 2010;16: 23–30.

9- Roberts D, Shepherd RW, and Shepherd K. Anthropometry and obesity in myelomeningocele. J Paediatr Child Health. 1991;27(2) :83-90;

10- Jones, KL. Meningomyelocele, Anencephaly, Iniencephaly Sequences, in Smith's Recognizable Patterns of Human Malformation, .1998: 548, 659-60,

11- McAbee GN, Chan A, Erde EL. "Prolonged survival with hydranencephaly: report of two patients and literature review". Pediatr. Neurol. 2000; 23 (1): 80–4.

12- Tietjen, I.; Bodell, A.; Apse, K.; Mendonza, A. M.; Chang, B. S.; Shaw, G. M.; Barkovich, A. J.;

Lammer, E. J.; Walsh, C. A. : Comprehensive EMX2 genotyping of a large schizencephaly case series. Am. J. Med. Genet.2007; 143A: 1313-16.

13- Cowchock, S; Ainbender, E; Prescott, G; Crandall, B; Lau, L; Heller, R; Muir, WA; and Kloza,. "The recurrence risk for neural tube defects in the United States: A collaborative study". A.J. M.G 1980: 5 (3): 309–14.

14- Stephen D. Ratcliff. Family medicine obstetrics (3rd). Philadephia: Mosby Elsevier.2008; 323-36.

15- Keeling JW. Central Nervous System Anomalies: Fetal Pathology, 1994 :pg. 33-34

16- Shaffer LG, Marazita ML, Bodurtha J, Newlin A, and Nance WE "Evidence for a major gene in familial anencephaly". Am. J. Med. Genet 1990: 36 (1): 97–101.

17- Wasserman CR, Shaw GM, Selvin S, Gould JB,andSyme SL. Socioeconomic status, neighborhood social conditions, and neural tube defects. Am J Public Health 1998; 88:1674-80.

18- Kulkarni ML, Mathew MA Ramchandran B. High incidence of neural tube defect in south India.2007; 49-52.

19- Tadanori Tomita, Hideki Ogiwara, Marc C Patterson, Leonard E Weisman, Alison G Hoppin. Anencephaly and encephalocele.[last updated: Mar 14, 2012].

20- Romero R, Pilu G, Phillippe S, Alessandro G, and Hobbins J. Anencephaly, Prenatal Diagnosis of Congenital Anomalies, 1988; 43- 45. From Riordan S. Weeks J. Anencephaly.

21- Kramer Ms; The epidemiology of adverse pregnancy outcomes: an overview. J Nutr. 2003 May; 133(5 Suppl 2):1592S-1596S.

22- Parker SE, Mai CT, Canfield MA, et al; for the National Birth Defects Prevention Network. Updated national birth prevalence estimates for selected birth defects in the United States, 2004-2006. Birth Defects Res A ClinMolTeratol. 2010; 88:1008-16.

23- Lowell E. Sever .An epidemiologic study of neural tube defects in Los Angeles County II. Etiologic factors in an area with low prevalence at birth Teratology 2005; 25: 3: 323–34.

24- Bakhouche Houcher1, Samia Begag1, Yonca Egin2 and Nejat Akar2. Neural Tube Defects in Algeria. At:

www.intechopen.com/download/pdf/33110

25- Jallo, G.I. &Becske, T. Neural Tube Defects. (2008). EMedicine Neurology.

26- Virginia E.Elgin sander connolly William S .Millar Neil A . Fedstein J. Dwork. Extramedullary Hematopoiesis within a Frontoethmoidal Encephalocele in a Newborn with Holoprosencephaly P.D.P May 2001; 4 :(3) 289-97.

27- Giroud A: Anencephaly. In Vinken PJ, Bruyn GW, Myrianthopoulos NC (eds): "Handbook of Clinical Neurology, Congenital Malformations of the Brain and Skull Part I." Amsterdam: Elsevier, 1977; 130:173-208.