

Birth defects and epidemiological factors in Tunisia

Anomalies congénitales et facteurs épidémiologiques en Tunisie

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ABSTRACT

Aim: To identify the birth defects listed in the embryo-fetopathology department of the maternity and neonatology center of Tunis (Tunisia), and to study the epidemiological factors.

Methods: We carried out a retrospective study on 2489 malformed cases including fetuses, stillborns and deceased newborns among 5750 ones autopsied in the embryo-fetopathology department of the maternity and neonatology center of Tunis.

Results: The sex ratio of autopsied cases was 1.06. 41% of them weighed less than 500 grams. The gestational age was between 22-28 weeks of amenorrhea in 41.3% of cases. Among the maternal characteristics, we noted an average maternal age of 30.1 years old (with extremes ranging from 16 to 51 years old), and a predominance of O blood group. Parental consanguinity and history of reproductive failure were found respectively in 37.4% and 32.5% of cases.

Antenatal diagnosis was established in 62% of cases. It was positive in 59.5% of cases (all types of malformations combined).

Among the 2489 malformed cases, 4568 birth defects were identified. Neurological anomalies were the most common (26.01%) followed by nephro-urological anomalies (13.16%) and cardiovascular anomalies (11.47%).

During the study period, 164 cases of polymalformative syndromes were counted and 217 cases of chromosomal aberrations were classified.

Conclusion: This study allowed us to assess the frequency of birth defects, categorize them based on their type and determine the different epidemiological factors during a long period of nine years, even though our nation does not have a national register of birth defects. In Tunisia, it is important to carry out a national multicenter study in order to set a national register representing the real statistics of these anomalies.

Key words: Birth defects, risk factors, epidemiology, prevention, Tunisia.

RÉSUMÉ

Objectif: Identifier les anomalies congénitales recensées au service d'embryo-foetopathologie, du centre de maternité et de néonatalogie de Tunis (Tunisie), et étudier les caractéristiques épidémiologiques.

Méthodes: Nous avons réalisé une étude rétrospective portant sur 2489 cas d'anomalies congénitales incluant des fœtus, des mort-nés et des nouveau-nés décédés malformés parmi 5750 autopsiés au service d'embryo-foetopathologie de la maternité et de néonatalogie de Tunis.

Résultats: Le sex-ratio des cas autopsiés était de 1,06. 41% d'entre eux pesaient moins de 500 grammes. L'âge gestationnel était compris entre 22 et 28 semaines d'aménorrhée dans 41,3% des cas. Parmi les caractéristiques maternelles, nous avons noté un âge maternel moyen de 30,1 ans (avec des extrêmes allant de 16 ans à 51 ans), et une prédominance du groupe sanguin O. La consanguinité parentale et les antécédents d'échec de la reproduction étaient retrouvés respectivement dans 37,4% et 32,5% des cas. Un diagnostic anténatal a été posé dans 62% des cas. Il était positif dans 59,5% des cas (tous types de malformations confondus). Parmi les 2489 cas malformés, 4568 anomalies congénitales ont été identifiées. Les anomalies neurologiques étaient les plus fréquentes (26,01%) suivies des anomalies néphro-urologiques (13,16%) et des anomalies cardiovasculaires (11,47%). Au cours de la période d'étude, 164 cas de syndromes polymalformatifs ont été dénombrés et 217 cas d'aberrations chromosomiques ont été classifiés.

Conclusion: Cette étude nous a permis d'évaluer la fréquence d'anomalies congénitales, les catégoriser selon leur type et déterminer les différents facteurs épidémiologiques sur une longue période de neuf ans, même si notre pays ne dispose pas d'un registre national d'anomalies congénitales. En Tunisie, il est important de réaliser une étude nationale multicentrique afin d'établir un registre national représentant les statistiques réelles de ces anomalies.

Mots clés: Anomalies congénitales, facteurs de risque, épidémiologie, prévention, Tunisie.

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INTRODUCTION

Nowadays, fetopathology is becoming a discipline that presents an increasing interest to physicians. The progress made in the medical field to fight against infectious diseases, and to prevent the sequelae of prematurity and obstetrical accidents, have permitted to highlight birth defects and hereditary diseases [1].

Although congenital pathology had always existed, an attitude of fatalistic resignation was manifested against perinatal mortality and birth defects for centuries. Interest in perinatal care has only recently increased with the change of minds that has contributed to updating this specialty [2].

Fetopathological examination is indicated in cases of reproductive failure. It confirms, completes or corrects a prenatal diagnosis. Faced with the antenatal discovery of an anomaly, a multidisciplinary confrontation is required between obstetricians, neonatologists, pediatricians, foetopathologists and geneticists, in order to specify an exhaustive diagnosis and to consider a management strategy for the current pregnancy and subsequent pregnancies [3].

The fetopathological examination focuses on congenital pathology, and particularly on birth defects which include all structural deviations due to a developmental disorder occurring before birth [4].

The abnormal development of an embryo could be due to various causes : a defect in the genetic material inherited or occurring de novo, chromosomal anomalies, and the action of exogenous agents. But in most cases, birth defects have a multifactorial origin, in particular an interaction between genetic and environmental factors [5].

This study aimed to describe the different types of birth defects, to determine their frequencies during each year of the study period, and to study epidemiological factors that could be linked to their occurrence.

METHODS

We conducted a retrospective study of all malformed cases including fetuses, stillborns and deceased newborns autopsied at the embryo-fetopathology department of the maternity and neonatology center La Rabta (Tunis), over a period of 9 years (January 1, 2001 to December 31, 2009).

The department maintains a register documenting all fetuses, stillborns and deceased newborns autopsied for malformative or etiological assessments.

To trace the profile of malformed cases and their mothers, we have analysed medical registers in order to identify the different birth defects.

We included all cases with postnatally diagnosed congenital anomalies as well as those resulting from a medical termination of pregnancy for antenatally diagnosed congenital anomalies.

Recruitment was mainly ensured by the neonatology department and the gynecology-obstetrics departments of the maternity center. Some cases were sent by some other public hospitals and by certain private establishments in

the capital Tunis, Tunisia.

Data collection

For each autopsied fetus, stillborn or deceased newborn, a sheet was drawn up on which the maternal and case characteristics were noted. The data collected was checked and supplemented if necessary, by studying the medical registers of the neonatology department and the gynecology-obstetrics departments of the maternity center. The maternal data considered included: age, parity, gestation, blood group, the existence of a history of spontaneous abortions, stillbirths, malformed infant, the presence of consanguinity and pregnancy pathology. For fetal characteristics, we systematically recorded: sex, birth weight, birth term, condition at birth (alive or stillborn), outcome of a single or multiple pregnancy. Careful clinical examination involves both the fetus and the placenta.

Criteria for inclusion

All malformed fetuses, stillborns and deceased newborns who have benefited from a fetopathological examination with parental consent, were included in our study.

Criteria for non-inclusion

We did not include products of miscarriages less than 7 weeks of amenorrhea (WA), and newborns dying beyond 28 days.

Criteria for exclusion : Malformed fetuses, stillborns and deceased newborns whose parents did not give their consent were excluded from our study.

Fetopathological examination

It is a specialized examination that requires a specific protocol combining the study of the placenta and the fetus.

Study of the annexes

The study of the annexes includes measuring the diameter and the length of the cord, examining its insertion zone on the placenta, and counting the vessels. Any abnormalities are noted (hematoma, cyst, knot, etc...).

Fetal examination

The systematic study protocol includes photographs, x-rays, karyotype and autopsy.

All cases with malformations benefited from photographs and x-rays. The autopsy remains the most clinical examination systematically carried out after the agreement of the parents. The meticulous clinical examination of the fetus is carried out in search of dysmorphism or external anomaly directing towards a chromosomal aberration or an internal malformation.

The usual measurements (vertex-heel, vertex-coccyx, head circumference and foot length) allow an assessment of fetal growth in relation to gestational age.

At the opening, the thoracic abdominal and pelvic viscera are examined in situ, which facilitates the study of the anatomical relations of the different organs and notes the presence of certain anomalies such as a common mesentery, a diaphragmatic hernia... evisceration one-piece is adopted.

Brain is removed in the case of a neurological abnormality mentioned during a prenatal diagnosis, following a postnatal clinical examination, a polymalformed case, a suspicion of a chromosomal aberration and in certain forms of osteochondrodysplasia.

Samples are systematically taken from all organs for histological study. The two stains used are hematoxylin eosin and Masson's trichrome.

Statistical analysis

The data were entered and analyzed using IBM SPSS statistics software, version 23.

We calculated the means, range (extreme values: minimum and maximum) and the standard deviation for the quantitative variable. Frequencies were expressed as percentages for qualitative variables.

Ethical consideration

Ethical approval for the study was obtained from the Ethics Committee of the Maternity and Neonatology Center in Tunis.

RESULTS

Our study focused on 2489 malformed cases including fetuses, stillborns and deceased newborns listed on 5750 fetopathological examinations carried out over a period of nine years.

Each malformed case had at least one malformation but could carry two or more malformations. Thus, 4268 birth defects were counted.

The percentage of malformed cases was 43.28% during the period (2001-2009).

Epidemiological factors

Characteristics of malformed cases (N= 2489) and their parents (2001-2009) were presented in Table 1.

Among the 2489 malformed cases identified in this study, 51.11% were male, 47.98% were female and 0.89% were asexual. The sex ratio was to 1.06.

The median weight was 801.65g with extremes ranging from 16 to 4800g.

The median gestational age was 25-26 weeks of amenorrhea (WA) with extremes ranging from 7 WA to 42 WA.

The median maternal age was 31.30 years with extremes ranging from 16 years to 51 years.

62.08% of mothers were multigravida and 37.91% were primigravida with a average gestation of 2.37 (±1.62).

38.83% of mothers were multiparous, 33.83% were primiparous and 27.23% were nulliparous. The average parity was 1.33 (±1.32).

Maternal blood group was specified in 1242 mothers. 41% were O+ blood group, 28% were A+, 15% were B+, 5% were AB+, 6% were O-, 3% were A-, and 1% for both B- and AB-.

Maternal medical history was documented in 809 mothers: 37.2% had stillbirths, 33.99% had miscarriages, 21.87% had malformed babies and 6.92% had neonatal deaths.

The consanguinity rate was 37.42%.

3.84% of malformed newborns were born alive and died secondarily.

Maternal pathologies were noted in 8.79% of mothers, dominated by diabetes and toxemia of pregnancy.

Table1. Characteristics of malformed cases and their parents (2001-2009), (N= 2489).

Characteristics	Percentage (%)
Sex	
Male	51.11
Female	47.98
Asexual	0.89
Weight	
<500	41.44
500-1000	27.26
1000-1500	10.59
1500-2000	7.11
>2000	13.57
Gestational age	
7-21	31.84
22-28	41.29
29-35	18.15
36-42	8.7
Characteristics of the parents	
Consanguinity	
(+)	37.42
(-)	62.57
Maternal characteristics	
Maternal age	
≤28	29.92
28-35	42.45
≥35	27.62
Gravidity	
G1	37.91
G>1	62.08
Parity	
P0	27.23
P1	33.83
P>1	38.83
Blood group	
O+	41
A+	28
B+	15
AB+	5
O-	6
A-	3
B-	1
AB-	1
Medical history	
Stillbirths	37.2
Miscarriages	33.99
Malformed babies	21.87
Neonatal deaths	6.92

Identification of birth defects

All of the 4568 birth defects identified in the laboratory were classified by system and in descending order (Table 2). Thus, neurological abnormalities were the most frequent, they represented 26.01% of malformations followed

by nephro-urological abnormalities (13.16%) and lung abnormalities (12.87%, dominated by pulmonary hypoplasia). Cardiac abnormalities occupied the 4th place with a rate of 11.47% followed by digestive and face abnormalities (10.33%).

Table 2. Identification of birth defects (2001-2009).

	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total	%
Neurological abnormalities	53	62	90	95	125	136	176	224	227	1188	26,01
Nephro-Urological Abnormalities	50	38	47	75	67	76	89	49	110	601	13,16
Lung Abnormalities	52	40	30	55	74	109	62	79	87	588	12,87
Cardiac Abnormalities	32	29	29	47	52	69	72	111	83	524	11,47
Digestive Abnormalities	23	28	19	35	43	68	96	67	93	472	10,33
Face Abnormalities	29	23	23	23	59	58	49	94	70	437	9,57
Skeletal Abnormalities	28	26	27	44	75	44	42	24	38	348	7,62
Extremity Abnormalities	10	14	24	30	39	18	61	35	47	278	6,09
Genital Abnormalities	3	3	5	10	12	20	26	19	29	127	0,28
Skin Abnormalities	1	0	0	0	3	0	0	0	1	5	0,11
Total	281	263	294	414	549	598	673	702	785	4568	100

In our study, neurological abnormalities were dominated by hydrocephalus (37.87%). Neural tube defect including anencephaly, cystic spina bifida, rachischisis and encephalocele occupied the 2nd place with a

rate of 34.1%. Anencephaly was the most common malformation in neural tube defects, its rate was 11.02% of all neurological abnormalities (Table 3).

Table 3. Neurological abnormalities, 2001-2009 (N=1188)

	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total	%
Hydrocephaly	14	30	41	36	59	39	57	91	83	450	37,87
Anencephaly	12	7	15	9	16	18	22	15	17	131	11,02
Cystic SB	4	7	12	9	12	14	16	21	21	116	9,76
RC	8	6	6	12	16	14	14	11	21	108	9,1
Encephalocele	3	4	2	6	4	9	6	12	4	50	4,21
TOTAL NTD*	27	24	35	36	48	55	58	59	63	405	34,1
Cerebellar abnormalities	3	1	2	7	3	12	24	20	28	100	8,41
Abnormalities of the corpus callosum	0	1	3	4	1	9	19	23	26	86	7,24
Microcephaly	3	1	1	5	8	7	5	11	8	49	4,13
Holoprosencephaly	2	2	8	5	4	5	7	0	12	45	3,79
Gyration abnormalities	4	2	0	2	1	5	5	17	6	42	3,54
Iniencephaly	0	1	0	0	1	2	1	3	0	8	0,68
Diastematomyelia	0	0	0	0	0	2	0	0	1	3	0,25
Total	53	62	90	95	125	136	176	224	227	1188	100

NB*: The neural tube defect (NTD) includes anencephaly, cystic Spina Bifida (SB), Rachischisis (RC) and encephalocele.

In our series, nephro-urological anomalies ranked second in all birth defects with a rate of 13.16% (Table 2).

We counted 115 cases of cystic renal dysplasia, i.e. 19.13% of nephro-urological anomalies and 4.62% of birth defects (Table 4).

Pulmonary abnormalities held the 3rd rank with a rate of 12.87% and are represented in 70.07% of cases by pulmonary hypoplasia (Table 5).

Cystic adenomatoid lung disease accounted for 2.38% of all lung malformations. It constitutes the 2nd pulmonary anomaly after abnormal pulmonary lobulation (24.66%) and constitutes the most frequent cystic bronchopulmonary anomaly (Table 5).

524 cases of heart defects were identified for a total number of 5750 fetopathological examinations, i.e. a

frequency of 9.11% during our study period.

Heart defects rank 4th after neurological, nephro-urological and pulmonary anomalies.

The most common heart defects, isolated or associated with other cardiac abnormalities, was ventricular septal defects (42.75%), followed by abnormalities of the aortico-pulmonary trunk (13.93%) and the atrioventricular canal (11.45%) (Table 6).

In our series, digestive abnormalities and those of the abdominal wall represented a frequency of 10.33% (Table 2). Coelosomy was counted in 20.97% of our cases. Diaphragmatic abnormalities accounted for 16.32%. Digestive stenosis, atresia or agenesis were listed in 16.95% of cases (Table 7).

Table 4. Nephro-Urological Abnormalities, 2001-2009 (N=601).

	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total	%
Cystic Renal Dysplasia	10	9	10	19	12	14	13	9	19	115	19.13
Ureteral abnormality	9	9	8	13	11	13	20	9	19	111	18.47
Renal Agenesis	9	9	8	13	11	13	13	9	19	104	17.3
Pyelocaliciel dilation	5	1	8	3	5	5	15	7	15	64	10.65
Horseshoe Kidney	1	4	4	7	5	6	9	4	15	55	9.15
Bladder abnormality	7	3	1	5	6	8	6	3	6	45	7.49
Renal Hypoplasia	3	2	3	6	8	7	6	2	7	44	7.32
Posterior Urethral Valve	4	1	4	4	4	6	6	1	0	30	5
Isolated Renal Ectopia	0	0	1	5	3	0	1	5	8	23	3.81
Renal Hyperplasia	1	0	0	0	0	4	0	0	0	5	0.83
Number anomaly	0	0	0	0	0	0	0	0	2	2	0.34
Renal Tumor	1	0	0	0	1	0	0	0	0	2	0.34
Isolated shape anomaly	0	0	0	0	1	0	0	0	0	1	0.17
Total	50	38	47	75	67	76	89	49	110	601	100

Table 5. Lung Abnormalities, 2001-2009 (N=588).

	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total	%
Pulmonary hypoplasia	44	34	20	49	55	63	35	47	65	412	70.07
Lobulation abnormality	4	3	9	5	15	40	23	30	16	145	24.66
Cystic adenomatoid lung disease	2	2	1	0	2	1	2	1	3	14	2.38
Pulmonary hyperplasia	2	1	0	0	0	0	1	1	0	5	0.85
Sequestration	0	0	0	0	1	1	0	0	1	3	0.51
Tracheoesophageal fistula	0	0	0	0	1	0	0	0	2	3	0.51
Isomerism	0	0	0	0	0	3	0	0	0	3	0.51
Unilateral pulmonary agenesis	0	0	0	1	0	1	1	0	0	3	0.51
Total	52	40	30	55	74	109	62	79	87	588	100

Table 6. Heart Abnormalities, 2001-2009 (N=524).

	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total	%
Ventricular septal defects	12	6	9	18	17	34	33	52	43	224	42,75
Aortic-pulmonary trunk	8	5	5	2	9	7	9	13	15	73	13,93
Atrioventricular canal	5	3	1	9	11	4	10	13	4	60	11,45
Atrial septal defect	0	2	2	2	6	12	7	6	6	43	8,20
Hypoplastic left heart syndrome	1	4	5	2	3	2	3	15	3	38	7,25
Ventricular abnormalities	0	1	4	5	2	3	1	3	6	25	4,78
Ear abnormalities	2	3	2	5	2	0	4	2	4	24	4,58
Dextrocardia	2	3	1	2	1	6	2	2	0	19	3,62
Venous return abnormalities	2	2	0	1	0	1	2	3	2	13	2,48
Acardius	0	0	0	1	1	0	1	2	0	5	0,96
Total	32	29	29	47	52	69	72	111	83	524	100

Tableau 7. Digestive abnormalities, 2001-2009 (N = 472).

Digestive abnormalities	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total	%
Splenic abnormalities	5	4	3	6	13	15	37	9	28	120	25,42
Liver abnormalities	3	1	2	3	5	10	20	15	22	81	17,16
Stenosis, atresia or agenesis	3	6	2	6	4	16	10	16	17	80	16,95
Diaphragmatic abnormalities	9	5	3	12	5	7	13	9	14	77	16,32
Coelosomy	3	9	5	5	14	6	10	13	10	75	15,89
Laparoschisis	0	1	1	1	1	13	4	2	1	24	5,08
Pancreatic abnormalities	0	2	3	0	0	0	2	0	1	8	1,7
Cloaca	0	0	0	1	1	1	0	3	0	6	1,27
Meckel's diverticulum	0	0	0	1	0	0	0	0	0	1	0,21
Total	23	28	19	35	43	68	96	67	93	472	100

DISCUSSION

Within 5750 fetuses, stillborns and deceased newborns autopsied, 43.28% were found to have congenital birth defects, totaling 4568 cases.

The overall percentage of malformed cases is varying significantly depending on the studied series, and on the population if concerned only stillbirths and living births or only living births. According to data from 1998 to 2011 provided by the European Surveillance of Congenital Anomalies, the rate of congenital anomaly was 1.27 per 1,000 births [6]. In Korea, 'congenital anomalies, deformities, and chromosomal abnormalities' was the third leading cause of infant mortality in 2020, accounting for 16.2% of all infant deaths [7].

The sex ratio was 1.06 in our series. The sex ratio at our center was between 0.96 and 1. A male predominance with 61.3% compared to 38.7% of female was noted in the study of Choi et al [8]. This result was also in concordance with study of Black et al [9].

A meta-analysis strengthened the hypothesis that pregnancies with a male fetus are more susceptible to abnormal placental development, which is associated with obstetric complications such as gestational hypertension, preeclampsia, gestational diabetes, and placental abruption [10].

Fetopathological examination was done in 41% of cases between 22-28 weeks of amenorrhea. The median gestational age was 25-26 WA with extremes ranging from 7 WA to 42 WA.

In the literature, the examination of the second trimester represents 63% of cases with an average gestational age of 23-36 WA. In the studies of Carles and Optiz [11, 12], the gestational age was 21.5 weeks.

In this current study, we have found that 42.7% of mothers were aged between 28 and 35 years old, while 27.5% were over 35 years old.

In a large prospective cohort study, Hollier et al. demonstrated that women aged 25 years or older at delivery had significantly and progressively greater risk of having fetuses with nonchromosomal malformations compared with women aged 20 to 24 years. By 35 years of age, the additional age-related risk of having infants with nonchromosomal malformations was approximately 1%, and for women aged 40 years or older, the increase in risk was approximately 2.5% over that of women younger than 25 years [13].

In the study of Choi et al, no fetal anomalies were detected by targeted ultrasonography in women younger than 20 years, and the highest rate of 2.8% was found in women who were older than 40 years [8].

In 41% of cases, the dominant blood group was group O. However, Bugnon et al [14] observed the predominance of B blood type in mothers of malformed children.

In our series, maternal pathology was found in 8.79% of cases, represented mainly by toxemia of pregnancy and diabetes. Bugnon et al, has reported a rate of 37% of toxemic mothers with malformed children [14]. Roux has shown that metrorrhagia was significantly more frequent during pregnancies with malformed fetuses [15].

Concerning diabetes, it has been proven that the

imbalance of diabetes in the preconception period was responsible for the appearance of fetal malformations.

The risk of congenital malformations was three to four times higher in children of diabetic mothers. It reached 80% in cases with long-term illness [15].

According to Kinnunen et al, the risk of major congenital anomalies was significantly higher in the gestational diabetes mellitus -exposed (5.09%) than in the non-exposed group (4.33%) [16].

In this current study, all the 4568 congenital birth defects identified in the laboratory were classified by system and in descending order.

Neurological abnormalities were the most frequent representing 26.01% of birth defects followed by nephro-urological abnormalities (13.16%), and pulmonary abnormalities (12.87%, dominated by pulmonary hypoplasia). Cardiac abnormalities occupied the 4th place with a rate of 11.47% followed by digestive and wall abnormalities (10.33%).

The rate of neurological malformations was the highest in our series. This could be explained by the deficiency of folic acid, vitamin B12, vitamin D and fatty acids levels in mothers [17]. This rate was 21.13% in the study of Kannane et al [18], and 12.4% in the study of Choi et al [8]. In our study, central nervous system malformations were dominated by hydrocephalus (37.87%), whereas those reported by Kannane et al, were dominated by spina bifida (11.44%) [18].

In our series, nephro-urological malformations ranked second in all congenital birth defects with a rate of 13.16%. This result was consistent with the study of Robert [19]. According to Carle, anomalies of the development of the urinary tract hold the 1st rank of malformative pathologies in a series of 1410 fetopathological examinations [11], the 2nd rank in Pierquin's series [20], and the 5th rank in the series of Gillerot [21, 22].

In our series, renal agenesis represented 17.30% of cases with a nephro-urological malformation. This finding was similar to the literature where renal agenesis rates were 13.8% and 10% [23].

The overall prevalence of renal agenesis has been extensively discussed in the literature. Numerous epidemiological studies have been conducted, where the occurrence of various congenital anomalies was analysed. These studies have reported the prevalence of this defect ranging from 0.00096% to 1.59% [24, 25]. In the meta-analysis of Plutecki et al, which was based on 15 641 184 subjects, the pooled prevalence of renal agenesis was 0.03% [26].

Among the extra urinary malformations associated with renal agenesis, we noted a higher frequency of genital anomalies, i.e. 75%. The same result was reported by Kohler [27].

In this study, digestive abnormalities and those of the abdominal wall represented a frequency of 10.33%. This finding was in contrast with those of Carles [11] which was 25.1%, 4.5% in the series of Gillerot [21], 3.8% in the study of Gillerot and Hustin [22] and 3.6% in the study of Choi et al [8].

In 91% of cases, omphalocele was accompanied by other malformations (neurological, nephro-urological, cardiac,

etc.). This particularity was underlined by Brun, and which was generally found in the context of chromosomal aberrations and in particular in the Trisomy 18 [28].

Intestinal atresia was associated in 22.22% of cases with renal malformations. Francannet reported a rate of 19% in his study [29].

Splenic, hepatic and pancreatic abnormalities were found in the context of syndromic or metabolic diseases.

We identified, in our sample, only 1 case of Meckel's diverticulum, i.e. 0.21%. The rate was between 1 to 2% of the population according to Grall's study [30].

The latter has shown that there was no malformation associated with Meckel's diverticulum, which was in contrast with what was noted in our series.

Strengths: Among the strengths of our study is the long period of study spread over 9 years and the high number of cases. Despite the absence of a national register of birth defects in our country, this study allowed us to evaluate the frequency of birth defects and to classify them according to their type.

Weaknesses: This study is carried out at the maternity and neonatology center of Tunis and is not representative of national statistics. A national multicenter study is needed to have statistics that reflect the reality of congenital anomalies, hence the interest in setting up a national register of birth defects in Tunisia.

CONCLUSION

This study allowed us to assess the frequency of birth defects, categorize them based on their type and determine the different epidemiological factors during a long period of nine years, even though our nation does not have a national register of birth defects. We denounce that there isn't a national record in Tunisia, so that we may clearly understand the frequency of various anomalies, their regional distribution, and their historical evolution. This is why, it is important to set a national register representing the real statistics of these anomalies.

Abbreviation

NTD: Neural Tube Defect

WA: Week of amenorrhoea

SB: Spina Bifida

RC: Rachischisis

Header: Birth defects in Tunisia

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