ORIGINAL ARTICLE

Contribution of fetopathological examination in identifying causes of neonatal deaths

Contribution de l'examen fœtopathologique dans l'identification des causes des décès néonataux

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Abstract

Objectives: To determine the concordance between the causes of death reported in the neonatal departement and the data obtained from the fetopathologic examination.

Methods: We included all newborns admitted to the Neonatal Resuscitation Unit who died there before the 28th day of life and in whom a fetopathological examination was performed.

Results: The causes of neonatal deaths were characterized by the dominance of respiratory pathologies (31%) then palliative cares (18%), neurological causes (9%), heart disease (9%), inherited diseases of metabolism (6%) and sudden deaths (6%). A total concordance between fetopathological and neonatological examinations was noted in 27% of the cases, a partial concordance in 40%, a total discordance in 27%, and in only 6% of the cases the fetopathological examination didn't show any abnormalities.

Conclusion: We emphasize of the importance of fetopathological examination in the determination of the cause of neonatal deaths by providing an exhaustive diagnosis essential to the management of future pregnancies.

Key words: Neonatal deaths; Neonatological clinical examination; Fetopathological examination.

Résumé

Objectifs: Déterminer la concordance entre les causes de décès néonataux annoncées dans le service de néonatologie et celles retenues par l'examen fœtopathologique.

Méthodes: Nous avons inclus tous les nouveau-nés admis en unité de réanimation néonatale qui y sont décédés avant le 28ème jour de vie et chez lesquels un examen fœtopathologique a été réalisé.

Résultats: Les causes des décès néonataux ont été caractérisées par la prédominance des pathologies respiratoires (31 %), des soins palliatifs (18 %), des causes neurologiques (9 %), des maladies cardiaques (9 %), des maladies héréditaires du métabolisme (6 %) et des morts subites (6 %). Une concordance totale entre les examens fœtopathologiques et néonatalogiques a été constatée dans 27% des cas, une concordance partielle dans 40%, une discordance totale dans 27% et dans seulement 6% des cas l'examen fœtopathologique n'a montré aucune anomalie.

Conclusion: Nous soulignons l'importance de l'examen fœtopathologique dans la détermination de la cause des décès néonataux en fournissant un diagnostic exhaustif indispensable à la gestion des futures grossesses.

Mots clés: Décès néonataux; Examen clinique néonatologique; Examen fœtopathologique.

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Introduction

The loss of a child during the neonatal period constitutes a traumatic event for the family, as well as for the medical team. The parents, especially the mother, experience this event as a failure and the identification of the cause helps them to grieve.
For this reason, the search for causes of death in newborns is a concern for every neonatologist. The doctor, in his quest for the causes of death, seeks among other reasons, to detect genetic diseases in order to establish genetic counseling and improve his treatment protocols.
In this case, the fetopathologic examination is a valuable tool. It confirms, completes or corrects the presumed cause of death and can sometimes in itself provide an answer. Its contribution is indisputable for establishing an exhaustive diagnosis essential for genetic counseling.
The objective of the fetopathological examination is to detect any discrepancy between the neonatological clinical examination before death [1]. This may correct or confirm a diagnosis, providing invaluable comfort for the family and the medical team. However, this examination may be unnecessary in certain cases [2].
The aim of this study was to determine the concordance between the cause of death reported in the neonatal unit and the data obtained from the fetopathologic examination.

Methods

This was a descriptive and retrospective study, carried out in the neonatology and the fetopathology departments in the Center of Maternity and Neonatology of Tunis (CMNT), over a period of 6 years from January 2011 to December 2016.
Our study consisted of two main parts:
- a descriptive part of epidemiological data, clinical, radiological characteristics of our patients in the neonatal intensive care unit during their hospitalization and data from the fetopathological examination.
- an analytical part, in which we used by analogy, a classification proposed by Brand et al [3] according to the degree of concordance of the comparison between the causes of death recorded in neonatology (or following the antenatal ultrasound examination) and the data from the fetopathological examination which consisted of an external examination of the newborn to detect any anomaly visible to the naked eye.
Thus, four groups were retained:
- Group A: the fetopathological examination confirmed the diagnosis made by the neonatologists:"Total concordance".
- Group B: the fetopathological examination confirms the initial diagnosis of the neonatologists, highlighted other anomalies and provided additional elements: "Partial concordance".
- Group C: the final diagnosis was rectified or corrected by the fetopathological examination: "Total Discordance".
- Group D: the fetopathological examination provided no pathologic evidence and no malformations.

Patients

Data were collected from patient files and the staff notebook of the neonatology and the fetopathology departments in the Center of Maternity and Neonatology of Tunis.
We included in this study livebirths and admitted to the neonatal intensive care unit, who died before the 28th day and underwent a fetopathological examination was performed.
We considered as born alive all newborns with a gestational age of at least 22 weeks of amenorrhea and/or a birth weight of at least 500 grams and who have had positive cardiac activity at some point.
Live births and deaths whose records were incomplete or not found, were not included in this study.
The fetopathological examination was performed in the fetopathology department, and included several stages: Radiographic examinations, photographs, biometric examinations, external macroscopic examination, examination of the central nervous system, histological examination, examination of the placenta with the cord and membranes.

Data collected

In this work, we studied the epidemiological, clinical, biological, radiological and fetopathological characteristics in newborns hospitalized in the neonatology department after neonatal deaths and in whom a fetopathological examination was carried out after written consent of the parents.

Results

53 files met the inclusion criteria but according to the exclusion criteria only 34 cases were retained. Their distribution over time was detailed in Figure 1.

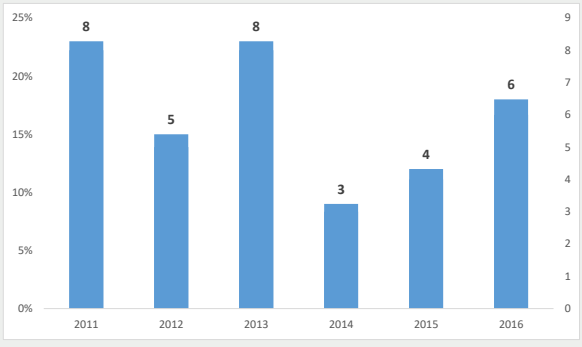

Figure 1. Distribution according to the year of study

Epidemiological characteristics were presented in Table 1. Median gestation was 2.4 with exremes ranging from 1 to 7 gestations while median parity was 1.8 with extemes ranging from 1 to 4 parities. The percentages of miscarriages, intrauterine fetal deaths and abortions were 12%, 9% and 27%, respectively. In addition, 21% of women reported a neonatal death during their previous pregnancies.

Table 1. Epidemiological characteristics

Characteristics	Percentage
Maternal Age (years old)	
20-30	50
30-35	13
>35	4
Medical-surgical history	
No history	76
Presence of Medical-surgical history :	24
Consanguine marriage	
Yes	38
No	62
Obstetric history	
Abortions	27
Previous neonatal death	21
Miscarriages	12
Intrauterine fetal deaths	9
Prenatal ultrasound	
Absent	12
Present	88
Pathological	56
Normal	32
Pathologies during pregnancy	
Gestational diabetes	12
Pre-eclampsia	9
Threat of premature delivery	15
Metrorrhagia	0
Particular habits	
Medication intake	21
Smoking	0
Alcohol consumption	0
Term of delivery (WG)	
<28	15
28-31	18
32-33	12
34-36	18
>37	37
Mode of delivery	
Vaginal	53
Cesarean section	47
Time of rupture of the amniotic sac	
No rupture	73
Rupture	27
<12 hours	18
12-18 hours	3
>18 hours	6
Quantity of amniotic fluid	
Normal	64
Polyhydramnios	21
Anamnios	12
Oligoamnios	3
Acute fetal distress	
Presence	44
Absence	56

WG : Weeks of gestation

Prenatal ultrasound was abnormal. The ultrasound abnormalities found in our series included: severe intrauterine growth retardation ; club feet, boot hands, abnormal brain structures ; multicystic left kidney, hydronephrosis, pyeloectasia of the ventricles ; polymalformative syndrome ; thickening of the neck and scalp; large lobulated mass with a large cystic component with an intraoral component and significant contingent of extraoral intraamniotic development ; hydrothorax ; macrosomia and low ear implantation ; oligoamnios, polyhydramnios, anamnios ; megabladder and bilateral dilatation of the pyelocalicial cavities ; bilateral pyelic ectasia ; anasarcis with significant thickening of the soft tissues and bilateral pleural effusion ; pulmonary atresia with intact septum, right ventricular hypoplasia, coronary anomalies; right diaphragmatic hernia.

In our study, gestational diabetes was detected in 12% of cases, pre-eclampsia in 9% of cases, a threat of premature delivery in 15% of cases and no cases of metrorrhagia were reported during these pregnancies.

Smoking as well as alcohol consumption were not reported in any of our cases.

Taking medicine during pregnancy was reported in seven women with a percentage of 21%.

Exposition to antenatal corticosteroids was reported in 21% of cases.

In our series, was reported in 63%of cases. The cesarean section rate was 47%.

Acute fetal distress was reported in 44% of cases. The membranes rupture accured in 27% of cases. Polyhydramnios was reported in 21% of cases, anamnios in 12% of cases and oligoamnios in 3% of cases.

The neonatal clinical examination was pathological in 96% of cases (Table 2). The five-minute Apgar score is shown in Figure 2.

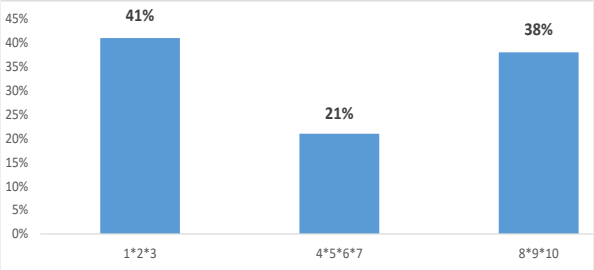

Figure 2.Apgar Score

50% of newborns had a birth weight greater than 2500 grams, and 15% of newborns had an extremely low birth weight of <1000 grams.

Intrauterine growth retardation was noted in 50% of cases. An abnormal head circumference was described in 38% of cases (microcephaly: 12% and macrocephaly: 26%). 3% of newborns presented with anal impermeability and 1% presented with choanal atresia. Facial dysmorphism was noted in 41% of newborns including: Microretrognatism, Microphthalmia, Macrocephaly, Hypertelorism, Triangular facies, Low ear implantation as well as poorly hemmed ears, Cleft palate and ogival palate (Figure 3).

Neonatal respiratory distress was noted in 85% of cases requiring tracheal intubation in 24% of cases and apnea in 30%. An abnormality of the cardiological examination was found in 47% of cases: Bradycardia in 14 cases, Hemodynamic disorder in 16 cases, and Heart murmur in two cases. On the other hand, 21% of newborns had

a pathological abdominal examination: Meteorized abdomen in four cases, hepatomegaly in two cases, and splenomegaly in two cases. The neurological examination was pathological in 82% of cases including decreased reactivity, hypotonia, decreased spontaneous mobility and lack of alertness. Most of the newborns were male with 65% of cases (sex ratio 1.8). Sexual ambiguity was reported in 3% of cases.

Table 2. Neonatal clinical examination

Characteristics	Percentage
Birth Weight (g)	
>2500	50
1500-2500	20
1000-1500	15
<1000	15
Head circumference	
Normal	62
Macrocephaly	26
Microcephaly	12
Orifice permeability	
Anal impermeability	3
Choanal atresia	1
Facial dysmorphism	41
Neonatal respiratory distress	81
Cardiological examination	
Normal	53
Pathological	47
Abdominal examination	
Normal	79
Pathological	21
Neurological examination	
Normal	18
Pathological	82
Sex	
Male	65
Female	32
Asexual	3
Abnormalities of the external genitalia	
Absence	88
sexual ambiguity	3
Unilateral cryptorchidism	9
Skin examination	
Normal	85
Jaundice	6
Other skin signs	6
Skin hemorrhage	3

G : grams

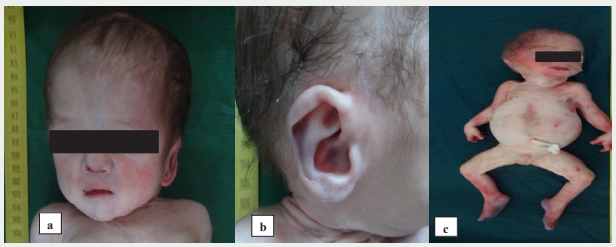

Figure 3. External examination: **a**) Microstomia ; **b**) abnormally shaped ear lobule; **c**) Potter facies, boot hands and congenital convex pes planus associated with abdominal distention.

In our series, 12% of newborns presented an anomaly of the external genitalia, including 3% of cases with anomaly of sexual differentiation and 9% of cases with unilateral cryptorchidism, as shown in Table 2.

In 85% of cases, the skin examination did not present any abnormality. Elsewhere, jaundice was noted in 6% of newborns, other skin signs were noted in 6% of other babies (including a collodion baby) and only 3% of newborns had a skin hemorrhage.

Additional tests like biological examination, radiological examination including chest x-ray, transfontanellar ultrasound, cardiac ultrasound and abdominal-renal ultrasound were presented in Table 3.

Table 3. Additional tests

Characteristics	Percentage
Biological examination	
Absence	47
Presence	53
Normal	23
Pathological	30
Radiological examination	
Chest x-ray	
Absence	28
Presence	72
Normal	11
Alveolar syndrome	26
Cardiomegaly	11
Bilateral hydrothorax	6
Pneumothorax	6
Unilateral pleurisy	6
Diaphragmatic hernia	3
Pneumonia	3
Transfontanellar ultrasound	
Absence	82
Presence	18
Normal	9
Pathological	9
Cardiac ultrasound	
Absence	82
Presence	18
Normal	6
Pathological	12
Abdominal-renal ultrasound	
Absence	91
Presence	9

The biological examination was carried out in 53% of newborns, returning pathological in 30% of cases with anemia, hyperbilirubinemia and inflammatory syndrome. A chest x-ray was performed in 72% of newborns showing various anomalies as shown in Table 3. Transfontanellar ultrasound was only performed in 18% of cases, returning abnormal in 9% of cases showing cerebral edema in one case and intraventricular hemorrhage in two cases. The cardiac ultrasound, which was only performed in 18% of cases, turned out to be pathological in 12% of cases distributed in Moderate pulmonary arterial hypertension (PAH), Reduced contractility, Dilated right cavity with doubt about supravalvular stenosis, PAH, dilation of the right heart chambers, global hypokinesis.

Abdominal-renal ultrasound was performed in 9% of cases. It was pathological in all cases showing: a large hydro-(metro)-colpos associated with significant bilateral urinary dilatation with thinning of the renal parenchyma; an overloaded liver; a neurological bladder.

As shown in Table 4, early neonatal mortality was reported in 41% and late neonatal mortality in 12%.

Different causes of death were retained in neonatology (Table 4).

Table 4. Neonatal deaths

Classifications	Percentage
Survival time	
<24 hours	41
1-7 days	47
8-28 days	12
Causes of death	
Respiratory causes	31
Palliative cares	18
Heart disease	9
Neuromuscular diseases	9
Sudden death	6
Hereditary metabolic disease	6
Others	21

In our series, the external examination of the face was normal in only 24% of newborns. External examination of the trunk was pathological in 50% of cases. External examination of the limbs and extremities was normal in 62% of newborns. 15% of newborns presented an abnormality of the external genitalia. Impermeability of the orifices was only noted in four cases (15%).

The concordance between the fetopathological and neonatological diagnosis was as follows:

- Group A: Total concordance observed in nine cases (27%).
- Group B: Partial concordance noted in 14 cases (40%).
- Group C: Total discordance observed in nine cases (27%).
- Group D: No pathological element or malformation observed in two cases (6%).

Discussion

This is the first study carried out in Tunisia which emphasizes the importance of fetopathological examination in neonatal deaths and the need for collaboration between the different stakeholders: gynecologists, neonatologists and fetopathologists.

According to previous studies, the increase in neonatal deaths was linked to a mother's age greater than 35 years, due to the increased risk of congenital malformations and lethal chromosomal aberrations responsible for neonatal deaths [4, 5].

As antecedents, high blood pressure constituted a major risk factor in neonatal and maternal mortality. This maternal pathology can be responsible for perinatal asphyxia, prematurity, hypotrophy and intrauterine growth retardation. This was in concordance with the study of Chahid et al, at the Souissi maternity ward in Rabat, which concluded that perinatal asphyxia, prematurity, hypotrophy, mortality and perinatal morbidity were more significant in hypertensive mothers with a statistically significant difference [6].

Most women with a history of abortion, neonatal death, miscarriage or in utero fetal death in previous pregnancies had a higher risk of neonatal mortality, which was described in the Algerian study of Noria [7].

In our study, consanguinity was present in 38% of cases. Consanguinity represented a very important risk factor in the occurrence of congenital malformations and even neonatal deaths, especially in developing countries according to Noria [7].

In addition, inbreeding would lead to an increase in the frequency of stillbirths, neonatal mortality and congenital malformations. The influence of genetic factors on perinatal mortality was evident by the close correlation that existed between the rate of mortality and consanguineous marriages according to a study carried out in Canada by Boisvert [8].

Certain drugs have been teratogenic [9] but in our study, we did not find any teratogenic drugs intake by mothers during pregnancy.

In this current study, 12% of women developed gestational diabetes during their pregnancies, 6% of them were on a diet and 6% on insulin. Each of these women gave birth to newborns carrying congenital malformations such as laryngeal stenosis, buccopharyngeal teratoma, chromosomal aberration and renal malformations. These results were almost similar to those found in the literature [10-14].

We noted that 9% of women presented a pre-eclampsia. Pre-eclampsia or pregnancy toxemia could be responsible for several fetal anomalies that could be implicated in neonatal deaths. This pathology presented the cause of prematurity and intrauterine growth retardation in 26% of cases according to the study of Odegard et al [15]. Neutropenia has often been noted in newborns born to toxemic mothers constituting a risk factor in the occurrence of neonatal infections, especially nosocomial infections and the hyaline membrane disease [16-18].

In our series, oligohydramnios was observed in 36% of cases and it was linked each time to a congenital anomaly responsible for the death, thus being in correlation with the literature [19,20].

In our study, we noted an Apgar score lower than seven in 62% of cases, including 41% lower than three. In the literature, a low Apgar score of less than seven at five minutes was a predictive factor of neonatal mortality. In the study of Casey, the risk of neonatal death among newborns with an Apgar score lower than three is eight times greater than among those with an Apgar score higher than seven [21].

The analytic part of our study demonstrated a concordance between the fetopathological and neonatological diagnosis, total or partial, in 67% of cases. In 27% of cases the fetopathological examination corrected the neonatological diagnosis. In only 6% of cases, it did not show anomalies or malformations, which was consistent with literature data [1, 2, 22].

In sudden deaths of newborns, the gold standard of exploration remains the fetopathological examination

given its multiple advantages. Indeed, this examination most often allows to determine the cause of death, providing the answer sought by the medical team as well as by the parents [23]. It also allows to avoid the occurrence of new cases of sudden death later by detecting hereditary pathologies or genetic malformations, by providing the genetic counseling to the parents by the medical team [24,25].

For congenital metabolic diseases, the interest of the fetopathological examination lies in its ability to guide the diagnosis by reducing the field of research given the great diversity of hereditary diseases. In our case, this examination allowed to guide the geneticists in their research by providing diagnostic elements in favor of glutaric aciduria type II. Thus, the medical teams can bring their advice to the family by planning subsequent pregnancies.

In cases following a medical termination of pregnancy (without feticide), the fetopathological examination provides additional information that can help us in the management of subsequent pregnancies. In our series, fetopathology provided additional information in four cases and corrected the antenatal diagnosis in one case. This demonstrates the usefulness of this examination, because it allows to better detect certain anomalies and to provide advices to parents in order to avoid the recurrence of this type of anomalies in the future. Unfortunately, this contribution has not been noted in the literature [26].

Perinatal mortality remains a public health problem in Tunisia and multitude of causes and risk factors were studied by Ben Hamida Nouaili et al [27]. To learn more about causes of neonatal deaths, a complete fetopathological examination is indicated to establish the diagnosis of malformative anomalies that could explain neonatal death and guide the management of later pregnancies.

That's why we should encourage the practice of fetopathological examination in neonatal deaths and explain to parents its usefulness so that they can grieve and take precautions in future pregnancies.

Conclusion

To conclude, we can emphasize the usefulness of the fetopathological examination and its contribution in determining the cause of neonatal deaths. This examination allows to establish an exhaustive diagnosis essential for the management of later pregnancies by perfecting genetic counseling, and to provide psychological comfort to the family and the medical team.

Abbreviation
CMNT : Center of Maternity and Neonatology of Tunis
PAH : Pulmonary Arterial Hypertension

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