

A Comparison Between Clinical Diagnosis of Death and Autopsy Diagnosis. A Retrospective Study of 131 Newborns, Stillborns and Aborted Fetuses

Mariana COSTACHE^{a,b}; Monica CIRSTOIU^c; Andreea CONTOLenco^b;
Anca Mihaela LAZAROIU^{a,b}; Simion GEORGE^b; Maria SAJIN^{a,b};
Oana Maria PATRASCU^b

^aDepartment of Pathology, "Carol Davila" University of Medicine and Pharmacy,
Bucharest, Romania

^bDepartment of Pathology, Emergency University Hospital, Bucharest, Romania

^cDepartment of Obstetrics-Gynecology III, Emergency University Hospital, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

ABSTRACT

In recent years, the autopsy was considered necessary only in medico-legal cases, or when the clinician requires it to better understand the pathology and cause of death (with the deceased family's consent). Although it has been shown in numerous studies that the autopsy and the postmortem histopathological examination are the only ones that can diagnose correctly and completely, the autopsy rate is declining. The primary motive of the family in consenting to a perinatal necropsy, may be to determine the cause of death of their child and to be aware of possible complications of their future pregnancy. This study shows the rate of concordance between clinical diagnosis and autopsy diagnosis, and the rate of concordance between macroscopic diagnosis and microscopic findings, pointing out once again the importance and the utility of the autopsy in medical practice.

Keywords: autopsy, clinical diagnosis, newborn, stillborn, dead fetuses, diagnostic study

Address for correspondence:

Mariana Costache, Department of Pathology, "Carol Davila" University of Medicine and Pharmacy, 8 Eroilor Sanitari Avenue, 5th District, Bucharest, Romania.

E-mail: m_costache_dermatopat@yahoo.com

Article received on the 25th of May 2014. Article accepted on the 23rd of June 2014.

INTRODUCTION

The autopsy, more correctly called necropsy, is a sequel and a completion of the study of disease after death. It consists of an examination of the corpses to determine the cause of death based on lesions found, in collaboration with clinical, radiological and laboratory data (1).

Until the 1960's, the autopsy was crucial for understanding and characterization of the disease, and it was the center of medical research. Medical doctors considered that it is important to recognize the differences between clinic diagnosis and autopsy diagnosis, to improve knowledge (2). In recent decades, the rate of the autopsies declines on account of the progress in disease diagnosis; also, the clinicians have avoided the autopsy due to possible medico-legal consequences (3); sometimes, the deceased's family opposes to autopsy (4).

Even after a great effort, in one third of cases, the clinicians can not find the cause of death (5). At the necropsy, the pathologist reports aspects that help diagnose the cause of death and associated pathologies. This allows to correctly inform the family about their misfortune and to evaluate the probability of a risk pregnancy's recurrence (6). Also, a correct diagnostic is significant for mortality statistics, which remain essential for public health.

The approach of fetal or perinatal autopsy is different from the approach of adult autopsy. Maternal health influences fetal development. The diseases and conditions considered in adults are different in the fetus. Genetic syndromes must be identified if present (7).

In the last twenty years high-quality anatomical information of all body structures, especially about the central nervous system of fetuses and neonates can be seen on postmortem MRI. This is less invasive and is more acceptable than necropsy to some parents and some religious groups (8-10).

Based on this background, we felt it is important to examine the discrepancies between the provisional clinical diagnosis of death and the necropsy findings, and to assess the value of necropsy and postmortem histology. Also, research of the bibliography showed that up to this moment, no studies such as this have been performed in Romania. □

MATERIAL AND METHODS

This retrospective study examined data from consecutive autopsies performed in the Department of Pathology, at the University Emergency Hospital Bucharest over one year period, from July 2012 to July 2013. Medical records were provided by the same hospital. Data were typed into a personal database and were processed with Microsoft Office Excel 2010 program.

The cases were divided into two categories. First category is represented by stillborns and dead fetuses, and second category, by dead newborns. We define a dead fetus as a fetus without signs of life, to which death occurred before the twenty-fourth week of pregnancy. A stillborn is a fetus that died at any time after the twenty two week of pregnancy, or birthweight >500 g if the gestational age was unknown (11). A dead newborn is a newborn without signs of life and to which death occurred in the first year of life.

Regarding stillborns and dead fetuses, the data collected was divided into: demographic (mother's age, residence, gestational age), associated pathologies and frequent histopathological findings. Information regarding the newborns was also divided into: demographic (mother's age, residence, newborn's age), associated pathologies, cause of death and histopathological findings.

The concordance between clinical diagnosis of death and the diagnosis established after performing the autopsy was classified as: total, representing the concordance in most diagnoses; partial, maximum two diagnoses correlated; without concordance, when no clinical diagnosis correlated with autopsy diagnosis. Same classification was applied to the correlation of macroscopic and microscopic diagnoses.

Research of bibliography and search conducted on the Internet using keywords "stillborn autopsy", "newborn autopsy", "cause of death, autopsy, clinical diagnosis" showed that up to this moment, no studies such as this have been performed in Romania. □

RESULTS

Stillborns and dead fetuses

The descriptive analysis of the stillborns and dead fetuses showed that 52.29% of the cases were requested induced abortions and 47.71%

of the cases were therapeutic or spontaneous abortions. Most women who have had a requested induced abortion were aged between 20-30 years in 43.86% of the cases and 30-40 years in 42.11%. Decades two and five were found with a frequency of 10.53%, respectively 3.51%. Most cases were from urban areas (57.89%); 42.11% from rural areas.

Therapeutic or spontaneous abortions have been performed on women with ages between 30-40 years (46.15%) and 20-30 years (40.38%). In 7.69% and 5.77% of the cases, women were 10-20 years old, respectively 40-50 years old. Most women (65.38%) were from urban zone and 34.62%, from rural zone. The average gestational age of stillborn and dead fetuses was 20-30 weeks in 50% of the cases. In 29.92% gestational age was 10-20 weeks and in 23.08%, 30-40 weeks.

Most commonly associated pathological findings were: fetal (98.07%), maternal (34.61%) and placental (19.23%). There were 2 cases without clinical diagnosis, and in another 7 cases the clinical diagnosis was metrorrhagia.

Maternal associated pathological findings were uterine (11.90%), such as cicatricial uterus; cardiovascular (9.52%): hemophilia, aortic insufficiency with cardiac insufficiency, tricuspid atresia, preeclampsia; renal (2.38%): chronic renal insufficiency with hemodialysis. Other maternal pathological aspects were found in 21.43%: antiphospholipid syndrome, ulcerative colitis, abortive disease (Table 1).

Placental associated pathological aspects were vascular (5.88%): infarction, placental hematoma; placenta praevia (3.92%); oligohydramnios (3.92%); other aspects (5.88%), such as: calcified placenta, chorioamnionitis, polyhydramnios (Table 2).

We classified fetal associated pathological findings in: pulmonary atelectasis (96.08%), meningo-cerebral hemorrhage (64.71%), malformations (27.45%), Down Syndrome (11.76%) and other genetic syndromes (3.92%), such as Williams Syndrome, Trisomy 18, Patau Syndrome. Among the malformation, we mention: neurological malformation in 17.65% of cases (anencephaly, holoprosencephaly, lissencephaly, bifid spine, mielomeningocele), renal malformations 11.76% (horseshoe kidney, uni and bilateral renal agenesis, renal hypoplasia, polycystic kidney), digestive malformations 9.8% (omphalocele, imperforate anus, pyloric stenosis, gastroschisis) and other malformation 11.76% (palatoschisis, upper limb amelia, mi-

crognathia) (Table 2).

At histopathological examination we found as most frequent aspects: pulmonary atelectasis (88.46%), meningo-cerebral hemorrhage (50%), cerebral edema (40.38%), hepatic stasis (30.77%), renal stasis (28.85%), placental infarction (19.23%), chorioamnionitis (13.46%), placental hypoxia (9.62%) and pulmonary hemorrhage (5.77%).

Regarding the concordance between the cause of death established by the clinician and the cause of death established by the pathologist, in 75.68% of the cases there was a total concordance and 24.32 % partial correlated. There was no case of total discordance (Figure 2). The correlation between postmortem macroscopic diagnosis and histopathological diagnosis highlighted a percentage of 96.08% in the group of total concordance and 3.92% in the group of partial concordance.

Most frequent missed or misdiagnosed pathologies by the clinicians in case of stillborn and dead fetuses were malformations (11.64%).

Newborns

There were 22 cases of newborns: 50% were younger than a month, 36.36% were with ages between one and two months, and 16.64% were older than two months. Most cases were from urban areas (81.82%) and only 18.18%, from rural areas.

Most of the deaths were caused by neurological (100%), pulmonary (77.27%), cardiac (44.55%) and other causes (13.64%) (Figure 1). Meningo-cerebral hemorrhage (90.9% of neurological causes), hydrocephalus (9.09%), cerebral edema (9.09%) and cerebral abscess (4.54%) were established as neurological causes of death. Pulmonary causes found were pulmonary hemorrhage (82.35%), hyaline membrane disease (11.76%) and bronchopneumonia (5.88%). There was only one newborn in our study who died as a result of cardiac pathology: transposition of the great arteries.

Uterine (11.9%)	Cardiovascular (9.52%)	Renal (2.8%)	Other (21.43%)
- cicatricial uterus	- hemophilia - aortic insufficiency - tricuspid atresia - preeclampsia	- chronic renal insufficiency	- antiphospholipid syndrome - ulcerative colitis - abortive disease

TABLE 1. Maternal associated pathological findings in stillborns and dead fetuses.

Fetal	Pulmonary atelectasis		96.08%
	Meningo-cerebral hemorrhage		64.71%
	Malformations	neurological malformation (anencephaly, holoprosencephaly, lissencephaly, bifid spine, mielomeningocele)	17.65%
		renal malformations (horseshoe kidney, uni- and bilateral renal agenesis, renal hypoplasia, polycystic kidney)	11.76%
		digestive malformations (omphalocele, imperforate anus, pyloric stenosis, gastroschisis)	9.8%
		other malformation (palatoschisis, upper limb amelia, micrognathia)	11.76%
	Down Syndrome		11.76%
	Other genetic syndromes (Williams Syndrome, Trisomy 18, Patau Syndrome)		3.92%
Placental	Vascular (infarction, placental hematoma)		5.88%
	Placenta Praevia		3.92%
	Oligohydramnios		3.92%
	Others (calcified placenta, chorioamnionitis, polyhydramnios)		5.88%

TABLE 2. Fetal and placental associated pathological findings in stillborns and dead fetuses.

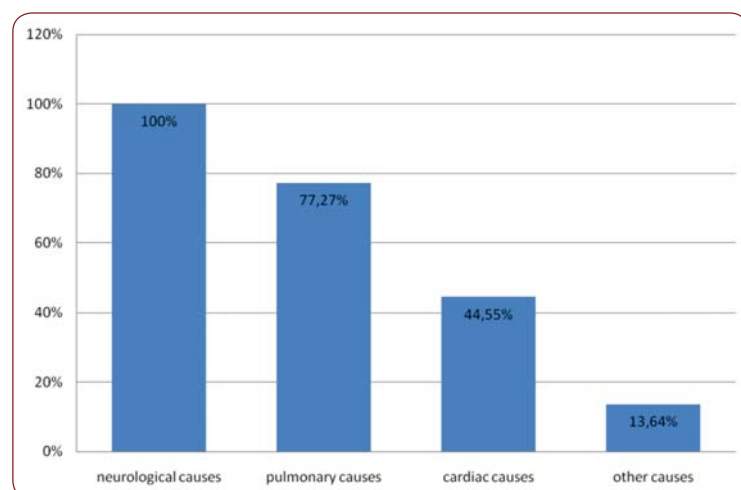


FIGURE 1. Most frequent causes of death in newborns.

Complications determined by generalized fetal edema were another cause of death (13.64%) (Table 3).

The majority of cases presented associated pathologies (linked or not linked to the pathology that caused death), such as neurological pathology (100%), pulmonary pathology (90.91%), prematurity (90.91%), infectious pathology (72.73%), perinatal hypoxia (59.09%), digestive pathology (22.73%), cardiovascular pathology (13.64%), renal pathology (4.55%) and others (4.55%).

At the histopathological examination, most frequent findings were meningo-cerebral hemorrhage (86.36%), pulmonary hemorrhage (77.27%) and hepatic stasis (77.27%). Other histopathological aspects were: renal stasis (68.18%), cerebral edema (40.91%), bronchopneumonia (13.64%) and pneumonia (9.09%).

Regarding the concordance between the cause of death established by the clinician and

the cause of death established by the pathologist, in 52.38% of the cases there was a total concordance and 47.62 % correlated partial. There was no case of total discordance (Figure 2). The correlation between postmortem macroscopic diagnosis and histopathological diagnosis highlighted a percentage of 87.71% in the group of total concordance and 14.29% in the group of partial concordance.

Most frequent missed or misdiagnosed pathologies by the clinicians in case of newborns were digestive pathologies in 27.27% of the cases, pulmonary (27.27%), cardiovascular (18.18%), renal pathologies (9.09%), generalized fetal edema (9.09%), hemorrhagic syndrome (9.09%).

DISCUSSIONS

According to the World Health Organization, Romania had the highest abortion rate in Europe in 2012: more than twice the EU average (11). In our study the percentage of requested induced abortions was 52.25%, higher than the percentage of therapeutic and spontaneous abortions. The abortion rate could be influenced by socio-economic factors (a low financial status), a lack of partner responsibilities in couple (children are mother's responsibility, father has a symbolic financial role), age (too young or too old), lack of desire in having children (12).

Stillbirths are one of the most common adverse pregnancy outcomes despite the intensification of obstetric surveillance. The causes of stillbirth are represented by pathophysiologic processes encountered in the mother, fetus and placenta (13-15). In a retrospective study of

stillbirths' deaths, there was complete concordance between clinical diagnoses and autopsy findings in 76%, partial agreement in 13% of necropsies, and in 11% of cases there was no correlation between diagnoses. In a second study, the concordance rate between clinical and pathological diagnoses was 56% and the discordance rate, 21%. As one would expect, in our study the necropsy showed less extra information about stillborns and dead fetuses than dead newborns. This fact is determined by a considerable number of antepartum deaths with signs of pulmonary atelectasis (96.08%) and meningo-cerebral hemorrhage (64.71%). Our results are comparable with the results obtained in other studies: total concordance between clinical and pathological diagnoses at stillborns and dead fetuses is 75.68%.

The number of deaths due to congenital abnormalities has increased (6). The accurate diagnosis of these disorders is relevant for parents to evaluate the probability of a risk pregnancy's recurrence. In this study in 11.54% of cases of stillborns and dead fetuses, the clinician missed or misdiagnosed the malformations. However, some of the congenital anomalies would have been difficult to pick up. The necropsy was clearly an essential investigation in these cases.

An author recommended in his study that histopathological examination should not be made on all cases, because it adds little information to the one obtained from gross examination (especially, when the fetus was normal). In our study, total concordance between gross and microscopic examination was 96.08% and partial in 3.92% of cases. These results sustain the idea that in some cases gross examination is enough to put a correct diagnostic.

On the dead newborns, total concordance between the clinical and pathological diagnoses occurred less often than it did among stillborns and dead fetuses: 52.38%. In retrospective analysis, some of the pathologies that have been missed or misdiagnosed could have been diagnosed during life (16, 17). Most frequent missed pathologies by the clinicians regarding the newborns were digestive pathologies in 27.27% of cases, pulmonary (27.27%), cardiovascular (18.18%), renal pathologies (9.09%), feto-placental anasarca (9.09%), hemorrhagic syndrome (9.09%). Bronchopneumonia was missed by the clinicians in all cases. Histopathological examination completed the diagnostic established at the gross examination in 14.29% of cases. $\square$

Neurological causes	Pulmonary causes	Cardiac causes	Other causes
- meningo-cerebral hemorrhage (90.9%)	- hemorrhage (82.35%)	- transposition of the great arteries (4.55%)	- anasarca (13.65%)
- hydrocephalus (9.09%)	- hyaline membrane disease (11.76%)		
- cerebral edema (9.09%)	- broncho-pneumonia (5.88%)		
- cerebral abscess (4.54%)			

TABLE 3. Causes of death in newborns.

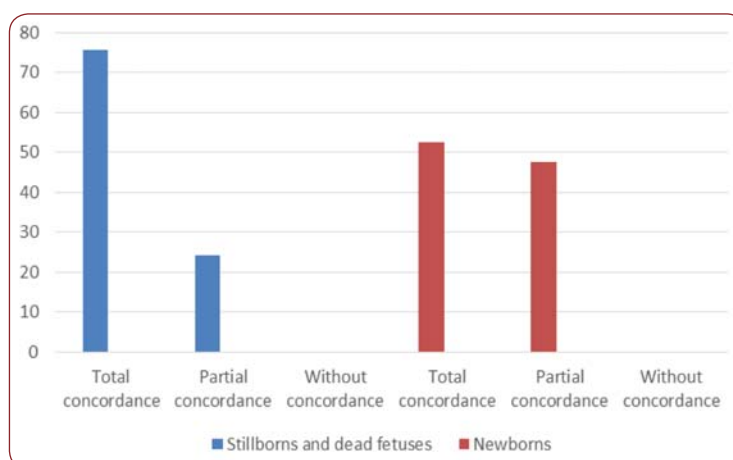


FIGURE 2. The concordance between clinical diagnosis and autopsy diagnosis in stillborns, dead fetuses and newborns.

CONCLUSIONS

This study has shown that necropsy and post-mortem examination had completed or had changed clinician's diagnoses in an important proportion, showing that these procedures are useful to determine the correct cause and contributing factors of stillborn, fetuses and newborn deaths. The obtained data will contribute to the understanding and prevention of these deaths. Necropsy and histological examinations are also useful in providing information that may be relevant for a future pregnancy. Also, a correct diagnostic is significant for mortality statistics, which remain essential for public health.

We encourage clinicians to consider the necropsy an important tool that extends the understanding of pathologies.

Conflict of interests: none declared.

Financial support: none declared.

REFERENCES

1. **Leibovici M** – Necropsia si semiologia anatomo-clinica, Ed. Medicala, Bucuresti, 1967; 11-14
2. **Hill RB, Anderson RE** – The autopsy – medical practice and public policy, Stoneham, MA, Butterworth Publishers, 1988
3. **Spiliopoulou C, Papadodima S, Kotakidis N, et al.** – Clinical diagnoses and autopsy findings: a retrospective analysis of 252 cases in Greece. *Arch Pathol Lab Med* 2005; 129:210-214
4. **Combes A, Mokhtari M, Couverlard A, et al.** – Clinical and autopsy diagnoses in the Intensive Care Unit. *Arch Intern Med.* 2004; 164:389-392
5. **Label RR** – Pregnancy loss and unsanctioned grief: the nature and consoling of unacknowledges loss, Springfield, IL, 1990
6. **Gordijn JS, Erwich HMJJ, Khong YT** – Value of the perinatal autopsy: critique. *Pediatr Dev Pathol* 2002; 5:480-488
7. **Porter HJ, Keeling JW** – Value of perinatal necropsy examination. *J Clin Pathol.* 1987; 40:180-184
8. **Thayyil S, Sebire JN, Chitty SL, et al.** – Post mortem magnetic resonance imaging in the fetus, infant and child: A comparative study with conventional autopsy (MaRIAS Protocol). *BMC Pediatr* 2011; 11:120
9. **Griffiths DP, Paley JNM, Whitby HE** – Post-mortem MRI as an adjunct to fetal or neonatal autopsy. *Lancet* 2005; 365:1271-73
10. **Whitby HE, Paley NM, Cohen M, et al.** – Postmortem MR imaging of the fetus: An adjunct or a replacement for conventional autopsy? *Semin Fetal Neonatal Med* 2005; 10:475-483
11. World Health Organization Regional Office for Europe, Jan. 2012 Europe health for all database (HFA-DB), World Health Organization Regional Office in Europe on line, (<http://data.euro.who.int/hfad/>)
12. **Nguyen RH, Wilcox AJ** – Terms in reproductive and perinatal epidemiology. *J Epidemiol Community Health* 2005; 59:1019-1021
13. **Mueller RF, Sybert VP, Johnson J, et al.** – Evaluation of a protocol for postmortem examination of stillbirths, *New Engl J Med.* 1983; 309:586-590
14. **Goldenberg RL, Kirby R, Culhane JF** – Stillbirth: a review. *J Matern Fetal Neonatal Med.* 2004; 16:79-94
15. **Vergani P, Cozzolino S, Pozzi E, et al.** – Identifying the causes of stillbirth: a comparison of four classification systems. *Am J Obstet Gynecol.* 2008; 199:319.e1-4
16. **Gau G** – Is the perinatal necropsy really necessary? *Arch Dis Child.* 1983; 58:649-650
17. **Korteweg FJ, Gordijn JS, Timmer A, et al.** – A placental cause of intrauterine fetal death depends on the perinatal mortality classification system used. *Placenta.* 2008; 29:71-80.

