

COMPARATIVE STUDY BETWEEN SPANISH FLU PANDEMIC AND COVID-19 PANDEMIC AS RECORDED IN THE ARCHIVES OF THE “MINA MINOVICI” NATIONAL INSTITUTE OF LEGAL MEDICINE IN BUCHAREST

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BACKGROUND

In January 2021 nearly 2 million deaths have been reported over the world because of SARS-CoV-2, caused by severe acute respiratory syndrome due to SARS-CoV-2. COVID-19 pandemic is now a reality and humanity is searching and fighting for valid solutions. COVID-19 pandemic is 7th influenza A respiratory virus world spread disease and the 6th influenza A pandemics within the last 130 years [1-3]. Chronologically the first respiratory virus flu is the “Russian” pandemic flu in 1889-1891 (1 million mortality, H3 virus), the “Spanish flu” pandemics from February 1918 - April 1920 with all its 4 epidemiological waves (infecting 1/3 of the world's population, 20-50 million mortality, H1N1 virus), Asiatic flu pandemic in 1957-1958 (H2N2 virus) [4], Hong Kong pandemic flu 1968-1969 (1 million mortality, H3N2 virus) [4], aviary flu 1997-2007 names SARS-severe acute respiratory syndrome- (from birds to humans, but not human to human, especially in 2002-2004, infecting 8098 people, 774 mortality, H5N1 virus) [4-6], Mexico porcine flu pandemic 2009 (infecting 42-86 million, 8250-17.620 mortality, novel H1N1 virus [5, 6], COVID-19 pandemic (infecting 126.852.304, mortality 2.782.188 [7], SARS-CoV-2 virus); flu pandemics are determined by subtypes of A virus which resorts their genome with animal reservoir [4]. A comparison between the “Spanish flu” pandemic and the COVID-19 pandemic as recorded by the National Institute of Legal Medicine in Bucharest is proposed.

The Bucharest's Morgue and the Institute of Legal Medicine prof. Mina Minovici: a brief history of the Institute and of its archive

In 1890 Mina Minovici (1858-1933), recently

licensed in Pharmacy and Medicine in Bucharest, Romania, fulfil in 1888 in Paris his Ph.D. under the coordination of Professor Paul Brouardel. Upon his return, he looks to meet gen. Carol Davila (Carlo Antonio Francesco d'Avila) the official person entitled at that time to organize the medical and sanitary system in the country and of medical teaching.

A recent doctor in medical science Mina Minovici asks permission to build the Morgue of Bucharest explaining the social need for such an institution. It was then the time when talented natives after an abroad academic enlightening, always returned home to support the national development. Gen. Carol Davila supported dr. Mina Minovici idea and recommended him to the Mayor of Bucharest and the Ministry of Justice.

The Mayor of Bucharest, Emanoil Pache Protopopescu (1845-1893), was at that time the unique person who in his 3 years mandate (1888-1891) succeeded to modernize the city of Bucharest (building both cardinal axes with large boulevards, 28 schools, a night asylum, public electric lightning, paving all major streets with granite stone and the tramway as public transportation).

He then, entrust Mina Minovici because of his boldness and determination and will allocate a public plot for the City Morgue. In near 2 years, 1890-1892, with public financial aid from the Bucharest City (63%) and the Ministry of Justice (37%), the “City Morgue of Bucharest” is raised up under the plans of a Romanian famous architect, Hristea Cerchez (Fig. 1) and 20th December became its founding day.

In 1892 Mina Minovici was appointed Director of the Morgue until his death, 40 years later in 1933 (Fig. 2). In 1896 he become a professor of legal medicine at

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the Faculty of Law at the University of Bucharest and begins his institutional reform of legal medicine in Romania: he will rename in 1897 the Morgue as the first Institute of Legal Medicine (worldrecordacademy.org) able to take over on a public base all the justice requests and to perform training of specialists in legal medicine (forensic pathologists) which will gain officially an occupational standard ever since. In 1899 he is appointed full professor of legal medicine at the Faculty of Medicine of the University of Pharmacy and Medicine Carol Davila (founded in 1856 by gen. Carol Davila). A royal decree will rename the Institute in 1930 as "Institute of Legal Medicine professor M. Minovici" to honour him.



In 1989 a new building is raised after the demolition of the historical building and in 2000 the first specific legislation emerged, and the Institute renamed as today, the National Institute of Legal Medicine Mina Minovici (Fig. 3). The National Institute succeeded to keep up its archives mostly intact since the foundation. The present study is based on its old archives and necropsy files documenting the "Spanish flu" period time, 1918-1920, and nevertheless its modern archives from 2020 documenting the COVID-19 pandemic.



Some clinical and gross pathological historical records about the Spanish flu

Some historical reports on Spanish Flu symptoms and pathology findings that we could find access observe general weakness, cough, fever, shivering, headaches. Generally, they disappeared in up to 5-10 days. Other symptoms are bloodshot eyes, nose bleeds, dry tongue, or deafness. Fever reaches up to 39-40 degrees, though some who do not get high-temperature symptoms can continue their normal activities. Those with high fever experienced a worse condition as the throat inflammation goes deeper to the bronchial branches causing pneumonia when it reaches the alveoli. Some experienced high fever at first, they got better for a few days, but the fever returned

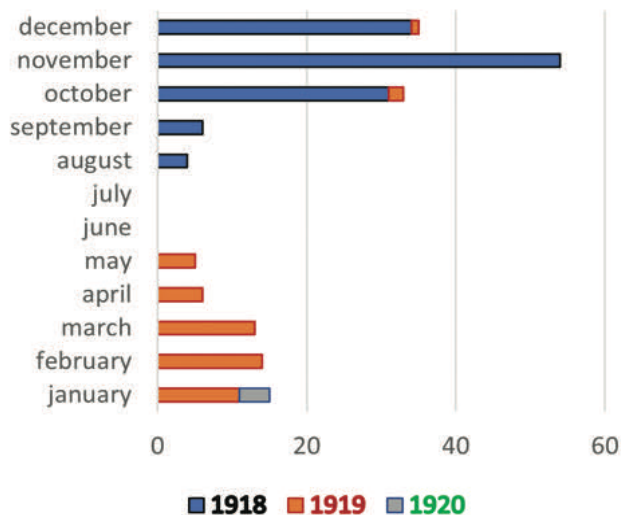
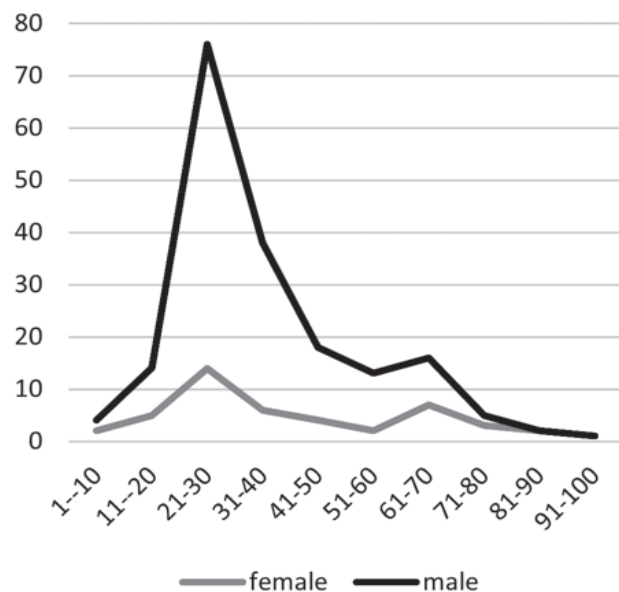
indicating conditions like pneumonia which ends after 3-10 days but also causes death (Dimitrije Antic cited by 8).

Relating about Spanish flu pandemics in 1919 in the Hospital the Journal of medical students [9], Victor Babes (1854-1926, author with VA Cornil of the first bacteriology treatise in time, 1885 [10] and author of passive immunity concept and antibiosis) describes a large diversity of clinical cases. He notes symptoms such as shiver, fever 39-40, accelerated pulse, frontal headache, leukopenia, cough, bronchitis. In 2-3 daytime the fever decreases with sweats and getting-over. In some other cases, usually young women, high fever, tiredness, pulmonary infiltrates, pleurisy, and enlarged spleen followed usually by death due to asphyxia because of haemorrhage and abundant fluid tracheal secretion. Myocarditis was rarely noticed compared to the common flu. Victor Babes expresses that he failed to find Pfeiffer bacillus in Spanish flu samples cases: additionally, he finds Pfeiffer bacillus in other diseases also and concludes not to be specific for flu or Spanish flu whatsoever. He then reckons, "What may be the biological agent of Spanish flu?". He notices a high rate of bacterial heterogeneity in flu pneumonia, and he adds two more bacilli frequently observed in severe sepsis cases (i.e., not specific) he named "Bacillus transparent septicus" and Bacillus lanceolatus septicus". He noticed an abundant mucosal secretion in alveoli and small bronchi with asphyxia as a death mechanism. He finally considers that in some cases there is a unique aetiology however in many other a multiple aetiology.

Old archives of the National Institute of Legal Medicine Mina Minovici Bucharest: a study on Spanish flu death

Statistics. In the old archives of the National Institute of Legal Medicine Mina Minovici from Bucharest, we found 185 forensic autopsies between 1918-1920 recognizing Spanish flu infection as a cause of death, Fig. 1 (the Institute was the only one to perform autopsies in Bucharest region (capital of Romania), nearly 2000/year, similar as in present time).

Following the analysis of those 185 necropsy files, we found a male: female ratio, 1.9:1 (84: 45), (Fig. 2) aged 1-95 years the majority without recorded flu symptoms before death. We noted a heterogeneity of death circumstances (Table 1). Most of the autopsy files have not a full report. Some files have a brief description of the history of the case and that of necropsy findings. All medico-legal cases have an order basis issued by a law enforcement force (police or prosecutor).

Annual distribution of Spanish flu deaths (medico-legal cases) in Bucharest**Male/ female distribution "Spanish" Flu****Figure 1.** Spanish flu deaths: annual case distribution (medico-legal cases).**Figure 2.** Spanish flu deaths: male/female ratio (medico-legal cases).**Table 1.** Death circumstances – Spanish flu deaths. Necroptic findings in the old archives of the NILM MM

Spanish flu at soldiers 36,2 %: prisoners 22,3% (Germans, Russians, Italians, Hungarians)
Spanish flu with symptoms - 8,1%; with no symptoms or no symptoms documented 91,8%. Symptoms: high fever (40° Celsius), shiver, articular pains, thoracic pain, nausea, headache, muscular cramps.
Spanish flu and typhoid fever suspicion 1,08%
Spanish flu with sudden death – other causes than Spanish flu 16,2 %
Spanish flu while working accidents 0,5%
Spanish flu and intoxication suspicion 0,5% v
Spanish flu and suspect to be violent death -confirmed Spanish flu 3,7 %
Spanish flu and death in custody (asylum) – confirmed Spanish flu 3,7 %
Spanish flu and unknown identity bodies 6 %
Spanish flu and others (comorbidities, no next of kin, no medical documents, etc.) 24,02 %

Table 2. Spanish flu necropsy findings in the old archives of the NILM MM

Necropsy findings in Spanish flu cases: old archives of the “Mina Minovici” National Institute of Legal Medicine Bucharest	
Brain	Cerebral edema (frequent). Bronchopneumonia is associated with hemorrhagic foci (frequent). Lobular pneumonia - red hepatization stage (more frequently in the lower lung lobes). Multiple lung infarctions. Multiple pleural adhesions.
Lungs	Pleural effusion. Marked pulmonary stasis. Lung edema. Some patients had calcified granulomas or TB cavities. Diffuse pulmonary sclerosis
Heart and main vessels	Cardiomegaly. Myocarditis. Acute aortitis. Chronic aortitis (with aneurysmal dilatation), Advanced aortic atherosclerosis
Liver	Fatty liver dystrophy and hepatomegaly (frequent in young adults). Passive congestion of the liver. Cirrhosis. Hydatid cysts (extremely rare)
Spleen	Splenomegaly (up to 800 grams). Hemorrhagic infarction.
Kidney	Renal stasis. Nephritis. Advanced renal sclerosis in the elderly.
Skin	Purple-colored spots (some cases)

Death circumstances. Several death circumstances have been observed. A lack of flu-specific symptoms creates a suspect case scenario or a sudden death scenario in most of the cases. It was the period of World I War and some very contagious infectious

diseases such as typhoid fever.

Necropsy findings in Spanish flu cases. The most frequent necropsy findings that we noticed in the old archive of the institute are listed in Table 2.

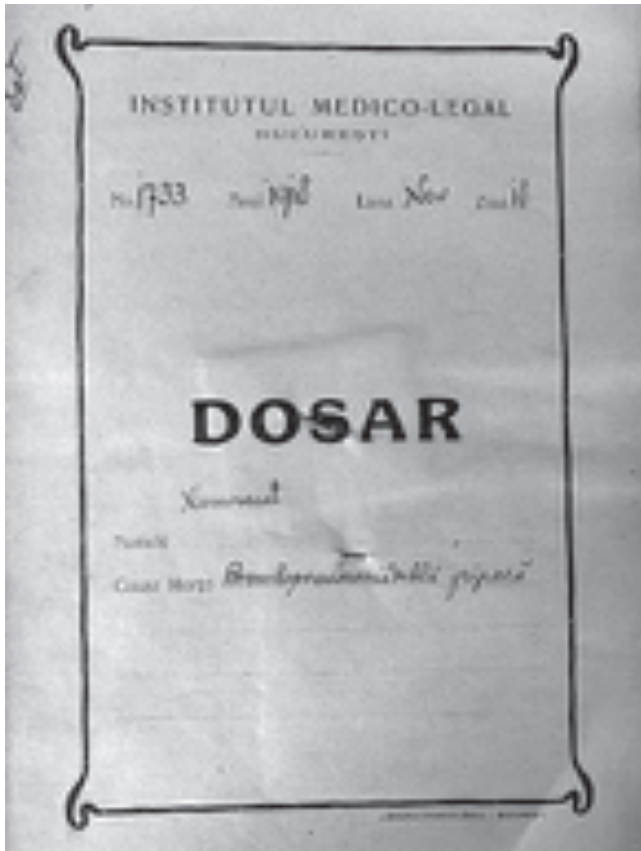


Figure 3. A cover of an autopsy report from 1918: we may notice the case number, date, and head for the name. At the bottom of the page is the cause of death.



Figure 4. The bodies with unknown identities were photographed, and the black and white photographs were attached to the autopsy report and inscribed with the case number and the date of the autopsy. Sometimes ocular prostheses were used for a better physiognomy result.

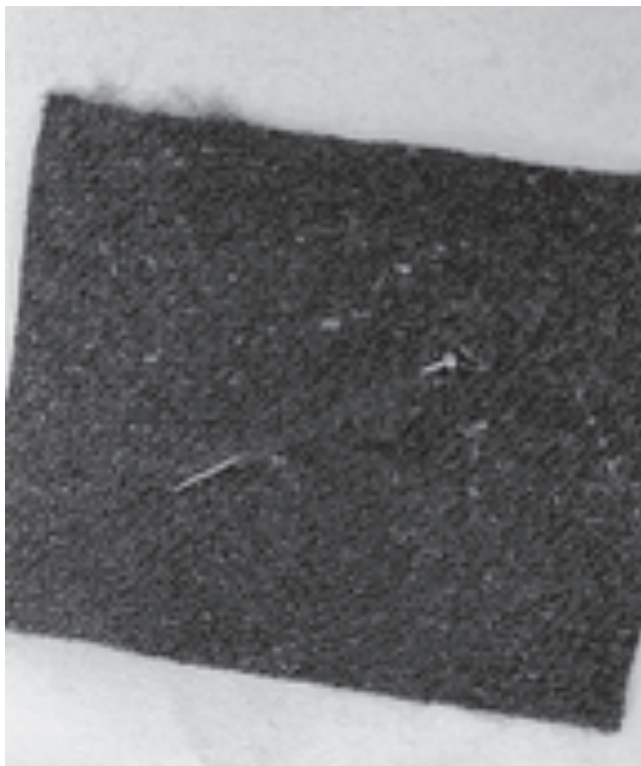


Figure 5. Piece of textile material from the body clothing.

Short case presentations of Spanish flu death from the old archives of the National Institute of Legal Medicine Mina Minovici from Bucharest

Case 1

In the first case, the forensic autopsy was performed to identify the body of a man aged 60-70, who died in hospital.

In the autopsy report (Fig. 3), we found: a black and white photograph of the corpse (Fig. 4), a piece of textile material from the man's clothes (Fig. 5), as well as the description of the particular signs (Fig. 6).

On the cover of the autopsy report is the cause of death: "Double flu bronchopneumonia" (Fig.3).

Case 2

24-year-old male, whose sudden death happened while traveling by train in November 1918. An acute medication poisoning was suspected.

Autopsy findings: both lungs showed significant edema. Predominantly in the right upper and left inferior lobe, numerous foci of hemorrhage and bronchopneumonia, calcified granulomas

INSTITUTUL MEDICO-LEGAL

Nr. 1733

Numele Prenumele *Necunoscut*

Mort la *Spit Calautine*

Starea civilă

Etatea *60. 70 ani*

Părinți

Profesia *lucrat ?*

Mort în ziua de *15/12 Nov. 918*

Naționalitatea

Ados de *Cara 19*

Religia

Anul *1918* Luna *Nov* ziua *18* ora *10 am*

Protecție

Unde se înmormântează *Învorul Nov*

Local nașterii

Cauza înmormântării *Adus*

Domiciliul

Exit din viață la *19/12 Nov. 918*

Autopsiat la *19 Nov 918*

Greutate

Talia

Trusestate

Haine și Obiecte ce poartă :

Adus

Observațiuni—Cauza Morții

*Căderea unei bătrân de 60-70 ani
ochi albaștri, cărunt, mai mult
alb derivat dintr-un blond plin de
pădurechi, într-o stare deplorabilă.*

Pneumonie datorită gripale

Figure 6. Autopsy report – identification and description data: particular signs of the person and relevant aspects found during the autopsy “The body of an old man, 60-70 years old, blue eyes, grey-haired, mostly white, derived from blond hair, with parasites, body decay. Double flu pneumonia”.

[illegible]

Figure 8. Communication addresses: Left: NILM MM to police: “Sir, Royal Commissioner, as a response to your address with no. 2355/20th Nov. 1918, “I have the honor to communicate that we have not received yet in the Institute the pills expected from your address. Additionally, we communicate that in the Institute has been brought sublieutenant MM (not C) regiment 80 Infantry to whom by autopsy we noticed the cause of death as Flu Bronchopneumonia “. Right: “No. 296/20th Nov. 1918 Martial Court Bucharest, Chemistry lab. Institute of Legal Medicine, we have the honor to kindly ask to perform urgent analyzes of pills believed to have determined the death of sublieutenant MC, reg. 80 infantry”.

(tuberculosis). The pleural cavities contained citrine serous fluid.

Macroscopic aspects of other organs: splenomegaly, hepatic steatosis and marked visceral stasis, erosive gastritis. Toxicological test results are negative.

Cause of death: Severe bronchopneumonia due to influenza virus infection.

Case 3

A 35-year-old woman, whose death occurred shortly after hospitalization, without a clear diagnosis. A legal autopsy was ordered by authorities (Fig. 7). In the autopsy report, we found the communication of the hospital to the forensic doctor (Fig. 8).

Autopsy findings: the skin located on the trunk and limbs of the body was covered with petechiae and purpura. Pulmonary: bronchopneumonia and pulmonary edema.

Received of *John A. Kim*
 the sum of *100* Dollars
 for *rent of land*
 this *10th* day of *June* 18*82*
 Witness my hand and seal of office
 at *St. Louis* this *10th* day of *June* 18*82*
John A. Kim
 Clerk of the Court

Figure 7. Communication addresses: police to NILM MM: „Toward the Institute of Legal Medicine, file 1712, received with no. 1396, on 13/26th No. 1918: „We have the honour to bring you the body of sublieutenant MM reg. 80 Infantry brought in Bucharest from Piatra Olt (a city). The papers have been send to the Military Garrison of Bucharest Market, the death being suspect. Colonel.....“

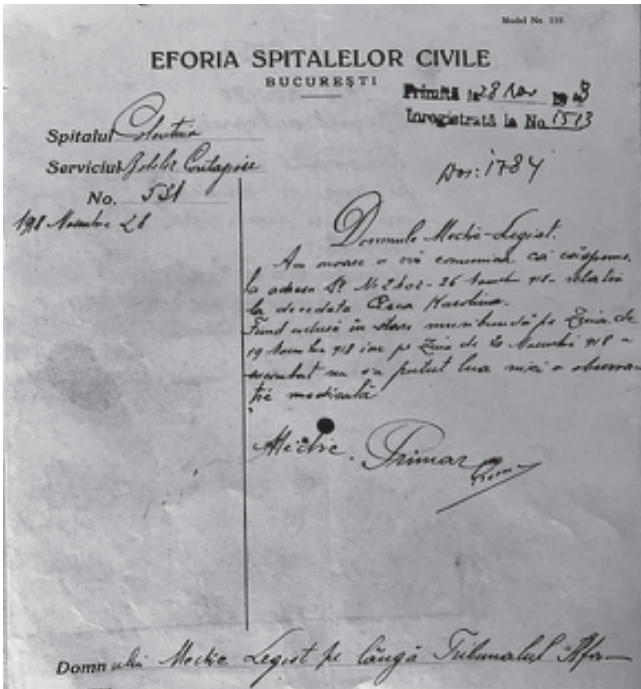


Figure 9. The communication order from the Colentina hospital, Infectious disease department, issued with no. 531/28th Nov. 1918, file 1784 and received in the NILM MM on 28th Nov. 1918 with no. 1513 states: "Toward the legal medicine doctor of the Public Ministry of Ilfov County, Dear forensic doctor, we have the honor to communicate to your address no. 2402/26th Nov. 1918 that Mrs. CM has been brought to us dying on 19th Nov. 1918 and passed away the next day on 20th Nov. 1918 without any medical records. Doctor..."

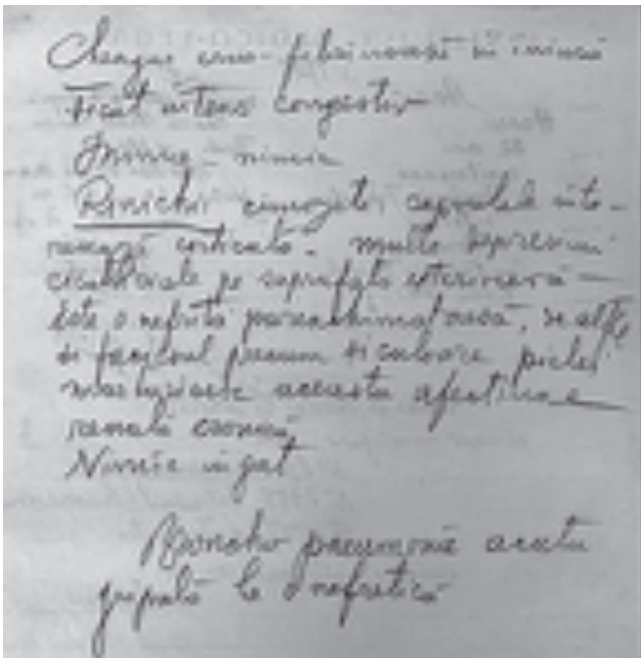


Figure 11. Autopsy report and cause of death (continuation). Cruor and fibrinous clots in the heart. Highly congestive liver. Anatomical normal heart. Kidney with cyanosis, a lot of scars on the exterior kidney surface. A parenchyma chronic nephritis. Facies and skin color prove a chronic kidney pathology. Acute flu bronchopneumonia to a nephritic person.

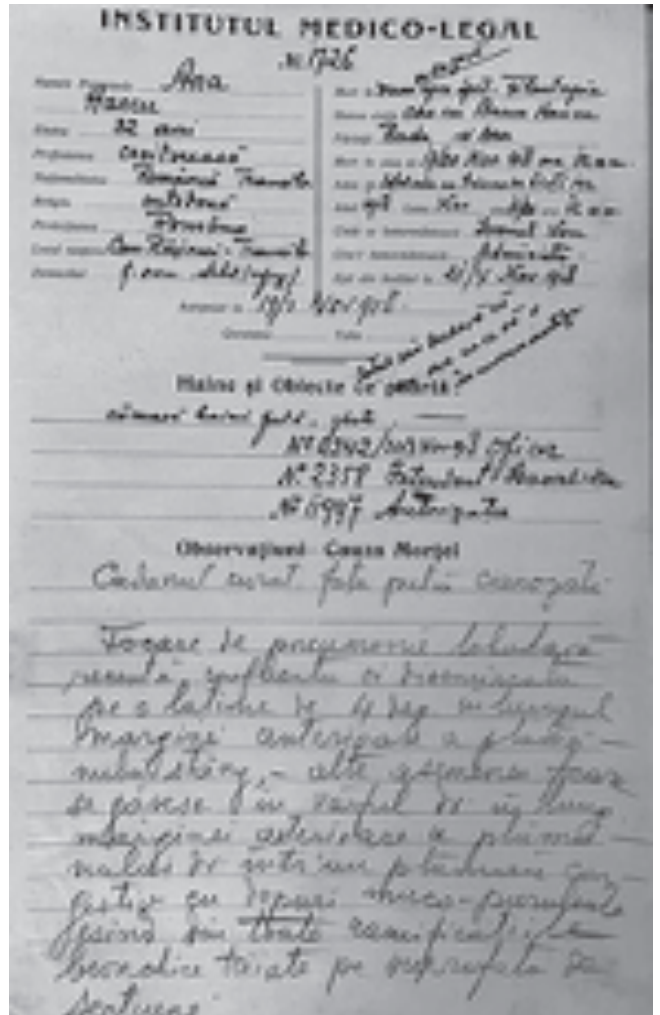


Figure 10. An autopsy report and cause of death. No. 1726 AH. 32 years old. Taylor. Romanian. Orthodox. Romania. Village ... from Transilvania. Refugee. Autopsy on 19/2 Nov. 1918. Death from the railway station to Filantropia Hospital. Married with BH. Parents R and A. Dead on 17/80 Nov. 1918 10 a.m. brought by her husband with the tramway no. 142. Issued in 1918, Nov. 17/80 12 a.m. to be buried in ... by the Administration. Exit from the NILM MM on 21/4 Nov. 1918. Her husband declares he has no financial means for funerals. Wears a shirt, skirt, and boots. Observations and cause of death: the body clean, facial cyanosis, foci of recent lobular pneumonia confluent and disseminated over a 4 fingers depth alongside the anterior margin of the left lung. Many similar foci are to be found in the apex of the lung alongside the anterior margin of the right lung with congestion and purulent and mucosal floats exiting all the bronchial ramifications on the section cut (to be continued).

Macroscopic aspects of other organs: cerebral edema, cardiomegaly, atherosclerosis, hepatic steatosis, and kidney vessel sclerosis.

Cause of death: Bronchopneumonia due to influenza virus infection.

Case 4

The case described in the report was of a 32-year-old woman who suddenly and unexpectedly died (Fig. 9).

Autopsy findings: Multiple foci of bronchopneumonia were found in both lungs. From the descriptions in the report (Figs 10 and 11), the forensic pathologist observed visceral stasis, as well as suggestive changes of chronic kidney disease, skin coloration, and renal surface with multiple scar depressions.

The cause of death was bronchopneumonia, due to influenza virus infection.

New archives of the National Institute of Legal Medicine Mina Minovici Bucharest: a study on COVID-19 death

Statistics

In the new archives of the National Institute of Legal Medicine Mina Minovici from Bucharest, we found in 2020 some 82 cases COVID-19 confirmed of which 61 cases with COVID-19 as a cause of death (Ic. Primary or underlying cause of death) and 21 violent cases with SARS-CoV-2 infection in progress (II Contributory cause of death) and in 2021, the first 3 months (January 2021-March 2021) some 94 cases, 2020-2021, actually one year of COVID-19 pandemia (March 2020- March 2021), totally 176 cases.

Necropsy findings in COVID-19 cases. In Table 3, we present some macroscopic and microscopic aspects of the organ fragments collected from some of the COVID-19 cases autopsied in the National Institute of Forensic Medicine.

Annual case distribution - COVID-19 in 2020/2021 * (NILM statistics)

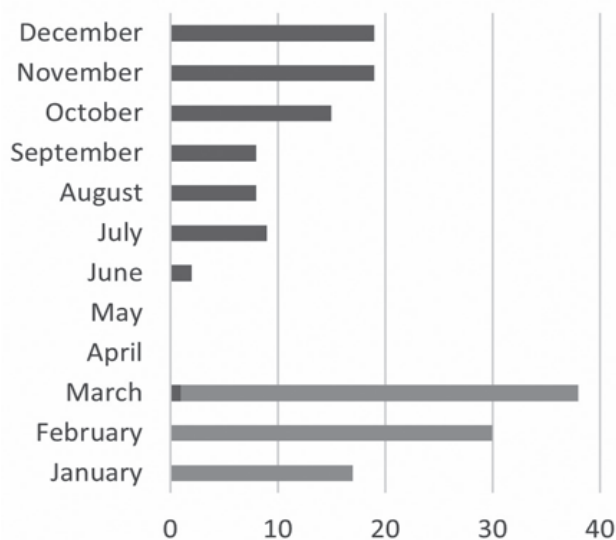


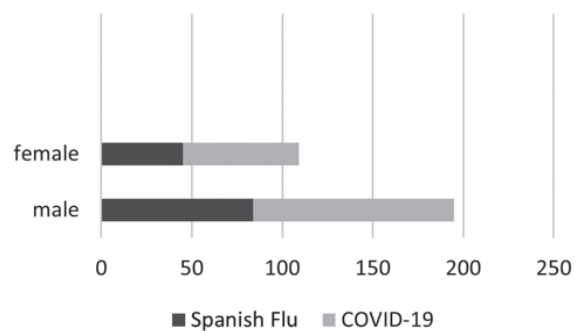
Figure 12. COVID-19 annual case distribution - (medico-legal cases); * in 2021 only the first 3 months.

DISCUSSION

A comparison between the Spanish Influenza pandemic (1918-1920) and the SARS-CoV-2 pandemic (defined as so by the World Health Organization [2]) draws up similarities and disparities (Table 4).

To compare the archives of the NILM Mina Minovici between 1918 pandemics and 1919 pandemics, 185 autopsy cases in Spanish flu deaths over 3 years (1918-1920, in a working flow of 1800-2000 autopsies cases/year) v. 176 cases in one-year time (March 2020- March 2021) in a similar working flow as in 1918-1920 time). That proves that in COVID-19 pandemic, in present time, more legal medicine autopsy cases (forensic cases) are ordered by the law-enforcement forces to verify and to determine the cause of death (most probably based on suspicions and a public request) and proves also to be

Comparison between male/female ratio in the two pandemics (NILM statistics)



male/ female distribution COVID-19 in 2020 (NILM statistics)

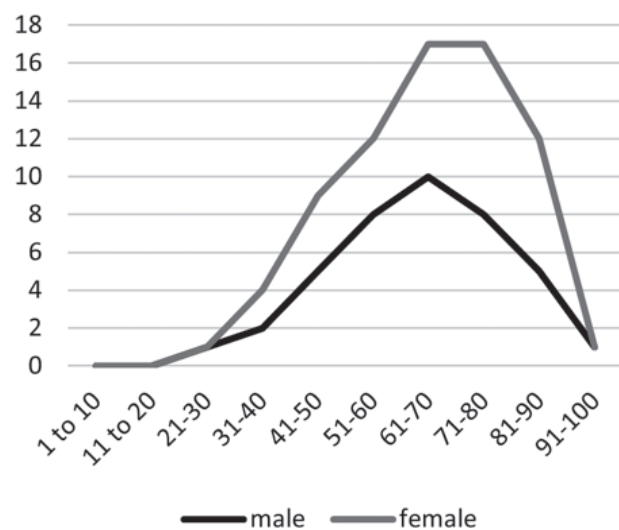


Figure 13. COVID-19 in 2020 male/female deaths ratio (medico-legal cases).

Table 3. COVID-19 deaths. Necropsy findings in COVID-19 cases: new archives of the NILM MM (a series of 100 cases from total cases. A complete report is not yet released, histopathology analyzes being still in work)

Organ	Forensic pathological aspects	Histopathological aspects
Brain	Most frequent: stasis, edema (83%), micro thrombosis (41%) usually associated with thrombosis in different organs (kidney, etc.), and minimal cerebral hemorrhages (33%). Meningitis and encephalitis in 2 cases.	Perivascular cellular infiltrates particularly in basal cerebral ganglia to patients with olfactive neuropathy. Cerebral ischemia. Chronic inflammation perivascular inflammation.
Lungs	Lungs are by far the most damaged organs. Diffuse alveolar lesions in different stages of DAD (diffuse alveolar disease) (29%), Pulmonary edema, patching, hemorrhages, diffuse consolidations sometimes reticular consolidations, thrombosis, pulmonary infarct, nonspecific pneumonia, bronchopneumonia (13%), viral pneumonia aspects (47%) with consolidation and intense dark-reddish aspects.	Diffuse alveolar lesions, DAD, pneumonia, bacterial or fungi bronchopneumonia. Thrombosis. Alveolar or interstitial hemorrhages, microthrombi (30-35%). Type 2 pneumocytes desquamation with viral cytopathic effect (cytomegalic cell, enlarged nuclei, eosinophilic nuclei). Elongated capillaries with altered morphology and stenosis, monilial morphology. Interstitial myofibroblastic reaction. Honeycomb aspect. An alveolar granulation tissue. Vascular alterations (periarterial lymphoplasmocytic infiltrates). Multinucleate giant cells, macrophages CD 68+; rare lymphocyte infiltrates.
Heart	Coronary atherosclerosis (78%), dissecting myocardial fibrosis (86%). Hypoxic ischemia (>50%).	Acute ischemia, acute necrosis, myocardial infarct, heart rupture, and hemopericardium (1 case). Microthrombosis (28%) in heart vessels usually associated with pulmonary thrombosis. No myocarditis.
Trachea	Erythema. Inflammation and hemorrhage.	Mucosal destruction, desquamation and denudation of basal lamina, vascular hyperemia, microthrombosis in submucosal vessels. Subacute tracheitis.
Liver	In our experience, the liver is after the lung, the second organ pathologically involved in COVID-19. Target liver presents stasis, dystrophy, vacuolar degeneration (70%), hemorrhages, necrosis, portal hyperactivity, fibrosis, cirrhosis, liver insufficiency.	Liver degeneration. Liver necrosis. Nodal proliferation of Kupfer cells. Portal lymphocytic proliferation. Ductular proliferation. Syncytial liver cells. Micro and macrovesicular steatosis. Microthrombosis. Central lobular necrosis (20%), capillary leukostasis (30%), thrombosis (10%).
Kidney	Acute tubular necrosis (61%).	Ischemia alterations with lesser capillary looping, plasma accumulation in Bowman space. Arterioles and capillaries thrombosis. Acute tubular lesions with lost brush edge, vacuolar degeneration, enlarged tubular lumen, necrosis, and tubular epithelium detachment. Rare (<20%) inflammatory infiltrates, hematic cylinders, or hyaline cylinders, tubular necrosis, exudative glomerulonephritis, glomerular cells edema, proteinic cylinders, erythrocyte cylinders, erythrocytic aggregation in glomerular capillaries, hemosiderin granules in the tubular epithelium.
Pancreas	No modifications. Autolysis.	Focal degeneration of the pancreatic cells. Focal pancreatitis.
Small bowel	Acute ischemia, necrosis, and mucosal hemorrhages.	Rare degeneration of the small bowel epithelium, necrosis of the gastric and bowel mucosal layer; dilatation and hyperemia of the small vessels in submucosa and lamina propria. Lymphocyte infiltrates with monocyte and plasmacytes.
Spleen	Microhemorrhages (66%).	Rare lymphocyte depletion (33%) is confirmed using IHC with CD45
Ganglia	Usually no modifications, rarely adenopathy	Frequent acute lymphocytes depletion; loss of follicular structure

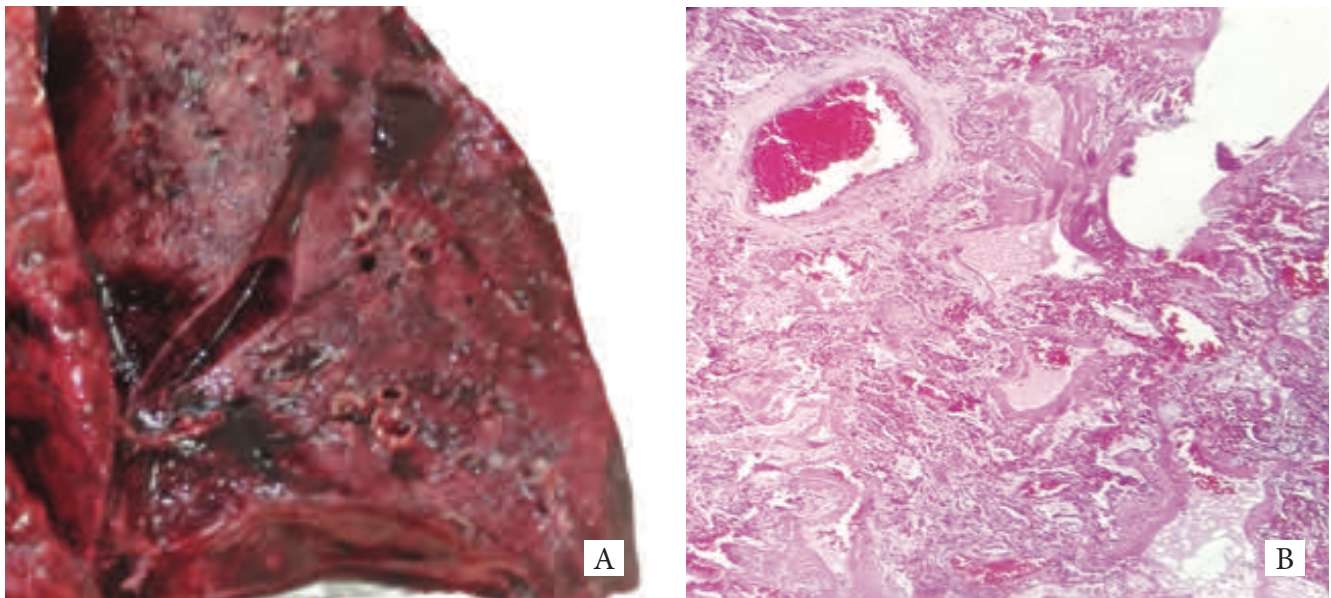


Figure 14. A) Macroscopic view: Lung section – Pulmonary consolidation. Bronchopneumonia. B) Microscopic view: 10x magnification- H&E staining of lung tissue section. Thick hyaline membranes lining the alveolar walls - advanced exudative phase.

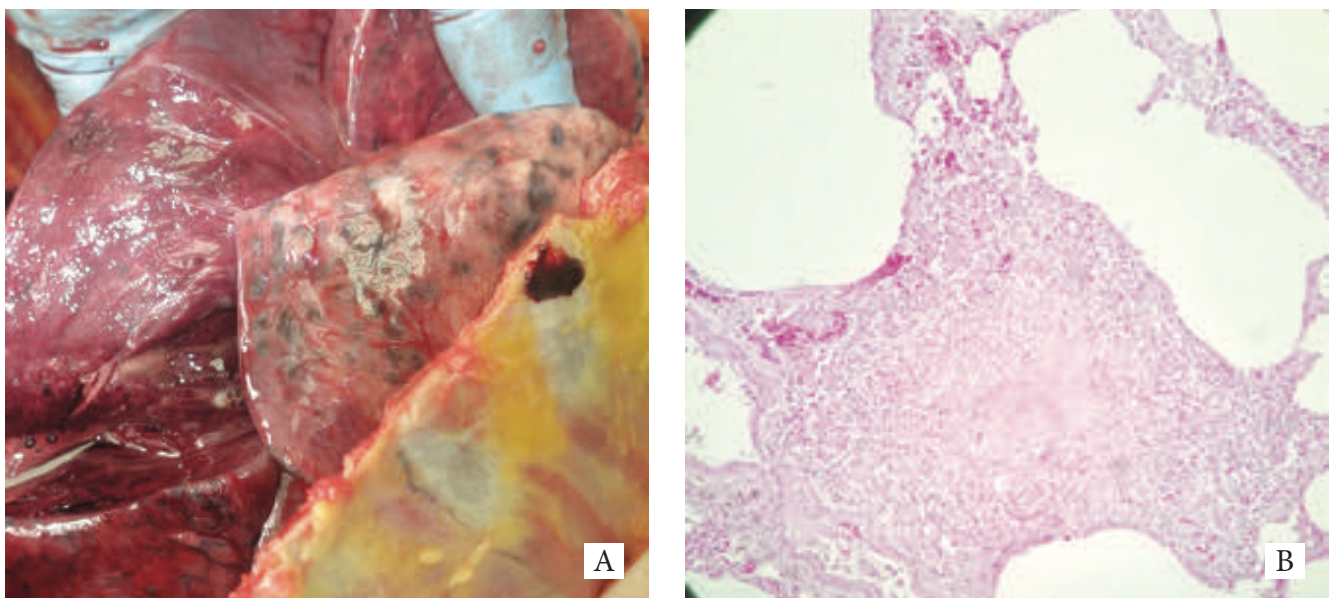


Figure 15. A) Macroscopic view: in situ dissection: lung section: Pulmonary TB granuloma. B) Microscopic view: 10x magnification- H&E staining of lung tissue: TB granuloma (central caseous necrosis, lympho-monocytes and giant Langhans cells at the periphery).

at least 3 times more frequent than in 1918 (if this order rate is to be continued): a 3-time increase of the judicial suspicious rate as in the former pandemic.

20-40 years old mortality *vs.* > 60 years old mortality is another difference, probably due to comorbidities in elder persons.

We did not find histopathological reports in the archives of the “Mina Minovici” National Institute of Legal Medicine. Most likely, diagnoses of death (in cases of patients who died as a result of influenza virus infection) were established based on the aspects of the

target organs (the lungs), with the help of investigative data.

The data obtained from the analysis of autopsied COVID-19 cases in the years 2020-2021 are much more complex to compare with 1918 due to complementary examinations.

1918-1920 did not gather, as today, so much fundamental science knowledge, virology (i.e. Pfeiffer agent, Hemophilus influenza, was considered a causative agent for Flu), or pathophysiology, so less specific treatment (no antibiotics to prevent and treat

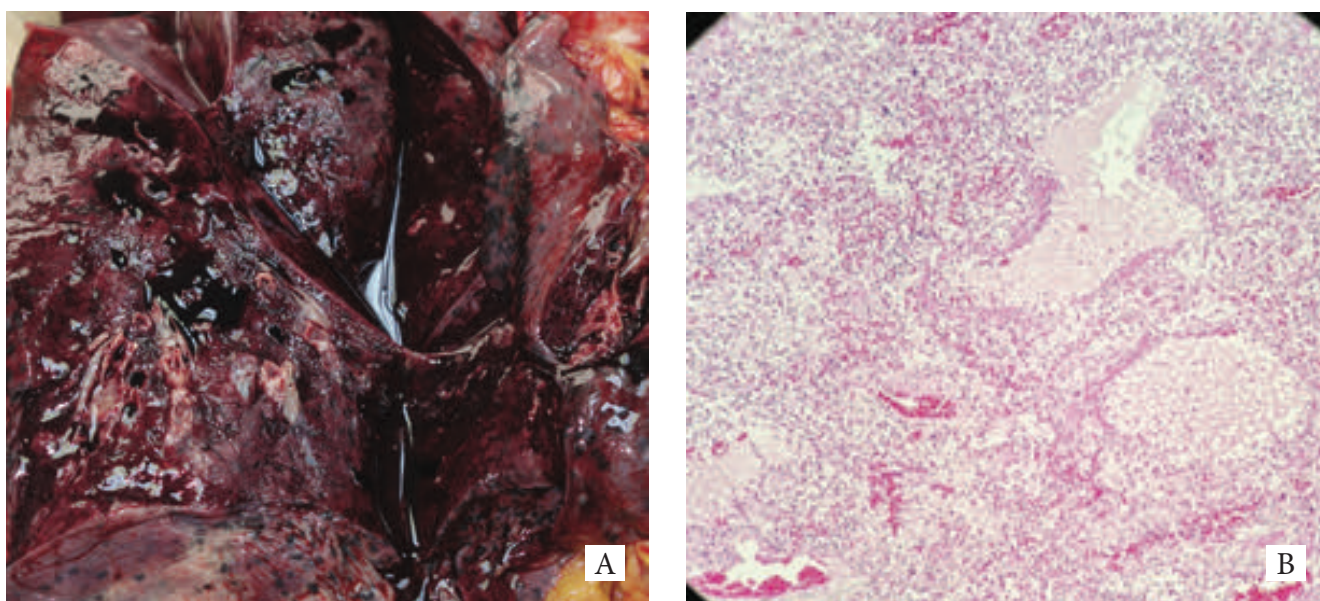


Figure 16. A) Macroscopic view: lung section: Pulmonary stasis. Scleroemphysema. Pulmonary consolidation. B) Microscopic view: 10x magnification- H&E staining of lung tissue: Hyaline membranes lining the alveolar walls.

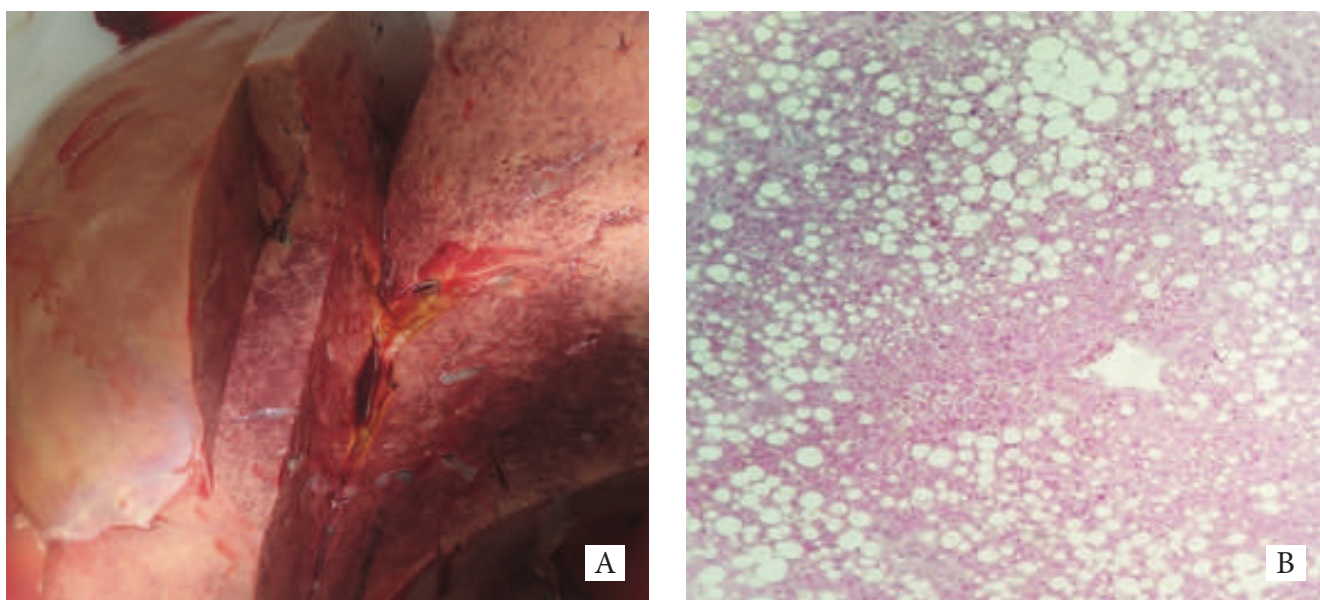


Figure 17. A) Macroscopic view: Liver section - Area of hemorrhagic necrosis. Fatty liver. B) Microscopic view: 10x magnification- H&E staining of liver tissue section - Centrilobular hemorrhagic necrosis area. Liver steatosis.

over infections) or vaccination policies (Edward Jenner, 1798, conceived the first vaccine for smallpox, Louis Pasteur, 1897 for cholera and on 1904 for anthrax; after the Spanish flu pandemic in 1923 Alexander Glenny develops a vaccine against diphtheria, pertussis vaccine in 1948 and Salk and Sabin the polio vaccine during 1950-1985) [20, 38, 39] and bioethics was not then yet emerged. Even though epidemiological measures like mask-wearing, quarantine, and isolation or interdiction of public gatherings were taken into consideration [20, 38, 39].

It was a difficult time overlapping with World War I, Spanish flu spreading, typhoid fever, and other vicious infectious diseases, and severe economical depression, therefore a lot of pressure to overcome. Nevertheless, nowadays the pressure is also important due to the general menace, the human rights recognition, and largely support and economical depression. Nowadays bioethics brings important support for a right balance between individual rights and public rights, beneficence vs. non-maleficence or beneficence vs. the principle of justice (present research

Table 4. Similarities and disparities between Spanish Influenza and SARS-Cov-2

	Spanish flu pandemic	COVID-19 pandemic*
Virus	Influenza A H1N1 [11], [12] discovered in 1951 by Hultin [13], initially characterized by Taubenberger in 1997 [14], sequencing in 2001 by Basler [15], with complete characterization in 2005 [16]	SARS CoV-2 [17, 18]
Natural reservoir	Avian [19]	Possibly bats [19]
First outbreak	United States [20]	China [18]
Period	1918-1920 [21]	2019- [19]
Waves of break through	4 [21]	3° [22]
Infected persons	500 millions [20]	126 millions [7]
Deaths	50 millions [20]	2.7 millions [7]
Incubation period	2 days [19]	2-11 days [23]
Mortality	>2.5% [24]	3% [7]
Host receptor	sialic acid [19]	angiotensin-converting enzyme 2 [17]
The people most affected	Young healthy individuals (near 28 years old at the pandemic time) [25, 26].	Elder persons with comorbidities as chronic conditions such as diabetes, heart diseases or cancer [27].
Symptoms	General weakness [8], cough [8], fever [8], shivering [8], headaches [8], bloodshot eyes [8], nose bleeds [8], dry tongue [8], epistaxis [8], cyanosis [25]	Fever [28], cough [28], vomiting [28], abdominal pain [28], headaches [28], anosmia [29], hyposmia [29] and dysgeusia [29]
Paraclinical changes	Lymphopenia, eosinopenia [19]	Lymphopenia [28] and increases in WBC (white blood cell), CRP (C-reactive protein), LDH (lactate dehydrogenase) and D-dimer level [30], Transmission: mainly through respiratory droplets [30]; other ways: fecal-oral, materno-fetal, contaminated surfaces [30]. Body systems and organs affected: the respiratory system, the cardiovascular system, the gastrointestinal system, nervous system [18].
Pathophysiology	Transmission: through respiratory droplets. [11]. Body systems and organs affected: the respiratory system, the cardiovascular system and the spleen [31].	Pulmonary stasis and edema [33], desquamation of pneumocytes [34], interstitial mononuclear infiltrate [34], diffuse alveolar damage [33], alveolar hemorrhage [35], bronchopneumonia [35], lymphocytic myocarditis [36], liver fibrosis [36]. Most deceased patients are men with cardiovascular diseases [37].
Autopsy findings	Tracheobronchitis [32], necrotizing bronchiolitis [32], Alveolitis [32], extensive hemorrhage [32], pleuritis [31], splenomegaly [31], heart hypertrophy [31]. Most deceased patients were men and only a small portion was overweight [31].	

*currently data gathered according to references; © present data.

on topics such as “bioethics and COVID-19” gather on PubMed 530 results, “bioethics and SARS-CoV-2”, do find 330 results, etc. [41]). We now have scientific literature for years to come just on this specific topic of COVID-19 and still is to be issued.

With no cure for the Spanish flu, aspirin (trademarked by Bayer in 1899, a patent that expired in 1917) was prescribed up to 30 grams per day (7 fold the normal prescription dose, i.e. a toxic dose). Aspirin intoxication (hyperventilation and pulmonary edema, hemorrhages, liver dysfunction) may mimic Flu symptoms and this could explain the severity of the 3rd wave of the Spanish flu [42]. Nevertheless, Spanish flu

Influenza virus reconstruction [13-16] allow science to explain its virulence. Hemagglutinin [43] and RNA polymerase allow the virus to make new particles and spread infection [43] and facilitate bacterial pneumonia which at that time was without any antibiotic-specific treatment [42]. Despite its high virulence more than 97% of the people infected with H1N1 influenza virus pandemic survived implying probably some host genetics contribution to prognosis [44].

1918 pandemic determined afterward a right focus on prevention such as developing of the washing machines with a mass availability, improving sanitation requirements by changing wooden beds in hospital

with metal beds, requirements for specific legislation to improve on a better epidemiological concept the urban housing (fire escape, separate bathrooms, etc.), crinoline wear by women, social distancing, etc.

Due to COVID-19, epidemiological measures, working from home, online connectivity of people, and the shift to online delivery of everyday items (food, usual shopping basket items, medicine, etc.), drive-in facilities are nowadays prevention measures still in progress to implement or to develop. Bioethics developments, new policies may be, will take into consideration all of these changing values of the present society.

In conclusion, if symptoms based on case definitions and laboratory investigations (RT-PCR) in case of COVID-19 pandemic are of major importance nowadays for detection and diagnosis, in 1918-1919-1920 pandemic the detection of influenza virus infection was based not so much on symptoms (somehow non-specific), not so much on the virus itself that they did not know but on epidemiological data (when available) and on necropsy gross pathology findings when autopsy was performed (primary lungs as target organs).

The role of legal medicine proved to be invaluable in such deadly scenario as pandemics because may provide autopsy examination body samples collection and thorough investigations, diagnosis clues and pathophysiology mechanisms. Legal medicine autopsy has the role to give answers to the justice system but also to provide explanations for medical purpose and a better knowledge (in 2020 Romania 5 autopsies performed in a hospital environment v. 143 forensic or legal medicine autopsies on an order base).

Nowadays, in our experience most of the legal medicine autopsies are performed at the request of the families of the deceased, which call into question the appropriate treatment and nevertheless the existence of the COVID-19 virus itself or the causality i.e. primary infection or secondary coinfection (nosocomial).

In some cases, the contribution of the novel coronavirus infection to death cannot be assessed.

When the 1918 flu hit, doctors and scientists were unsure what caused it (Pfeiffer agent was still in use) or how to treat it (no antibiotics). Unlike today, there were also no effective vaccines and antivirals (the first licensed flu vaccine appeared in America in the 1940's).

Therefore this comparison between the two pandemics brings us in a privileged position considering the knowledge, the science progresses and the bioethics insight that is able probably to sustain justice principle as a main ethics paradigm in COVID-19 pandemics.

Conflict of interest

The authors declare that they have no conflict of interest.

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