

Characteristics and management of pyogenic liver abscess

A European experience

Cristina Serraino, MD^{a,*}, Chiara Elia, MD^b, Christian Bracco, MD^a, Gianluca Rinaldi, MD^a, Fulvio Pomerio, MD^a, Alberto Silvestri, MD^a, Remo Melchio, MD^a, Luigi Maria Fenoglio, MD^a

Abstract

Pyogenic liver abscess (PLA) are space-occupying lesions in the liver associated with high morbidity and mortality. The aim of this study is to review an Italian hospital experience in epidemiological, clinical patterns, and management of PLA.

We performed a retrospective, descriptive case series at a single center assessing demographic characteristics, presentation patterns, etiological factors, microbiological etiology, and management for patients treated for PLA between 2000 and 2016.

Around 109 patients were identified. The majority of patients presented with fever (73%); right upper abdominal pain in 63.3%, vomiting and nausea in 28.4%. The most common laboratory abnormality among included items was increased C-reactive protein and fibrinogen blood levels, respectively, in 98% and 93.9% of cases. Abdominal ultrasound was the diagnostic investigation in 42.4% of cases; CT scan and MR imaging were performed in 51.1% and 3.3% of cases respectively. We observed blood or pus culture study in 99 cases of which only 53.5% came with positive microbial reports. The most common organism identified was *Escherichia coli* (26.5%), followed by *Streptococcus* spp (13.2%). Early antibiotic treatment started on all patients and 66.7% of cases required different approaches, Ultrasound or CT-guided needle aspiration of PLA was performed in 13 patients (11%) and percutaneous abscess drainage was performed on 72 patients (67%).

PLA is a diagnostically challenging problem due to nonspecific presenting characteristics. The microbiological yield identified was a typical European spectrum with a preponderance of *Escherichia coli* infections. Once recognized, percutaneous drainage and antibiotic treatment are the mainstay of management for PLA.

Abbreviations: CCIS = Charlson comorbidity index score, CT = computed tomography, ERCP = endoscopic retrograde cholangiopancreatography, MR = magnetic resonance, PCD = percutaneous catheter drainage, PLA = pyogenic liver abscess, PNA = percutaneous needle aspiration, SD = standard deviation.

Keywords: clinical presentation, microbiology, percutaneous drainage, pyogenic liver abscess, risk factors

1. Introduction

Pyogenic liver abscess (PLA), a suppurating infection of the hepatic parenchyma, remains a mortality associated condition and nowadays develops as a complication of biliary tract diseases for about 40% of cases.^[1] Recently, the etiologies of PLA have shifted from intra-abdominal infections such as acute appendicitis and trauma to pathologic conditions of the biliary tract; however, up to 55% of patients with PLA have no clear risk factors and these cases are called cryptogenic.^[2–4]

The incidence of PLA varies from 8 to 22 patients per 1,000,000 people belonging to a geographical area with substantially higher rates having been reported in Taiwan.^[5–8]

Early diagnosis and treatment is a crucial step in the management of these patients, since the presentation may be subtle and not specific (abdominal pain, fever, nausea, and vomiting), so currently constitutes a challenge for physicians: a high index of suspicion is the cornerstone of prevention for misdiagnosis and improvement of prognosis.^[9] In recent decades, combined antibiotic therapy and percutaneous drainage have become the first-line treatment in most cases and has greatly improved patients' prognosis: the mortality rate has dropped from 70% to 6.31%.^[10] In terms of causative pathogens, bacteria most frequently associated with PLA are *Escherichia coli*, *Enterobacteriaceae*, anaerobes, and other members of the gastrointestinal flora. Over the past 2 decades *Klebsiella pneumoniae* has been emerging as the predominant pathogen responsible for 50% to 88% of PLA in the Asian population and it has been reported with increasing frequency in South Africa, Europe, and the United States.^[7] Because such experiences have not yet been reported in Italy, we reviewed the cases of PLA seen at our institution. The present study is a retrospective analysis of demographic characteristics, etiological factors, presentation patterns, microbiological etiology, and the treatment of PLA cases which were presented in an Italian hospital over a 16-year-period.

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^a Department of Internal Medicine, Santa Croce and Carle Hospital, Cuneo,

^b Department of Emergency Medicine, Regina Montis Regalis Hospital, Mondovì, Italy.

* Correspondence: Cristina Serraino, Department of Internal Medicine, Santa Croce and Carle General Hospital, Cuneo, Italy (e-mail: cris.serraino@gmail.com).

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2. Materials and methods

2.1. Study population

The study includes 109 consecutive patients with pyogenic liver abscess admitted to the Santa Croce and Carle Hospital of Cuneo from January 2000 to December 2016. These patients were identified by searching the International Classification of Disease code (ICD 9-1997) for the diagnosis of “pyogenic liver abscess” (572.0.0) from the hospital database during that period. The protocol was approved by the Institutional Review Board of Santa Croce and Carle General Hospital, Cuneo, Italy (IRB No. 38132).

The diagnosis of PLA was based upon clinical aspects, imaging studies, and microbiology on blood or aspirate culture results.

Exclusion criteria were: patients with age < 18 years, amoebic liver abscess, hydatid liver abscess, previous episode of PLA, and previous liver transplantation.

Medical records were evaluated by the Hospital Archival records system. Data collected included demographic characteristics, etiopathologic factors, clinical features, laboratory data, number, size and location of lesions, microbiological findings, diagnostic and therapeutic methods, treatment response and mortality.

The presumptive etiology of the liver abscess was a judgement made, at the time of retrospective study by the investigator using a standard protocol. PLA was considered secondary to biliary tract disease in patients with a clinical picture of cholecystitis or cholangitis or a documented biliary duct abnormality. It was considered secondary to hematogenous spread when another source of infection was found. Cases that were judged ambiguous were reviewed by a secondary investigator to confirm the etiology. We defined a cryptogenic abscess as a PLA for which no obvious source of infection was found, despite evaluation by imaging methods and the collection of medical history in immunocompetent patients.

Radiological findings included abdominal ultrasound, computed tomography (CT), and magnetic resonance (MR).

Cultures were isolated for aerobic and anaerobic organisms using the standard diagnostic techniques. If both blood and pus cultures were positive, organisms recovered from the abscess were assumed to be the etiologic.

All patients received antibiotic therapy: the type, duration, and mode of administration were recorded for each case. PLA were treated empirically with antibiotics and, if there was no response to the initial treatment, the antibiotic was changed according to the results of cultures or empirically if cultures were negative. No response to the initial treatment was defined as a patient having persistent signs of sepsis after 5 days of intravenous antibiotics.

Ultrasound-guided percutaneous needle aspiration and drainage were performed in the radiology department.

Cure was defined as the absence of signs and symptoms together with image studies without findings compatible with PLA.

Case fatality was defined as death during hospitalization and related to PLA.

2.2. Statistical analysis

Comparisons of variables between groups were made with standard statistical tests. Survival probability curves were calculated with the Kaplan–Meier method and compared with log-rank test. Multivariate Cox proportional hazards model was used to assess variables independently related to 3-month survival. All statistical analyses were performed using SPSS 20.0 software. Results for continuous variables are expressed as mean \pm standard deviation. The significance level for all statistical tests was set at 0.05 two-tailed.

3. Results

3.1. Demographic and clinical features

From January 2000 to December 2016 inclusive, 109 patients were diagnosed with PLA at Santa Croce and Carle General Hospital, of which 62 patients (56.9%) were males and 47 patients (43.1%) were females. The patient’s age was ranging from 18 to 92, and mean age was 65.4 (standard deviation, SD: \pm 14.3).

As shown in Figure 1, the majority of patients with PLA presented with fever, 73%; right upper abdominal pain was reported in 69 cases (63.3%), vomiting and nausea in 31 (28.4%), while asthenia in 29 patients (26.6%), loss of weight in 19 patients (17.4%), and jaundice in 14 cases (12.8%).

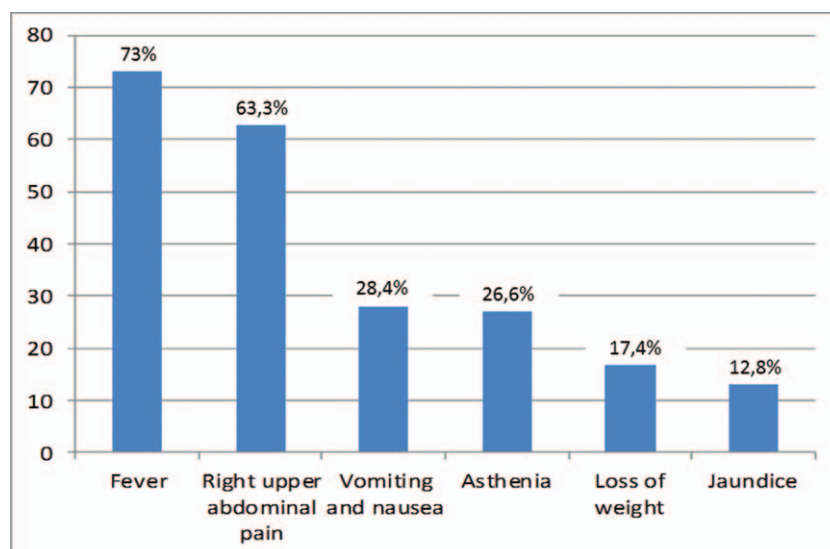


Figure 1. Percentage of patients with various clinical features on presentation.

Table 1
Summary of laboratory results at presentation in patients with liver abscess.

Results	Range	Mean ± DS	No. of cases outside range (%)
White cell count (× 10 ³ /L)	4.0–10.0	16 ± 9	84 (77)
Hemoglobin, g/L	<12	11.4 ± 1.9	67 (61,5)
C-reactive protein, mg/L	≤ 10	156.1 ± 84.9	98 (98)
Procalcitonine, ng/mL	<0.046	25.05 ± 52.7	34 (100)
Fibrinogen, mg/dL	150–450	693.8 ± 176.7	62 (93.9)
Albumin, g/L	< 35	26.5 ± 5.4	79 (96,3)
AST, U/L	> 40	96.7 ± 179.6	62 (56.9)
ALT, U/L	9–56	78.5 ± 94.8	49 (45)
ALP, U/L	38–126	258.5 ± 200.4	69 (67)
Bilirubin, mg/dL	0,2–1,3	1.5 ± 1.6	35 (33)

ALP=alkaline phosphatase, ALT=alanine transaminase, AST=aspartate transaminase.

A total of 25 patients (23%) had diabetes mellitus. Among the diabetic patients, 57% did not have good glycemic control (good glycemic control is categorized as glycated hemoglobin (HbA1c) ≤ 7%).^[11]

Charlson comorbidity index score (CCIS) was used to determine overall systemic health: with each increased level of CCSI, there was a step-wise increase in the cumulative mortality: score 0 with a 10 year survival rate of 99%, and score 5 with a 10-year survival rate of 34%, respectively.^[12] Among the study population, 19 patients (17.4%) had 0–1 CCIS, suggestive of low comorbidity, 22 patients (20.2%) had 2–3 CCIS, and 68 cases (62.4%) had high CCIS >3, suggestive of high comorbidity and cumulative mortality.

3.2. Laboratory and radiological features

The most common laboratory abnormality among included items was increased C-reactive protein and fibrinogen blood levels, respectively, in 98% and 93.9% of cases (Table 1). These were followed by abnormal total leucocytic count in 77% patients and elevated ALP in 67% of cases. The procalcitonine value was elevated in all patients in which it was tested 34 patients.

Abdominal ultrasound was the diagnostic investigation in 42.4% of cases; CT scan and/or MR imaging were performed if they were further needed for differential diagnosis. Around 51.1% of patients underwent CT scanning and 3.3% needed MR. The mean size of liver abscess was 7 ± 3.5 cm (range, 1.5–15 cm). In this series, 55% of abscesses were single at time of presentation. Two abscesses were found in 18.3% of cases and > 3 lesions in 26.6% of patients. The presence of gas in the abscess cavity was noted in 18.5% of cases. The majority of liver abscesses (65.4%) were found in the right lobe of the liver and about 19.6% were confined to the left lobe. Both lobes were involved in 15% of patients.

3.3. Microbiology and pathogenesis

We observed blood or pus-culture study in 99 cases of which only 53 cases (53.5%) came with positive microbial reports. Culture from aspirate of liver abscess was positive in 25 of 62 patients who underwent percutaneous aspiration of liver abscess (positive rate, 40.3%). The most common organism identified was *E coli* (26.5%), followed by *Streptococcus* spp (13.2%) and anaerobics (13.2%). Other organisms were *Enterococcus* spp (11.3%), *Staphylococcus* (7.5%) (Fig. 2).

As shown in Figure 3, of all PLA, in 28 cases (25.7%) the cause was not clear: cryptogenic abscess. Biliary tract diseases, including cholelithiasis, cholecystitis, and malignancies, were identified in 55% of cases (Table 2). In 12% of cases the cause of PLA was assigned to be hematogenous. In 7.3% of PLA the only known risk factor for PLA was diabetes mellitus. Among 28 cryptogenic abscesses, a total of 8 individuals (28.5%) underwent the colonoscopy: nobody was found to have incidental colon cancer or high-grade dysplasia.

3.4. Management

Intravenous antibiotic therapy started on all patients and 66.7% of cases required intervention in different forms. An empirical antibiotic treatment was started at the onset of the clinical sign of infection and was changed upon the results of antibiotic susceptibility tests. The reason for not performing image-guided

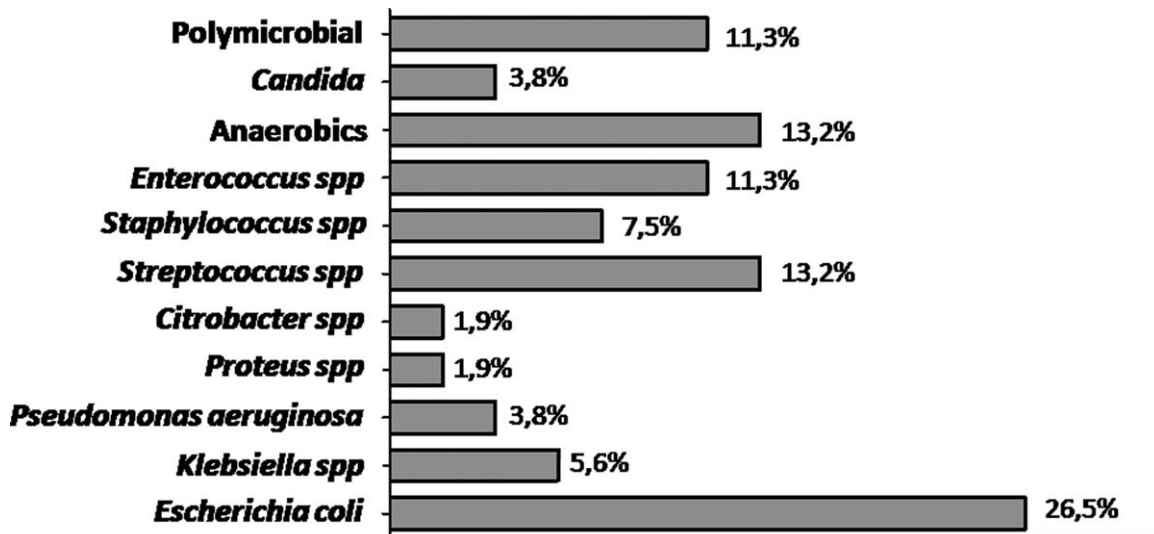


Figure 2. Organisms isolated from all positive cultures.

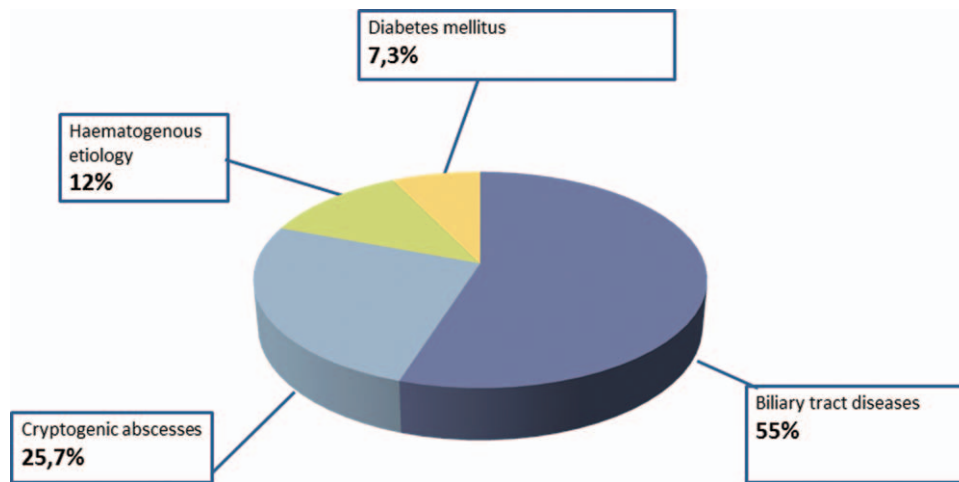


Figure 3. Causes of pyogenic liver abscesses.

aspiration and drainage was due to the small size of the abscess, clinical improvement with antibiotics or advanced malignancy. The range of antibiotic treatment duration was 29.7 days (SD: ± 19.8).

Radiological drainage was the most frequent initial intervention: ultrasound or CT-guided needle aspiration of PLA was performed in 13 patients (11%) and percutaneous abscess drainage was performed on 72 patients (67%). Generally, a percutaneous French 7 pigtail catheter was inserted. The removal of the percutaneous drain was based on the patient's clinical and laboratory response. The median of drainage duration was 12.6 \pm 14 days. Of all 72 cases that underwent radiological drainage, 7 patients required surgical intervention because of failure of resolution and recurrence of the abscess. Endoscopic retrograde cholangiopancreatography (ERCP) was used to treat liver abscess in 6 patients (5.6%), in which there was a lithiasic or neoplastic biliary obstruction.

The time interval between antibiotic administration and drainage was 8.5 days (SD: ± 11.7).

3.5. Complications and outcomes

There were 2 cases of major complication of interventional drainages: right pneumothorax, which resolved without drainage

Table 2

Detailed biliary tract diseases causes of pyogenic liver abscess. Values are given as number and percentages.

Disease	N (%)
Benign	
Cholecystitis	7 (21.9)
Cholangitis	5 (15.6)
Lithiasis of the biliary tract	11 (34.4)
Scar biliary stenosis	7 (21.9)
Hepatic cysts	2 (6.3)
Malignant	
Cholangiocarcinoma	8 (29.6)
Pancreatic cancer	7 (25.9)
Hepatocellular carcinoma	2 (7.4)
Liver metastases*	8 (29.6)
Gallbladder carcinoma	2 (7.4)

* Primary tumors were localized in 4 cases in the colon and in 2 cases in the rectum.

tube, and another patient developed biliary fistulae which resolved after ERCP decompression and nose-biliary drainage. There were no cases of abscess rupture or thoracic empyema. Eleven patients (10.1%) developed pneumonia during hospitalization and 4 cases (3.7%) developed splenic multiple abscesses.

The mean duration of hospitalization was 28 days (SD: ± 21). There was no correlation between length of hospital stay and PLA management; (antibiotic treatment alone versus interventional drainage, $P=NS$).

Eleven patients died during the hospital admission, such death resulting directly from the abscess or from a complication of treatment. The mean age of patients who died was 65.3 \pm 9. Seven were males. The mean hospital stay was 24 days (SD: ± 12.8).

4. Discussion

In this study, the clinical characteristics, etiology, microbiology, treatment, and mortality of 109 patients with PLA are reviewed and reported.

The average age of PLA patients in our sample was 65.4. This supports other series in demonstrating that the main age of patients who develop PLA has risen: in our study the average presentation was in the seventh decade. Again, a preponderance of males was noted.^[13,14]

Presenting symptoms of PLA were multiple and low specific, including fever, right upper abdominal pain, vomiting, nausea and asthenia, while on physical examination jaundice was recognized in 12.8% cases. In association to presenting symptoms, the presence of a raised C-reactive protein, white blood cell and alkaline phosphatase should suggest the possibility of PLA.

Perhaps the low index of suspicion of PLA due to the nonspecific presentation characteristics, the diagnosis could be suggested by the underlying predisposing disease processes. We identified predisposing diseases associated with the abscess formation, hepatic-pancreatic-biliary system problems were present in the majority of cases (55%).^[13]

Although it has been suggested that cryptogenic liver abscess is a sign of occult gastrointestinal malignancy,^[15,16] few patients with cryptogenic abscess underwent colonoscopy during their indexed hospitalization (28.5%); no colon cancer or polyp with high grade dysplasia was found.

The confirmation of the diagnosis of PLA relies on imaging of the liver: ultrasound alone was the diagnostic investigation in 42.4% of cases; CT scan was performed in 51.1% patients, the reason being the diffuse availability and of course, in case needed further for differential diagnosis. We confirmed the suggestion that PLAs are mostly confined to the right hepatic lobe^[9] as the result of the portal vein anatomy, more hepatic mass and the denser network of bile canaliculi in this lobe.

In our study, microbiological yield from blood and abscess culture was 54.2%, lower compared with other studies. A contributory factor to our low microbiological yield may be the early use of antibiotics: as known, a rapid sterilization of blood cultures can occur within a few hours of the first antibiotic dose.^[17] There are little formal data regarding the optimum duration of antibiotic therapy, but most units use a regimen of 2 weeks' parenteral treatment, followed by a more prolonged course (4–6 weeks) of therapy, switching to oral antibiotics when clinical and inflammatory responses allow.^[18] In our study, the range of antibiotic treatment duration was 29.7 ± 19.8 days, we also considered long oral antibiotic courses lasted after discharge.

A typical European microbiological spectrum was identified in this study: we observed a preponderance of *E coli* infections. The other main isolates were *Streptococcus* spp, *Enterococcus* spp and anaerobics. In only 2 cases we identified *K pneumoniae*, the predominantly PLA infection seen in Southeast Asia.^[19] The high incident of *E coli* and *Enterococcus* spp is probably related to the high incidence of a biliary cause of PLA.^[20]

Percutaneous needle aspiration and catheter drainage has been shown to be beneficial in the treatment of PLA in association with antibiotics: this association is the present standard practice. Of our cohort, all patients received antibiotic treatment, 66.7% of patients underwent percutaneous aspiration or drainage, or surgical drainage. Belonging to a meta-analysis, there is a favored opinion for use of percutaneous catheter drainage (PCD) over percutaneous needle aspiration (PNA): PCD facilitates a higher success rate, reduces the time required to achieve clinical relief and supports a 50% reduction in abscess cavity size.^[21,22] Image-guided catheter drainage was favored over PNA at our institution. ERCP can be a useful investigation and treatment procedure for patients with PLA: in this series 6.5% of patients underwent ERCP to treat a lithiasic or neoplastic biliary obstruction, which was the cause leading to PLA.^[23]

The most frequent complications were pulmonary: pneumonia was seen in 11.9% of patients.

The in-hospital mortality rate was 10.1%. Nowadays, better imaging, more effective use of antibiotics and abscess percutaneous drainage improved AEP mortality rate from 40% to 10% to 25%.^[24,25] Previous studies reflected that septicaemia and underlying malignancy were strong indicators of in-hospital mortality during the period from 1993 to 2008 in one UK center.^[15] In another European study, from 1992 to 2005, mortality associated with PLA was high, 19%, and the main risk factors were the development of sepsis and/or septic shock.^[9]

The overall mean hospital stay was 24 days, which was also compatible with previous reports.^[26,27]

This is a retrospective study; there are few reports in recent years about PLA diagnosis and management in Europe. Our experience may provide valuable information to clinicians who encounter this uncommon condition.

The present study has some important limitations: it is a retrospective study and some relevant information may not have been documented in the patient's medical chart, strong conclusions cannot be made due to the small sample size and

the results represent the experience of a single-center and may not be generalized in reference to other areas with different epidemiological or clinical settings.

5. Conclusion

The study attempts to show our first-hand real, original experiences in this field and to provide useful information. In practice, clinicians should maintain a high index of suspicion for PLA in patients who present with the risk factors; in particular, hepatic-pancreatic-biliary system pathologies, and clinical scenarios of fever, right abdominal pain, increased levels of C-reactive protein and white blood cell count. Prompt diagnosis of liver lesion and administration of antibiotics and percutaneous drainage can conduce to successful treatment.

Author contributions

Conceptualization: Cristina Serraino, Luigi Maria Fenoglio.

Data curation: Cristina Serraino, Christian Bracco, Gianluca Rinaldi.

Formal analysis: Chiara Elia, Remo Melchio.

Methodology: Remo Melchio.

Supervision: Fulvio Pomero, Alberto Silvestri, Luigi Maria Fenoglio.

Writing – original draft: Cristina Serraino, Chiara Elia.

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