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FULL PAPER

The challenge of infectious diseases consultations in the emergency department: an Italian nationwide survey

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SUMMARY

Diagnosis and management of infectious diseases (ID) at the emergency department (ED) are challenging due to the peculiar setting and the available diagnostic tools. The involvement of an ID consultant has been described to improve clinical outcomes and antimicrobial stewardship (AMS) programs.
An online survey was sent to 100 Italian Departments of Infectious Diseases affiliated with the Italian Society of Infectious Diseases and Tropical Medicine (SIMIT).
The primary objective of our study was to describe the characteristics of ID services in Italian EDs to identify possible challenges and shortcomings and provide tips to improve the management of patients. Secondary objectives included the evaluation of diagnostic capability and the management of patients with suspected or confirmed ID.
Seventy-six out of the 100 SIMIT centers, 32 (42.1%) of which were teaching hospitals, answered the survey. In 62 (82.7%) centers, consultations were performed by the IDs specialist on call. In 29 (38.2%) centers, there was a formal AMS program, and 32 (42.7%) had protocols for antibiotic use in the ED. Microbiological tests to be performed before starting antibiotic treatment in the ED were clearly defined in 44 (57.9%) hospitals.
This survey highlighted several challenges in the current organization of ID consultations in Italian EDs.

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INTRODUCTION

How can infectious diseases (ID) consultations in the emergency department (ED) be improved in quality and efficacy? The heterogeneous clinical presentation of ID at the ED can be challenging in terms of diagnosis and treatment. Indeed, the choice of the

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most appropriate diagnostic tools and treatment, considering the increasing rate of antimicrobial resistant bacteria, have led to growing demand for ID consultancy (Kawamura *et al.*, 2015; Hamandi *et al.*, 2014; Farmakiotis *et al.*, 2015; Yapar *et al.*, 2006).

The role of ID consultants is the key to improve clinical management of patients with a suspected ID (Vehreschild *et al.*, 2013; Fariñas *et al.*, 2012; Kerremans et al., 2012; Sellier *et al.*, 2009): a significant reduction of 30-day mortality and clinical failure of patients with *Staphylococcus aureus* bacteremia and infective endocarditis have been observed (Hadano *et al.*, 2021; Abraham *et al.*, 2020; Kawasuji *et al.*, 2019; Sherbuk *et al.*, 2019; Okura *et al.*, 2021) after establishment of ID consultation. Similar results were shown for patients with enterococcal bacteremia, candidemia, and septic shock (Kawamura *et al.*, 2015; Kaya *et al.*, 2021; Kobayashi *et al.*, 2020; Mohr *et al.*, 2020; Madaline *et al.*, 2019; Mejia-Chew *et al.*, 2019; Conant *et al.*, 2016).

Implementation of an ID consultant service in the ED resulted in a reduction of 14-day mortality in case of severe sepsis or septic shock (Viale *et al.*, 2017).

Moreover, the involvement of an ID specialist in antimicrobial stewardship (AMS) programs is associated with reduction in antibiotic consumption and optimized antibiotic use (Bouchet *et al.*, 2020; Mani *et al.*, 2021; Kishida *et al.*, 2020; Tagashira *et al.*, 2016; Jump *et al.*, 2012; Menichetti *et al.*, 2018; Falcone *et al.*, 2019). The implementation of AMS strategies in the ED may improve appropriate antibiotic prescribing, promote beneficial collaborative relationships between ID specialists and ED colleagues, and reduce unnecessary admissions to medical wards. In the ED, the ID consultant frequently deals with issues regarding available diagnostic tools and treatments, which can be different from those encountered in ID outpatient services or ID wards. Due to the unavailability of culture results, antimicrobial susceptibility tests, serological and molecular tests that can support the initial clinical evaluation, diagnoses in the ED are typically presumptive, and therefore seeking the advice of an ID specialist may be strongly recommended. Unfortunately, the daily presence of ID consultants in the ED and the availability of microbiological diagnostic tools 24 hours a day/7 days a week (24/7) are not guaranteed in every hospital, depending on local resources and organization (Sexton, 1991).

The Coronavirus Disease-19 (COVID-19) pandemic posed further challenges to ID management in the ED. In particular, ID consultants had a key role in deciding for hospitalization, giving indications for home care, and limiting irrational use of antibiotics (Giacomelli *et al.*, 2021; Nguyen *et al.*, 2020; Abelenda-Alonso *et al.*, 2020).

The aim of the present study is to evaluate the current organization of ID services and diagnostic and therapeutic tools available in Italian EDs. The present survey was encouraged by the limited available evidence on the role of ID specialists in ERs in Italy. We also aimed to provide some essential suggestions to overcome this gap and improve ID consultations in the ED.

MATERIALS AND METHODS

Study design

This is an observational study conducted through an anonymous web-based survey. The survey was designed according to methodological recommendations for surveys (Pulcini *et al.*, 2016). In particular, we specified the design of the study ("nationwide survey") in the title and abstract, defined clear and relevant questions, and presented the results with reference to the study objectives. The sample selection and the method used for data analysis are specified in the following paragraphs.

Setting and sampling strategy

We inquired about Italian hospitals whose ID Departments are affiliated with the Italian Society of Infectious Diseases and Tropical Medicine (SIMIT). Both teaching (university) and non-teaching hospitals were invited to participate. The survey was conducted from November 9, 2020 to the December 9, 2020. The survey was sent by e-mail to all SIMIT members.

Participants

For each center, only one ID physician serving as a consultant in the ED was invited to respond to the survey.

Outcomes

The primary outcome was to evaluate the current characteristics of ID consultations in the ED (number of ID consultations performed per year, employment of an ID specialist for consultations in the ED, organization of follow up service, and related issues).

Secondary outcomes were:

1) to describe the number of AMS programs in the ED;
2) to describe the available diagnostic tools for specific IDs in the ED;
3) to evaluate the management paths for patients with suspected or confirmed infectious diseases followed by ID consultants in the ED (availability of rooms for respiratory isolation, possibility to increase the number of hospital beds in case of an epidemic caused by emerging pathogens, and related issues);
4) to evaluate the possibility to perform clinical trials in the ED for ID consultants.

Survey design

The questionnaire was designed with closed-ended questions and is available here as Supplementary

Material (*Tables S1-S4*). It was pre-tested at the coordinating site for clarity and technical functionality. The questionnaire included 66 items, divided into 9 sections. The nine sections of the survey were:

I) Demographic information of the ID specialist filling in the survey (two questions);
II) Characteristics of the hospital (sixteen questions);
III) AMS programs in the hospital (twelve questions);
IV) Travel medicine (four questions);
V) Management of contagious patients in the ED (five questions);
VI) Virological diagnostic capability (eleven questions);
VII) Bacterial diagnostic capacity (nine questions);
VIII) Laboratory diagnostic capability at the ED (four questions);
IX) Clinical trials at the ED (two questions).

Ethical approval and informed consent

This study was designed as a service evaluation.
No informed consent was needed due to the absence of sensitive information or patients' data. No ethical approval was needed due to the nature of the data. No remuneration was provided to participants.

Survey administration and response rate

The online survey was distributed to 100 SIMIT-affiliated centers. Response rates were calculated as the number of hospitals from which an answer was recorded/total number of participating hospitals. Information on hospital name and country was used to screen for duplicate entries, but all data remained anonymous and it was not possible to link the participant physicians to the given answers.

Statistical analysis

An ad hoc electronic form was adopted to collect the data. Categorical variables were reported as absolute and relative frequencies, whereas continuous variables as means (± standard deviations) or medians (interquartile ranges, IQR), depending on their normal distribution. Continuous variables were compared by the Student t-test or the Mann-Whitney U-test, as appropriate. Categorical data were compared using the chi-square test or Fisher exact test.
A comparison between the responses collected from teaching and non-teaching hospitals was performed. A two-tailed p-value (p) less than 0.05 was considered statistically significant.
Given the lack of pre-study estimates for the outcome of interest, it was not possible to formulate the assumptions for sample size determination.
All statistical computations were performed with the statistical software STATA version 14 (StatsCorp, Texas, US).

RESULTS

Seventy-six out of the 100 sites responded to the invitation and filled in the questionnaire (response rate: 76%), with 42 (57.9%) non-teaching hospitals. Full details of survey items are presented in *Tables S1-S4*.

Section I - Demographic information of the ID specialist filling in the survey

ID specialists answering the survey had a median age of 40 (IQR 34-51). Forty (52.6%) were male. The geographical distribution of the hospitals (34 teaching hospitals, 42 non-teaching hospitals) is shown in *Figure 1*. Centers from 17 out of 20 Italian regions answered the survey. The majority of data were retrieved from Northern Italy (57.9% participating centers), followed by Southern Italy and Islands (22.4%) and Central Italy (19.7%).

Section II - Characteristics of the Hospital

Seventy-one out of 76 (93.4%) participants reported a median (IQR) of 600 (360-900) hospital beds. The median (IQR) number was higher in teaching (775 (600-1,200)) than in non-teaching hospitals (450 (350-600); p: 0.0002). Seventy-three (96.1%) ID consultants worked in a hospital where the ED was present, and all of them regularly performed ID consultations there. Forty-seven out of 74 (63.5%) hospitals had a neurosurgical ward, 34/74 (46%) a cardio-surgical ward, 49/74 (66.2%) a hematology ward,

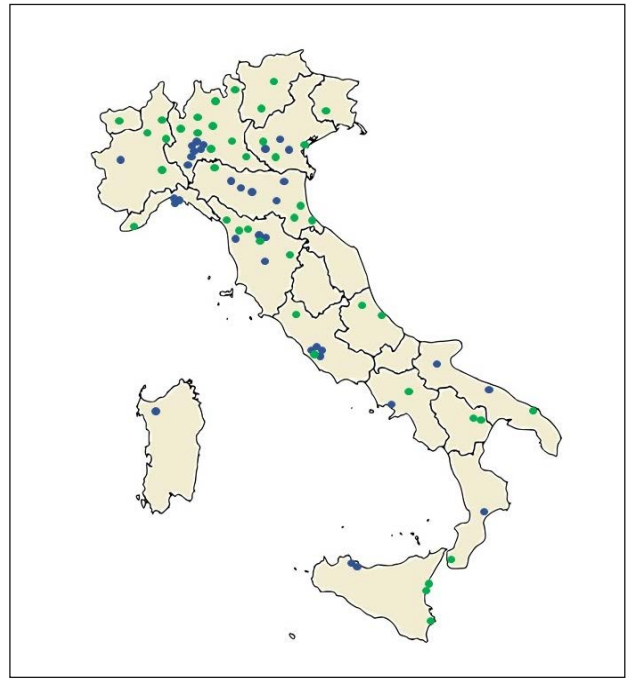

Figure 1 - Geographical distribution of the hospitals included in the survey. *Thirty-four teaching hospitals (blue dots) and 42 non-teaching hospitals (green dots) answered the anonymous web-based survey.*

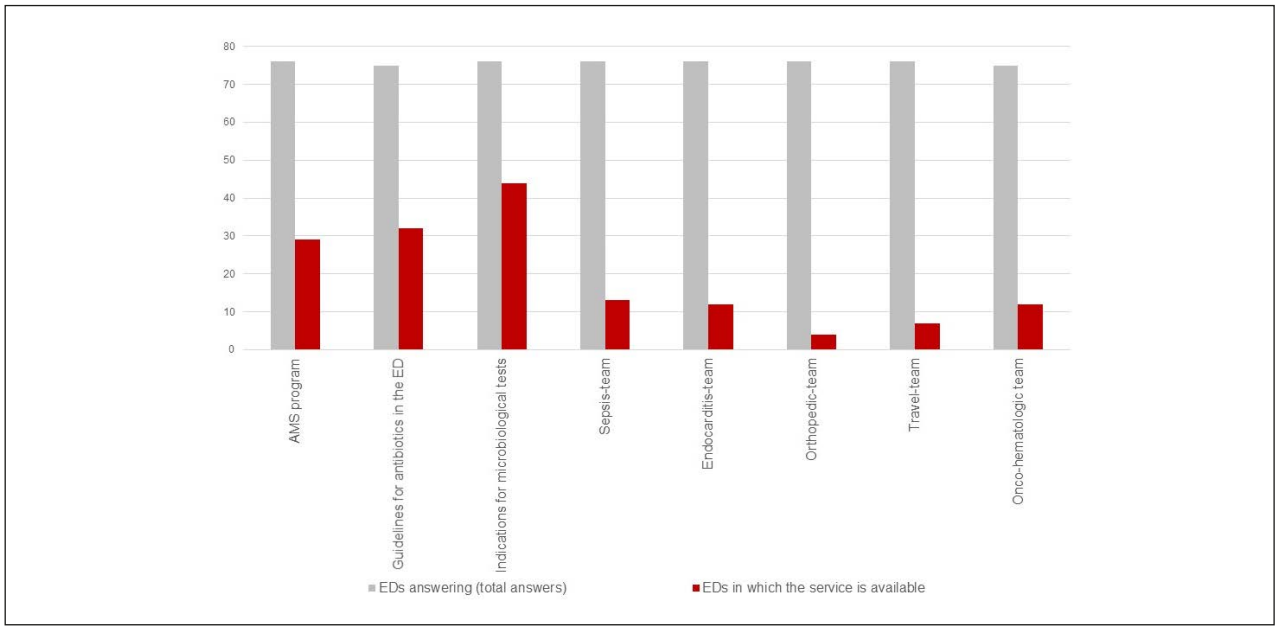

Figure 2 - Antimicrobial stewardship programs and Healthcare services in the participating Hospitals. *Clearly-defined AMS programs were reported in 29 (38.2%) hospitals. Full application of guidelines for the use of antibiotics in the ED was reported by 32 (42.7%) ID consultants. Forty-four (57.9%) EDs had formal indications on fundamental microbiological tests to be performed before starting antibiotic treatment. Specialistic healthcare teams (sepsis-team, endocarditis-team, orthopedic-team, travel-team, onco-hematologic team) were reported in less than 20% of participating hospitals. Percentages are calculated on the total number of answers given to each question. AMS: antimicrobial stewardship; ED: emergency department; ID: infectious diseases.*

74/74 (100%) an orthopedic ward, 24/74 (33.8%) a solid organ transplantation team, and 68/74 (91.9%) a pediatric ward. The neurosurgical, cardio-surgical, and solid organ transplantation wards were more frequently present in teaching hospitals, reaching statistical significance (p: 0.001 for neurosurgery and p<0.0001 for the other two units). The ID ward was present in 69 (90.8%) hospitals, with a median (IQR) number of 30 (22-40) hospital beds for teaching hospitals and 18 (14-23) for non-teaching hospitals (p: 0.0001). The ID specialist on call was in charge of ID consultation in ED for 62/75 (82.7%) sites. The ID consultant was specifically employed in the ED in 22 (29%) participating centers and in 17 (77.3%) the ID consultant was present 24/7. An ID or pediatric ID specialist was in charge of pediatric ID consultancies in 15/73 (20.6%) EDs, with a difference between teaching and non-teaching hospitals (p: 0.03). A median (IQR) of 42,468 (3,500-70,000) patients presented to the ED in 2019, and median (IQR) number of ID consultations was 1,100 (450-2,000). A median (IQR) of 5 (3-10) consultations per day was reported. An ID outpatient follow-up service was available in 32/75 (42.1%) hospitals.

Section III - AMS programs in the Hospital

Formal AMS programs (which should always include the definition of an antimicrobial stewardship team, collaboration between physicians, pharmacy and therapeutics committees, and administrative support to measure and track antimicrobial prescription) (Mendelson *et al*., 2020; Dellit *et al*., 2007) were reported in 62.5% of teaching and 20.5% of non-teaching hospitals (p<0.0001). Thirty-two out of 75 (42.7%) EDs followed local protocols for the use of antibiotics. Twenty-one (27.6%) sites reported the use of an online platform to check antimicrobial therapy from hospital wards. Prescription of antibiotics on an online platform was present only in 17 (22.4%) hospitals.

A flow chart indicating the microbiological tests to be performed before starting antibiotics was available in 44 (57.9%) EDs.

"Infection-teams" for the management of frequent and life-threatening infections have been set up in <20% of hospitals. Significant differences were observed between teaching and non-teaching hospitals for "sepsis-team" (p: 0.01), "orthopedic-team" (p: 0.03) and "onco-hematology infection team" (p: 0.02) (*Figure 2*).

Section IV - Travel medicine

Diagnosis of malaria relied mostly on rapid tests, which were available in 58/70 (82.9%) EDs. Thin and thick blood smears were performed in 41/70 (58.6%) and 35/70 (50%) EDs, respectively. Other less fre-

quently used diagnostic tools for malaria included loop-mediated isothermal amplification (LAMP), available in 4/70 hospitals, and quantitative buffy coat test (QBC), available in 2/70 hospitals. Polymerase chain reaction (PCR) for the diagnosis of Dengue, Zika, and Chikungunya infections was available in 14/74 (18.9%) EDs, whereas Dengue NS1 rapid antigen test was available in 10/74 (13.5%) EDs. Fecal samples were accepted 24/7 by laboratories for stool culture in 30/75 (40%) hospitals.

Section V - Suspected contagious patients in the ED

60/75 (80%) participants reported the availability of a formal emergency plan in case of highly contagious infections. Formal emergency plans increasing the availability of hospital beds during seasonal influenza and in case of epidemics were reported by 41/73 (56.2%) and 34/74 (46%) ID consultants, respectively.

Section VI - Virological diagnostic capacity at the ED

Rapid or serological tests for HIV were available in 51/74 (68.9%) EDs, and in 29/49 (59.2%) of them the result was available 24/7. Nasopharyngeal swabs for RSV or seasonal influenza virus could be performed in 38/74 (51.4%) and 49/74 (66.2%) EDs, respectively (*Figure 3*).

SARS-CoV-2 diagnostic capacity at the ED

Nasopharyngeal swab for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was available 24/7 in 72/74 (97.3) EDs. Serological test for SARS-CoV-2 was available 24/7 in 40/75 (53.3%) EDs. Twenty-nine participating consultants specified which serological test for SARS-CoV-2 was in use in their EDs: enzyme-linked immunosorbent assay (ELISA) and chemiluminescence sandwich-immunoassay (CLIA) were reported by 22/29 (75.9%) and 5/29 (17.2%) participating hospitals, respectively. One physician reported a combination of CLIA plus ELISA. One consultant reported a combination of a rapid test with a quantitative serological test.

Section VII - Bacterial diagnostic capacity at the ED

Blood cultures could be performed in 70/75 (93.3%) EDs. Nasal swab for methicillin-resistant *S. aureus* (MRSA) and rectal swab for MDR Gram-negatives and vancomycin-resistant *Enterococcus* spp. were available in 38/75 (50.7%), 41/74 (55.4%) and 27/73 (37%) EDs, respectively. Detection of *M. tuberculosis* in sputum by molecular and acid-fast coloration was available in 43/74 (58.1%) EDs. The possibility of testing for urinary antigens for *Legionella* spp. and *S. pneumoniae* was reported in 53/74 (71.6) EDs. Detection of pathogens typically involved in central nerv-

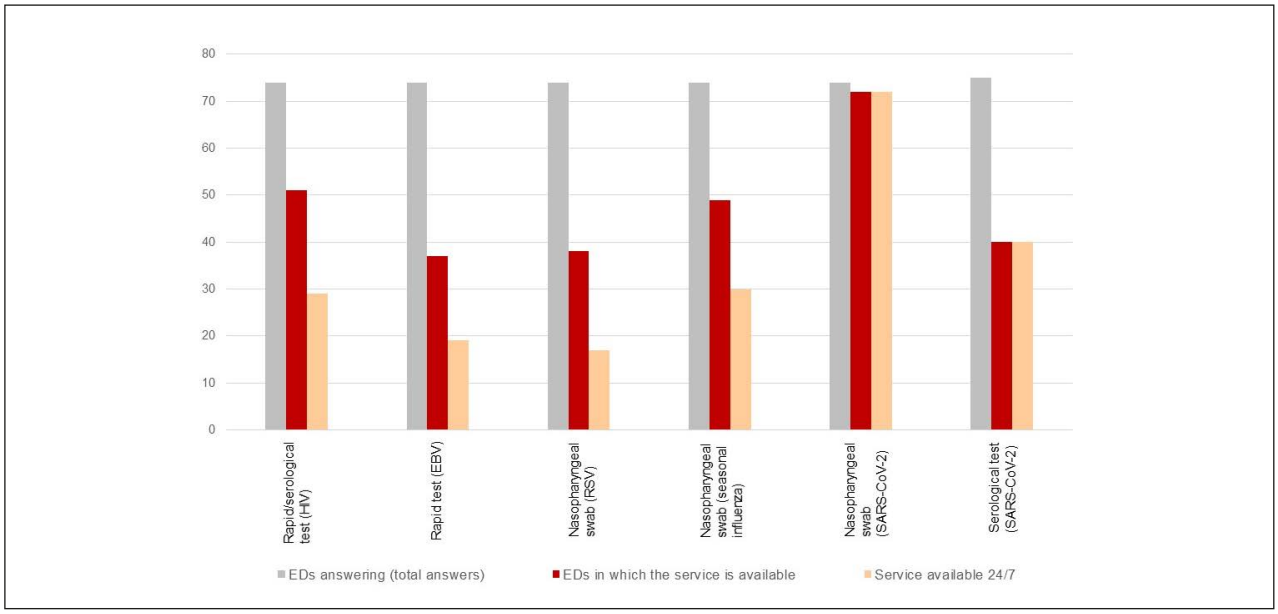

Figure 3 - Virological diagnostic capability at the Emergency Department. *Rapid or serological tests for HIV could be performed at the ED of 51 (68.9%) hospitals. Thirty-seven (50%) and 38 (51.4%) EDs reported the possibility to perform MonoTest and nasopharyngeal swab for RSV, respectively. Nasopharyngeal swab for seasonal influenza was performed in 49 (66.2%) EDs. All these tests were not available 24/7 in most EDs. With regard to the pandemic at the time the survey was conducted, nasopharyngeal swabs for the detection of SARS-CoV-2 and serological tests for SARS-CoV-2 were performed in 72 (97.3%) and 40 (53.3%) EDs, respectively. Percentages are calculated on the total number of answers given to each question. HIV: Human Immunodeficiency Virus; EBV: Epstein-Barr Virus; RSV: Respiratory Syncytial Virus; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; ED: emergency department.*

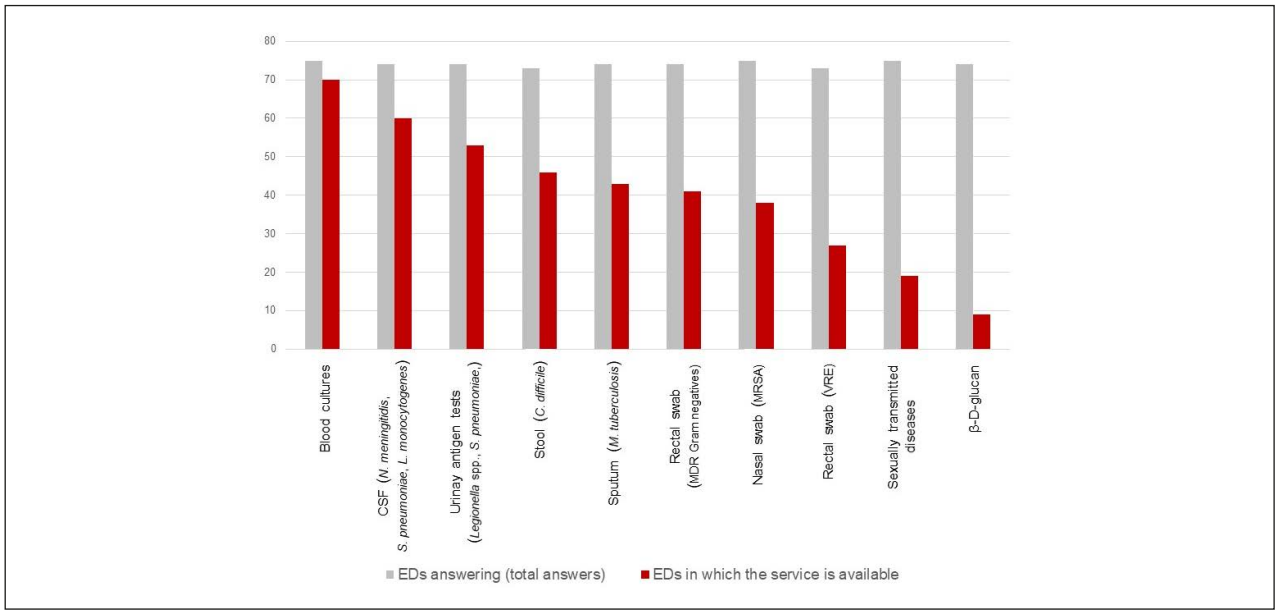

Figure 4 - Bacterial and fungal diagnostic capability at the ED. *The possibility to perform blood cultures in the ED was reported by 70 (93.3%) hospitals. Molecular tests to detect N. meningitidis, S. pneumoniae and L. monocytogenes on CSF were available in 60 (81.1%) EDs. Urinary antigen tests for Legionella spp. and S. pneumoniae were available in 53 (71.6%) EDs. C. difficile test on stool was available in 46 (63%) EDs. M. tuberculosis in sputum could be investigated in 43 (58.1%) EDs. Surveillance swabs could be performed in 37%-55% participating EDs. The possibility to test for sexually transmitted diseases was reported by 19 (25.3%) ID consultants. With regard to fungal diagnostic capability, 9 (12.2%) EDs reported the possibility to test for β-D-glucan from venous blood. Percentages are calculated on the total number of answers given to each question. MRSA: methicillin-resistant Staphylococcus aureus; MDR: multidrug-resistant; VRE: vancomycin-resistant Enterococcus spp.; CSF: cerebrospinal fluid; ED: emergency department.*

ous system infections (*N. meningitidis*, *S. pneumoniae*, *L. monocytogenes*) was performed with PCR on cerebrospinal fluid (CSF) in 60/74 (81.1%) EDs. Molecular tests for the detection of *C. difficile* and sexually transmitted pathogens (e.g., HIV, *C. trachomatis*, *N. gonorrhoeae*) were reported in 46/73 (63%) and 19/75 (25.3%) EDs, respectively (*Figure 4*).

Section VIII - Laboratory diagnostic capability at the ED

Blood count at bedside at the ED was available in 72/75 (96%) hospitals, whereas dosage of C-reactive protein and procalcitonin in 75/75 (100%) and 63/75 (84%) EDs, respectively. Dosage of β-D-glucan was reported from 9/74 (12.2%) participants.

Section IX - Clinical Trials at the ED

We investigated if there were ongoing clinical trials in the EDs of the participating centers. In particular, we addressed trials run by ID specialists and/or ED specialists about ID. Forty out of 71 (56.3%) hospitals reported the possibility of carrying out clinical trials in the ED setting, but only 13/67 (19.4%) reported ongoing clinical trials at the time the survey was completed.

DISCUSSION

This is the first Italian national survey investigating the organization of ID consultations in the ED of hospitals. Our study showed both strong and weak points of the current organization.

First, AMS programs were not clearly defined in all participating EDs, and informatic services can be enhanced in many EDs in order to ease the consultation of ongoing medications and laboratory findings. Second, although most EDs had formal emergency plans, these often did not include the possibility of increasing the number of hospital beds. Third, investigation of laboratory diagnostic capability showed some limits, with particular regard to fungal diagnostic tests and surveillance swabs. Finally, our survey highlighted statistically significant differences between teaching and non-teaching hospitals for several items. This can be partially explained by the fact that teaching hospitals usually receive more funds and their diagnostic capability and overall organization is enhanced compared to non-teaching hospitals.

We highlighted organizational aspects of ID consultation in ED that could be generally improved and issues that would make ID consultations more effective.

Six suggestions to improve organizational aspects

- At least one ID consultant should be dedicated to the ED (71% of EDs do not formally have a consultant), better if officially employed and not on call.
- The number of ID consultations in the ED should be computed (77.6% cannot estimate).
- Implementation of information technology to keep track of medical records and antibiotic therapy is needed (online platforms are used for medical records in 60% and for antimicrobial therapy in 27.6% of hospitals).
- AMS programs and clear recommendations on microbiological tests to be performed before starting antimicrobial treatment are needed (they are lacking in 57.3% and 42.1% of EDs, respectively).
- "Infection-teams" for frequent and life-threatening infections should be regularly active (82.9% of hospitals do not have a "sepsis-team"). Specific services such as endocarditis-team should be implemented in reference hospitals with a cardiac surgery team (they are present in less than 16% of hospitals).
- Formal emergency plan in case of epidemic/pandemic is a key point in the ED organization (20% do not have any plan and 54% do not have a formal plan to increase the number of hospital beds in case of emergency).

Tailoring AMS programs in the ED (e.g., local epidemiology, type of patients, available antibiotics for empiric therapy) is an essential element for successful AMS programs (May *et al*., 2020). AMS programs and guidelines for the management of patients with confirmed or suspected infectious diseases should be clearly defined and shared by both ID specialists and ED physicians, in order to ensure a coherent approach to these patients.

The number of ID consultations and the type of infectious diseases should be considered to assess the cost-effectiveness of ID consultants specifically employed in the ED.

In addition, while the training course to become an ID specialist is clearly defined (a four-year postgraduate course), in Italy there is not an official training period for physicians willing to become part of the "infection teams" we investigated in our survey. This depends on each hospital organization, on the area of specialization of the physicians employed, and on the cost-effectiveness of the teams. The definition of a nationally standardized training course is likely to make "infection teams" more effective.

Five suggestions to make ID consultations more effective

- Increase diagnostic capability for HIV, EBV, RSV, seasonal influenza virus (diagnostic tools for these infections are available 24/7 in 44.7%-62.5% of hospitals).
- Upgrade diagnostic tools for imported diseases in ED to give timely and appropriate diagnosis to returning travelers, migrants and expats (only 18.9% of EDs have 24/7 availability of molecular test for Dengue virus, Zika virus and Chikungunya virus; thin and thick blood smears to diagnose malaria were performed in less than 60% of EDs).
- Increase diagnostic capability for colonization by MDR microorganisms (nasal swab for MRSA is available in 50.7% of EDs, rectal swab for MDR Gram negative bacteria in 55.4% of EDs and rectal swab for VRE in 37% of EDs).
- Enhance the possibility to dose β-D-glucan from venous blood in hospitals with a high flow of patients with suspected invasive fungal infections (this is possible only in 12.2% of hospitals).
- Improved patient isolation in case of contagious/highly contagious IDs or MDR microorganism colonization is recommended.

Finally, the possibility of carrying out clinical trials on infectious diseases in EDs was reported in only 56.3% of participating centers. Enhancing the possibility to perform clinical trials in EDs may be of great importance. Although performing clinical trials in EDs may be challenging, the ED is a unique setting for clinical trials. As a matter of fact, identification of patients in the early phase of an infectious disease when no other previous therapy has been administered may reduce potential bias. Moreover, the ED is the most appropriate setting to recruit patients for trials on septic shock. The presence of an ID consultant dedicated to the ED may allow the successful implementation of clinical trials in this setting.

Limitations

A number of limitations should be addressed. First, the survey was conducted only in SIMIT-affiliated hospitals with a relatively high proportion of teaching hospitals. Thus, it is not generalizable to settings where ID services are absent. Second, although only three regions did not participate in the survey, a north-to-south lower response gradient was observed. Third, a number of respondents were not able to answer several questions. Finally, the survey was conducted at the time of the "second COVID-19 pandemic wave". This resulted, on the one hand, in limited availability of ID consultants to answer due to time constraints and, on the other, in partially different organizational issues.

The main strength of the survey is its user-friendly interface (web-based survey), which allowed a high response rate (76%) despite the dramatic pandemic situation.

Our survey also gives way to further studies. In fact, our study did not investigate the organization of ID consultations in Eds in other countries, so little is

known about the gaps that remain internationally or about good organizations that could be an example for other countries.

CONCLUSIONS

Our survey highlighted the strengths and weaknesses of the current organization for ID consultations in Italian EDs, offering recommendations to improve the organization and make ID consultations more effective. An under-implementation of AMS programs challenging the efficacy of ID consultations was observed, with a worrisome low percentage of hospitals with formal guidelines for both microbiological test indication and empirical antimicrobial treatment. This gap was particularly evident in non-teaching hospitals. Our data reveal the need for urgent implementation of information technology for antimicrobial prescription and implementation of AMS principles in the EDs, which have been demonstrated to improve patient care.

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