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The challenge of COVID-19 for a Clinical Microbiology Department

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ABSTRACT

Objectives: To quantify the workload and cost overload that the COVID-19 pandemic has meant for a Clinical Microbiology laboratory in a real-life scenario. *Methods:* We compared the number of samples received, their distribution, the human resources, and the budget of a Microbiology laboratory in the COVID pandemic (March–December 2020) with the same months of the previous year. *Results:* the total number of samples processed in the Clinical Microbiology laboratory in March to December 2020 increased 96.70% with respect to 2019 (from 246,060 to 483,993 samples), reflecting an increment of 127.50% when expressed as samples/1000 admissions (from 6057 to 13,780). The increase in workload was mainly at the expense of the virology (+2058%) and serology (+86%) areas. Despite additional personnel hiring, the samples processed per technician increased 12.5%. The extra cost attributed to Microbiology amounts to 6,616,511 euros (114.8%). *Conclusions:* This is the first study to provide quantitative figures about workload and cost increase caused by the COVID-19 in a Microbiology laboratory.

1. Introduction

In a very short period of time, Clinical Microbiology Departments had to adapt their structure to respond to an unprecedented massive diagnostic demand of a new disease (COVID-19) (Fang et al., 2020). However, up to the present time, we were not able to find reports quantifying the change for Clinical Microbiology Departments in aspects like variation in type of samples, human resources and cost. This paper compares the workload of the pandemic in our Microbiology Department (March–December 2020) with the same period of time of the previous year. We evaluate changes in samples submission, in personnel and in laboratory budget. We hope that our experience can be useful for other laboratories planning how to deal with possible future epidemics.

2. Material and methods

Setting: The Hospital General Universitario Gregorio Marañón (HGUGM) is a public tertiary and reference hospital in Madrid, Spain. The hospital attends a population of 350,000 inhabitants and, in normal circumstances, the Microbiology Department processes more than 300,000 samples per year. We report the activity of the Microbiology Department during the coronavirus pandemic in our country (March–December 2020), as compared to the same months in 2019. The data were obtained from the laboratory records.

Introduction of PCR techniques for SARS-CoV-2 PCR: When the first cases of COVID-19 were detected in Italy, 4 hospital laboratories in Madrid, including ours, prepared for performing SARS-CoV-2 PCR. We started performing PCRs at the end of February, 2020. Our laboratory had to use different RT-PCR systems. We started with the Light-Mix® Modular SARS-CoV (COVID19) E-gene (®Roche, Berlin, Germany) and with Applied Biosystems™ TaqMan™ 2019-nCoV Assay Kit v1 (ThermoFisher Scientific). In April we used simultaneously the Novel Coronavirus (2019-nCoV) Nucleic Acid Diagnostic

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Kit (PCRFluorescence Probing) S3103E by Sansure Biotech Inc. and GeneFinder™ COVID-19 PLUS RealAmp Kit (Korea). We also used RT-PCR TaqPath COVID-19 Multiplex Diagnostic Solution (ThermoFisher for), the Detection kit for 2019 Novel Coronavirus (2019-nCoV) RNA (PCR Fluorescence Probing), Daan Gene Co., Ltd. Of Sun Yat-Sen University and the Abbott Realtime SARS-C0V-2 assay. Finally, the GeneXpert PCR (Cepheid, California, USA) was incorporated and reserved for urgent results and for pooling.

As for nucleic acid extraction we used NUCLISENS® EASYMAG® and EMAG® by bioMérieux, VERSANT kPCR Molecular System KPCR, Siemens, Abbott M2000 System and KingFisher Flex by ThermoFisher Scientific.

For RT-PCR amplifications, Stratagene qPCR and QuantStudio 5 (Thermofisher Scientific) Real-Time thermocyclers as well as the automated Infinity GeneXpert device (Cepheid) were used.

The main diversity of techniques occurred specially in the first months of the pandemic coinciding with the greatest shortage of products on the market. Except for the very earliest start, when RUO tests were used, we have always used CE marked systems. Multiplex kits or combinations of singleplex kits have been always used, so samples were considered positive when at least 2 different targets were amplified. The runs always included positive and negative controls provided by the corresponding manufacturers, as well as laboratory own controls consisting of previously characterized, diluted and aliquoted samples. From May to June 2020 we preferentially used the TaqPath system by ThermoFisher, using the KingFisher as extraction system and QuantStudio-5 as Thermocycler as a standard technique and GeneXpert system by Cepheid on its platform Infinity as a rapid system. The latter, due to its higher price and its limitation for processing large numbers of samples at once, was used only when a very fast result was required, patients in the emergency room, imminent deliveries or preparation for unscheduled and urgent procedures.

Evaluation of laboratory samples: The workload of the laboratory was reported as samples processed per day, samples/1000 admissions and samples/100,000 inhabitants. Overall received samples and samples in each area of the laboratory were analyzed.

Serological testing: Detection of IgGs anti-SARS-CoV-2 was incorporated at our laboratory in mid-April. The Architect SARS-CoV-2 assay (Abbott, Illinois, USA) was used for such purpose.

Evaluation of the human resources requirements and of the laboratory budget: The variables for assessment the number of staff required during the pandemic were: number of persons (staff and technicians) working each day and number of samples per technician day. These were provided by the human resources department of the hospital.

The laboratory department budget was provided by the financial department of the hospital.

Ethics: The study was approved by the local Ethics Committee (code MICRO.HGUGM.2020-028).

Statistics: Contingency tables were statistically analyzed by means of exact Fisher exact test, and Mann-Whitney's *U* test was used with numerical variables.

3. Results

3.1. Overall number of samples

Table 1 summarizes the total number of samples processed in the Clinical Microbiology laboratory in both study periods. In the period March to December 2020 samples increased 96.70% with respect to 2019. The number of samples processed per day (including weekends) also raised 96.70%. A very significant increase was also observed in terms of number of samples per 1000 admissions (+127.50%) or samples per 100,000 inhabitants (+96.70%).

Fig. 1 shows the distribution of samples received in the different areas of the laboratory. The increase in workload was mainly at the expense of virology (2058.21%) and serology (84.07%). As for the other areas of the laboratory, all reduced their number of samples processed ranging from 1% (epidemiological surveillance samples) to 34% (genital tract samples). Activities different to the attention to COVID patients were clearly reduced in the Hospital including those related to surgery.

Table 1
Comparison of the workload in the Microbiology laboratory during March–December 2019 vs. March–December 2020 (COVID-19 pandemic).

	Mar–Dec 2019	Mar–Dec 2020	Difference
Hospital admissions	40,622	35,122	
Samples received in the Microbiology laboratory	**246,060**	**483,993**	+96.70%
Samples per day	806.75	1586.86	+96.70%
Samples/1000 admissions	6057.30	13,780.33	+127.50%
Samples per 100,000 inhabitants	70,302.85	138,283.71	+96.70%
Distribution of samples in the laboratory areas[a]			
Virology	11,523 (4.68 %)	248,691 (47.71%)	+2058.21%
Serology	48,340 (19.65%)	88,981 (17.07)	+84.07%
Respiratory samples and IV catheters	13,672 (5.56%)	11,746 (2.25%)	-11.09%
Epidemiological samples	9518 (3.87%)	6427 (1.81%)	-0.96%
Blood cultures	33,275 (13.52%)	29,703 (5.70%)	-10.73%
Urine cultures	51,607 (20.97%)	38,736 (7.43%)	-24.94%
Fungal cultures	8445 (3.43%)	5939 (1.14%)	-29.67%
Genital tract cultures	7777 (3.16%)	5132 (0.98%)	-34.01%
Mycobacterial cultures	44,438 (4.65%)	8798 (1.69%)	-23.08%
		7582 (1.45%)	-19.08%
Other exudates	9370 (3.81%)		
Other samples	41,095 (16.70%)	29,258 (6.05%)	-28.82%
Microbiology personnel			
Hired staff	17	20[b]	+15.5%
Microbiology technicians (average)	25	35,8	+43.2%
Cost of the Microbiology department	5,763,192€	12,379,703€	+114.8%
Personnel	3,247,436€	3,766,540€[c]	+15.9%
Laboratory material	2,515,756€	8,613,163€	+242.3%

[a] All differences in the distribution of samples were statistically significant with $P < 0.0001$.
[b] About 5973 extra hours were also hired for staff and residents, besides the new staff.
[c] About 385,343€ euros were dedicated to personnel hiring and extended shifts in March–December 2020 for the COVID-19 pandemic.

3.2. SARS-CoV-2 laboratory workload

The HGUGM processed a total of 237,015 samples for SARS-Cov2 PCR and 57.389 samples for SARS-CoV-2 IgG testing from March to December 2020. These samples accounted for 56.5% (45.5% and 11%, respectively) of the Microbiology samples during the 10 months of the study period.

Average turnaround times during the study period were 6.7 hours for PCR (ranging from 1.3 hours to 8.1 hours) and 1.4 hours for antibody testing (range, 57 minutes to 1.9 hours).

3.3. Workload for the laboratory staff and technicians

The number of laboratory technicians hired for our laboratory increased from 25 in 2019 to an average of 38.8 in March to

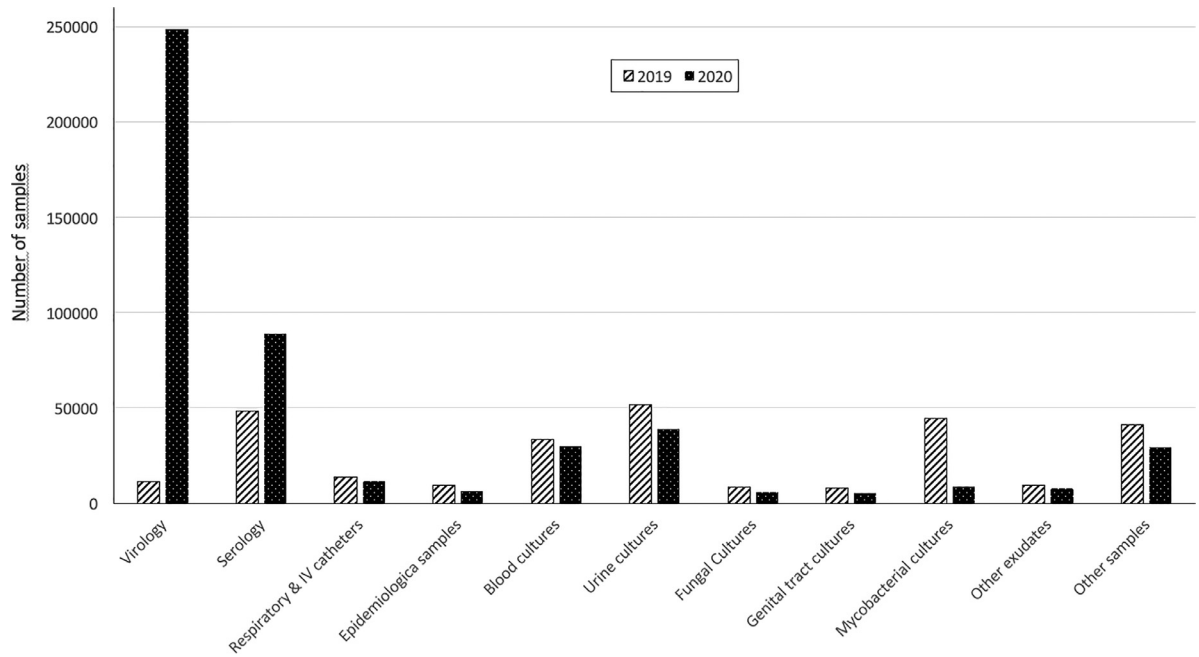

Fig. 1. Evolution of the samples received by the different areas of the Microbiology laboratory during March–December 2019 (Controls) vs. March–December 2020 (COVID pandemic). "Other samples" correspond to bacterial and viral (other than SARS-CoV-2) molecular diagnostic, stool cultures, antibacterial drug levels, Tuberculosis skin tests, epidemiology surveillance samples, and *C. difficile* and hepatitis testing.

December 2020. The number of samples processed per technician's day raised 12.5% despite the increase in hired personnel.

Staff was reinforced with the hiring of 3 clinical microbiologists (staff increased from 17 to 20) and with 5973 over hours during the study period. Extended shifts were distributed in 3307 for staff (10.8 extra hours/day) and 2666 for residents (8.7 extra hours/day). Research staff (7 persons) also helped in COVID-19 diagnosis during these months.

3.4. Laboratory materials and personnel budget

Overall, the Microbiology department costs increased 6,616,511 euros (114.8%). Of these, 519,104 euros were allocated to personnel hiring and extended shifts, and the rest to laboratory materials (+242%; from 2,515,756 to 8,613,163 euros). The most expensive items were: PCR reagents (60%), reagents for SARS-CoV-2 IgG detection (12%), SARS-CoV-2 extraction and purification (8%), and nasopharyngeal sampling swabs and transport media (15%).

4. Discussion

Our results reflect the enormous adaptation challenge that Microbiology laboratories had to tackle in a very short period of time to provide the diagnosis of a new disease within a worldwide epidemic. In 3 months, the samples received in the laboratory increased by 96.70%, work shifts were amplified, and need of procurement of diagnostic material in a very competitive market resulted in an excess expense of more than 6 and a half million euros in 10 months.

Several articles have been published analyzing adaptations required in emergency, radiology, and intensive care departments (Ashari et al., 2020; Wee et al., 2020; Vargas et al., 2020). However, we were not able to find virtually nothing about the great challenge that the pandemic has posed to Clinical Microbiology laboratories.

The Microbiology staff had to quickly adapt to the available information and the technologies being used. We had to implement practices never done before under normal circumstances, such as completing the installation of equipment by ourselves, or putting into operation veterinary diagnostic machinery (for nucleic acids extraction). Training plans for the personnel were fundamental. Most department members (staff, residents, and technicians) required specific training on nucleic acid extraction and PCR. Antibody detection procedures, the use of autoanalyzers for immunoassays and reinforcement in security procedures in the laboratory, were included in the training as well.

In a short timeframe the number of samples increased rapidly (37% in March, 63% in April) mostly due to high complexity samples such as SARS-CoV-2 PCR, which increased by 2058% in the whole period. In 10 months almost 240,000 SARS-CoV-2 PCRs and more than 55,000 serological tests were performed and results were provided every single day.

During the pandemic, there has been excellent communication and collaboration between the Microbiology and Infectious Diseases department and the Hospital management. The management has accepted the scientific and technical expertise of our department and we always have ensured the optimization of resources. In choosing the diagnostic platforms we have considered the reputation of the suppliers, the quality of the products and their adaptation to our circumstances and needs. Economic issues have also been taken into account, although they have not been a limiting factor for decision-making.

We have implemented some cost saving measures whenever possible. For instance, sample pooling was performed occasionally when the expected positivity rate was low. It was carried out in 2 low prevalence population studies, one carried out in employees of our Hospital (Estévez et al., 2021) and the other in asymptomatic volunteers. At some point, sterile saline solution was also used instead of transport medium due to the lack of supply.

The number of Microbiology laboratory technicians increased during the first 10 months of the pandemic, although not enough so as to stabilize the personnel workload, that increased by 12.5%. The daily number of samples processed by a microbiology technician to maintain a proper quality standard is not established (Carey et al., 2018). In fact, there very few reports have analyzed the workload of different infections in Microbiology laboratories. This field has traditionally been of interest to our group (Bouza et al., 2001, 2004, 2005).

Despite the extensive use of antimicrobials in patients with COVID-19 samples reflecting suspected concomitant nosocomial infection did not raise and even was reduced (blood cultures,

respiratory samples, intravenous catheters, and samples searching for colonization by multiresistant pathogens). In fact, it has been shown that critical COVID-19 patients frequently suffer from nosocomial infection (He et al., 2020) and in some centers the blood culture utilization has increased by up to 35%, with a high percentage of false positives (Sepulveda et al., 2020).

The areas of the laboratory that experienced exponential growth in their workload were those related to the diagnosis of COVID-19, specially the Virology and Serology units. The rest of the areas saw their demand clearly reduced, probably due to the reduction in surgical and outpatient clinics activity at the Hospital. This fact, together with the reinforcement of material and human resources, has allowed us to maintain the quality of care and our response times. We have not submitted samples at any time to external laboratories, however we have received samples from other canters and laboratories that do not usually depend on us.

There are virtually no data in the literature on the "normal budget" of a Clinical Microbiology laboratory. Undoubtedly, this budget is very much influenced locally by salaries and health care model. This epidemic has shown that hospitals must be prepared to spend large amounts of money to properly attend the diagnosis of the epidemic. In our center, Microbiology laboratory costs rose by 114% in 10 months, mainly due to the purchase of diagnostic tests (increase of 242%). This meant a cost increase of 6,616,511 euros over the normal Microbiology budget. The increase in the cost of diagnostic material was much more relevant than that of personnel (519,104 euros), which reflects the significant work overload assumed by the technicians and staff of the Microbiology laboratory.

The main limitation of our study is its unicentric nature, which reflects the experience of a Clinical Microbiology laboratory in a tertiary hospital located in Europe, in a country with public health care and which has suffered a large number of cases of COVID-19. However, we believe that it may be useful to other hospitals due to the absence of data in the literature, both on the overload that the emergence of the epidemic has meant and its cost.

This is the first study to provide quantitative figures about workload and cost increase caused by the first wave of the COVID-19 in a Microbiology laboratory.

Authors' contributions

Study conception and design: Pilar Catalán, Roberto Alonso, and Patricia Munoz. Laboratory work: Pilar Catalán, Roberto Alonso, Luís Alcalá, Mercedes Marín, Zaira Moure, Paula Pescador, and the Gregorio Maranon Microbiology-ID COVID 19 Study Group. Analysis and interpretation of results: Pilar Catalán, Roberto Alonso, Luís Alcalá, Emilio Bouza, and Patricia Munoz. Draft manuscript preparation: Roberto Alonso and Patricia Munoz. All authors reviewed the results and approved the final version of the manuscript.

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Declaration of Competing Interests

The authors report no conflicts of interest relevant to this article.

Supplementary materials

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