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Original Article

COVID-19 pandemic impact on cytopathology practice in the post-lockdown period: An international, multicenter study

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BACKGROUND: In a previous worldwide survey, the authors showed a drastic reduction in the number of cytological specimens processed during the coronavirus disease 2019 "lockdown" period along with an increase in malignancy rates. To assess the continued impact of the pandemic on cytological practices around the world, they undertook a second follow-up worldwide survey collecting data from the post-lockdown period (2020). **METHODS:** Participants were asked to provide data regarding their cytopathology activity during the first 12 weeks of their respective national post-lockdown period (2020), which ranged from April 4 to October 31. Differences between the post-lockdown period and the corresponding 2019 period were evaluated, and the authors specifically focused on rates of malignant diagnoses. **RESULTS:** A total of 29 respondents from 17 countries worldwide joined the survey. Overall, a lower number of cytological specimens (n = 236,352) were processed in comparison with the same period in 2019 (n = 321,466) for a relative reduction of 26.5%. The overall malignancy rate showed a statistically significant increase (12,442 [5.26%] vs 12,882 [4.01%]; $P < .001$) during the same time period. Similar results were obtained if both malignancy and suspicious for malignancy rates were considered together (15,759 [6.58%] vs 16,011 [4.98%]; $P < .001$). **CONCLUSIONS:** The data showed a persistent reduction in the cytological specimen volume during the post-lockdown period (2020). However, the relative increase in the cytological workload in the late part of the post-lockdown is a promising finding of a slow return to normality. ***Cancer Cytopathol* 2022;130:344-351**. © *2022 American Cancer Society*.

KEY WORDS: cancer screening program; coronavirus disease 2019 (COVID-19); cytopathology; fine-needle aspiration; malignancy rate.

INTRODUCTION

The end of 2019 was characterized by the rise of the novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2.[1-3] The pandemic status was officially declared by the World Health Organization on March 11, 2020.[4] At the time of this writing (July 2021), more than 185 million people had been reported to be test-positive, with more than 4 million deaths worldwide.[5]

The COVID-19 pandemic has significantly affected medical and laboratory practices around the world, including cytopathology practices.[6-9] In fact, to "flatten the curve," governments worldwide have imposed severe countermeasures limiting freedom of movement and everyday activities to reduce the spread of the disease. A major consequence of these limitations is the postponement of "nonurgent" medical and elective surgical procedures, which has resulted in a significant reduction in the activity of cytopathology services.[8-12] For example, in our previous survey of 41 laboratories from 23 different countries, there was a drastic reduction in the number of cytological specimens processed during the "lockdown" period along with a higher malignancy rate in comparison with the pre-lockdown period because of the prioritization of cytological specimens from individuals with a high cancer risk.[8]

The post-lockdown period in the second part of 2020 saw less restrictive measures. All medical services, including cytopathology, increased their services but still experienced a reduction in cytological specimens with respect to the corresponding prepandemic period and continued to see a persistently higher malignancy rate.[13,14] However, these data reflect only a single institution's experience, and global data regarding cytological practices in the post-lockdown period are limited. To fill this knowledge gap, a worldwide survey was taken to investigate the state of cytopathology laboratories during the COVID-19 pandemic post-lockdown period (2020).

MATERIALS AND METHODS

In this study, we applied the same methodology followed in our previous survey.[8] Briefly, an Excel questionnaire template was sent via email to the cytopathologists who had participated in the previous survey; these included the CytoESP Working Group (cytopathologists from the European Society of Pathology; https://www.esp-pathology.org/working-groups/esp-working-groups/cytopathology.html) and the cytopathologists who had participated in at least 1 of the 9 Annual National Molecular Cytopathology meetings in Naples, Italy (https://www.molecularcytopathology.com/), regardless of the single-participant sample workload. Only a single invitation email with no subsequent reminders was sent. Participants were asked to provide data regarding their cytopathology activity during the first 12 weeks of their respective national post-lockdown period and to stratify the data by consecutive 3-week intervals. The study period was individualized for each institution because of the variability of lockdowns among countries. In countries in which a lockdown did not take place, cytopathologists were asked to provide data from the first 12 weeks after the peak infection spread. Only data obtained from laboratories that had participated in both surveys were compared with those reported in the corresponding baseline period in 2019. Questions included in the survey are listed in Figure 1. All information regarding human material was managed with anonymous numerical codes, and all samples were handled in compliance with the

Declaration of Helsinki. The data were grouped into four 3-week periods, as previously reported.[13] Briefly, the overall workload rates for each specimen type were compared, and the total number of processed samples was recorded. Moreover, as far as the distribution of diagnostic classes was concerned, the numbers of suspicious and malignant non-gynecological diagnoses were compiled.

Differences between the post-lockdown period (2020) and the corresponding 2019 period were evaluated on the basis of absolute numbers. Differences in the rates of malignant diagnoses were assessed via the χ^2 test; *P* values lower than .05 were deemed to be statistically significant.

RESULTS

A total of 29 respondents from 17 countries worldwide (Azerbaijan [1 respondent], Belgium [1 respondent], Croatia [1 respondent], France [1 respondent], Finland [1 respondent], Germany [1 respondent], Italy [6 respondents, including previously reported data[13]], Japan [1 respondent], Moldova [1 respondent], Netherlands [1 respondent], Portugal [1 respondent], Spain [2 respondents], Slovenia [1 respondent], Turkey [2 respondents], Ukraine [1 respondent], the United Kingdom [2 respondents], and the United States [5 respondents]) joined the survey. For the most part, the data reflected single-institution activity except in 1 instance in which multi-institutional data were provided (Pathological National Automated Archive Public Pathology Database of the Netherlands; https://www.palga.nl/en/public-database.html). Because the timing of COVID-19 lockdowns differed among countries, each institution selected its most representative first 12 weeks of post-lockdown practice between April 4 and October 31, 2020.

Overall, a lower number of cytological specimens (n = 236,352) were processed during the post-lockdown period (2020) with respect to the same period in 2019 (n = 321,466) for a reduction of 26.5% (Table 1). The reduction was significant in each of the consecutive 3-week periods (period I, 49,724 vs 82,720; –39.9%; period II, 60,882 vs 88,744; –31.4%; period III, 60,715 vs 77,917; –22.1%; period IV, 65,031 vs 72,085; –9.8%; Table 2), although there was a trend toward a return to baseline volumes. Overall, the greatest reductions in the number of processed samples were observed for thyroid (–32.8%), cervical-vaginal tract (–30.7%), breast (–20.8%), serous cavity (–16.8%), salivary gland (–14.4%), respiratory tract (–12.2%), urine (–10.5%), and lymph node specimens (–7.5%); only 4 sample categories (central nervous system, gastrointestinal tract, biliary tract, and bone marrow specimens) showed an increase in the number of processed cytological samples (Table 3).

The overall malignancy rate of all samples obtained during the study period showed a statistically significant

COVID-19 POST-LOCKDOWN PERIOD					n°
Total number of cytological samples - 12 weeks					
Different sample sites (n°)	post-lockdown weeks n° 1-2-3	post-lockdown weeks n° 4-5-6	post-lockdown weeks n° 7-8-9	post-lockdown weeks n° 10-11-12	
Cervicovaginal tract					
Urinary tract					
Serous cavities					
Breast					
Lymph node					
Thyroid					
Respiratory tract					
Salivary gland					
Soft tissue					
Central nervous system					
Gastrointestinal tract					
Pancreas					
Liver					
Biliary tract					
Anal-rectal region					
Bone marrow					
Other sites					
Number of malignant diagnoses					
Number of suspicious for malignancy diagnoses					

CORRESPONDING PERIODS IN 2019				n°
Total number of cytological samples - 12 weeks				
Different sample sites (n°)	weeks n° 1-2-3	weeks n° 4-5-6	weeks n° 7-8-9	weeks n° 10-11-12
Cervicovaginal tract				
Urinary tract				
Serous cavities				
Breast				
Lymph node				
Thyroid				
Respiratory tract				
Salivary gland				
Soft tissue				
Central nervous system				
Gastrointestinal tract				
Pancreas				
Liver				
Biliary tract				
Anal-rectal region				
Bone marrow				
Other sites				
Number of malignant diagnoses				
Number of suspicious for malignancy diagnoses				

Figure 1. Survey questions. Participants were asked to provide data regarding their cytopathology activity during the first 12 weeks of their respective national post-lockdown period, with the data stratified by consecutive 3-week intervals. COVID-19 indicates coronavirus disease 2019.

TABLE 1. Total Numbers of Cytological Samples During 12 Weeks of the Post-Lockdown Period and the Corresponding Period in 2019 for Each Respondent

Respondent	Post-Lockdown Period (2020), N°.	Corresponding Period (2019), N°.	Difference, %	Difference Observed During Emergency Period (Lockdown)—Data From Previous Survey, %[a]
1	7823	7202	8.6	–83.1
2	2975	3491	–14.8	–67.7
3	103	132	–22.0	–98.0
4	573	738	–22.4	–80.2
5	1013	1073	–5.6	–73.6
6	1109	1476	–24.9	–75.4
7	1990	2180	–8.7	–43.3
8	5399	8541	–36.8	–83.0
9	4296	7082	–39.3	–79.5
10	1134	2803	–59.5	–79.8
11	2641	2805	–5.8	–89.4
12	3386	5298	–36.1	–0.1
13	1392	1334	4.3	–70.0
14	1930	1478	30.6	–79.9
15	4551	7833	–41.9	–74.8
16	1377	1299	6.0	–10.2
17	147,362	209,068	–29.5	–65.6
18	1476	1376	7.27	–58.6
19	655	1105	–40.7	–70.0
20	28,041	24,075	16.5	–59.2
21	1416	1876	–24.5	–67.9
22	373	582	–35.9	–16.1
23	6004	8383	–28.4	–75.4
24	938	2212	–57.6	–71.6
25	364	425	–14.4	–65.4
26	1887	3695	–48.9	–99.8
27	3538	7049	–49.8	–88.5
28	1239	4514	–72.6	–89.5
29	1367	2341	–41.6	–84.7
Total	236,352	321,466	–26.5	–64.6

[a]For the previous survey, see Vigliar et al.[8]

TABLE 2. Overall Cytological Sample Workload During the 12-Week Post-Lockdown Period Compared With the Corresponding Period in 2019

	Total Samples		
	Post-Lockdown Period (2020), N°.	Corresponding Period (2019), N°.	Difference, %
Period I	49,724	82,720	–39.9
Period II	60,882	88,744	–31.4
Period III	60,715	77,917	–22.1
Period IV	65,031	72,085	–9.8
Total	236,352	321,466	–26.5

The data are grouped into four 3-week periods.

increase in comparison with the corresponding period in 2019 (12,442 [5.26%] vs 12,882 [4.01%]; $P < .001$). Similar results were obtained when malignant and suspicious for malignancy samples were considered together (15,759 [6.58%] vs 16,011 [4.98%]; $P < .001$). With respect to the malignancy and malignant and suspicious rates, in 2 cases, data were reported merged for all 4 analyzed periods. Overall, among the 27 respondent laboratories, the malignancy rate and the malignant and suspicious rate during the COVID-19 post-lockdown period (2020) were higher in all examined periods in comparison with the corresponding period in 2019 (Table 4). Notably, the highest values were observed in period I (Table 4).

DISCUSSION

To the best of our knowledge, this is the first international, multicenter study to evaluate the cytopathological laboratory practices around the world during the immediate post-lockdown period. Notably, an overall reduction of processed cytological samples (26.5%) was observed between the post-lockdown period in 2020 and the corresponding period in 2019, with differences ranging from –72.6% to +30.6%. The absolute reduction in the number of processed specimens is alarming because of the increased risk for delayed treatment of patients with cancer. Only 4 specimen categories (central nervous system, gastrointestinal tract, biliary tract, and bone marrow specimens) did not show a decrease in the number of processed cytological samples in comparison with the prepandemic baseline. Overall, the highest reduction in samples was reported during the first 6 weeks in the post-lockdown period

TABLE 3. Overall Numbers and Proportions of Samples From Each Body Site During the Post-Lockdown Period and the Corresponding Period in 2019

Site	Overall Numbers			Difference Observed During Emergency Period (Lockdown)—Data From Previous Survey, %[a]
	Post-Lockdown Period (2020), N°.	Corresponding Period (2019), N°.	Difference, %	
Cervicovaginal tract	162,381	234,234	–30.7	–87.5
Urinary tract	18,712	20,916	–10.5	–53.5
Serous cavities	9701	11,659	–16.8	–33.6
Breast	4467	5642	–20.8	–57.1
Lymph node	9377	10,136	–7.5	–37.1
Thyroid	8954	13,328	–32.8	–80.5
Respiratory tract	11,143	12,693	–12.2	–50.7
Salivary gland	1315	1537	–14.4	–57.2
Soft tissue	770	894	–13.9	–59.6
Central nervous system	2532	2345	7.9	–30.1
Gastrointestinal tract	438	379	15.6	–51.6
Pancreas	1179	1268	–7.0	–23.5
Liver	367	434	–15.4	–3.3
Biliary tract	815	797	2.3	–42.6
Anal-rectal region	525	1004	–47.7	–98.7
Bone marrow	923	757	21.9	–81.4
Other sites	2753	3443	–20.0	–85.4
Total	236,352	321,466		

[a]The data come from the 29 respondents who participated in both surveys. For the previous survey, see Vigliar et al.[8]

TABLE 4. Malignancy Rates and Malignant and Suspicious Rates During the COVID-19 Post-Lockdown Period and the Corresponding Period in 2019 Grouped Into 4 Consecutive 3-Week Periods

	Post-Lockdown Period (2020)		Corresponding Period (2019)	
	Malignancy Rate	Malignant and Suspicious Rate	Malignancy Rate	Malignant and Suspicious Rate
Period I	5.7	7.4	3.5	3.5
Period II	5.0	6.4	3.6	3.6
Period III	4.9	6.3	4.0	4.0
Period IV	4.8	6.0	4.2	4.2

Abbreviation: COVID-19, coronavirus disease 2019.
The volume resulted from 27 respondents who provided data for each period.

(period I, –39.9%; period II, –31.4%) in comparison with the other 6 examined weeks (period III, –22.1%; period IV, –9.8; Table 2). Interestingly, other than different values of the overall reduction in cytology volume from each body site, different trends were observed in cytology practice recovery (Fig. 2). For example, Papanicolaou smears and thyroid samples showed a slow return to pre–COVID-19 levels; a possible explanation for the persistent reduction in the number of processed samples, particularly during the first 6 weeks of the post-lockdown period, may be the gradual reactivation of screening programs. Conversely, samples at high oncological risk, such as lymph node, breast, and respiratory tract fine-needle aspirates and serous fluids, showed a faster tendency to recover to pre–COVID-19 practice levels, as evident in the immediate post-lockdown period (period I or II); moreover, a steady trend during the subsequent periods was observed. This phenomenon probably reflected the attitudes of clinicians and cytopathologists for prioritizing specific specimen types. A fluctuating trend, with only a slight reduction in comparison with the pre–COVID-19 era (2019), was finally observed for sites such as the soft tissue, central nervous system, liver, pancreas, and gastrointestinal and biliary tract; however, the low volumes analyzed probably do not enable distinctive kinetics to be demonstrated. Overall, for the majority of sample types, there seemed to be quite significant variation from the lockdown time period to period I and the post-lockdown period (2020; Fig. 2 and Tables 2 and 3).

As for the malignancy rate and the malignant and suspicious rate during the COVID-19 post-lockdown period, a higher value in all examined periods was observed

in comparison with the corresponding period in 2019 (Table 4). Notably, the highest values were observed in period I (Table 4).

Despite the interesting results, several limitations affect our article. First of all, the number of participants was limited with respect to the previous survey. Second, more than half of the examined cases belonged to a single institution (laboratory #17). However, even without this laboratory, an overall reduction of 20.8% (88,990 vs 112,398) was observed. Similarly, there was a statistically significant increase (5.9% vs 5.1%; $P < .001$) in the overall malignancy rate and in the overall malignant and suspicious for malignancy sample rates when they were considered together (8.8% vs 7.2%; $P < .001$) in comparison with the corresponding period in 2019.

In conclusion, the COVID-19 pandemic era was characterized by decreases and delays in identifying new cancers.[15-17] Data generated from the present international, multicenter study showed that the postponement of "nonurgent" medical procedures was still observed during the post-lockdown period. Nonetheless, the policy of prioritizing high-risk patients has proven to be effective and should be pursued in the future, if necessary. In fact, when we consider the overall data, there was a significant increase in the malignancy rate between 2019 and 2020 when only malignant cases or when both malignant and suspicious for malignancy diagnoses were considered. These data strongly support the role of cytology in the diagnostic management of high-risk patients with cancer, even during this unprecedented health care emergency.[18,19] However, despite these results, the continued reduction of processed cytological samples in the post-lockdown period, which is related to national health care system countermeasures and the persistent reluctance of patients to go to the hospital, represents a global health care issue and serves as an important reminder of the potential consequences that such national policy measures can have on individuals with cancer.



Figure 2. Line charts of the overall workload for each cytological sample type normalized on a per-week basis and including data points from the COVID-19 lockdown period from the previous survey and 4 consecutive post-lockdown (2020) periods (red line). Data are compared with the corresponding period in 2019 (green line). COVID-19 indicates coronavirus disease 2019.



Figure 2.

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CONFLICT OF INTEREST DISCLOSURES

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AUTHOR CONTRIBUTIONS

Conceptualization: **Elena Vigliar**, **William C. Faquin**, **Martha Bishop Pitman**, and **Giancarlo Troncone**. Methodology: All authors. Software and formal analysis: **Elena Vigliar** and **Filippo Dello Iacovo**. Validation: All authors. Investigation: All authors. Resources: All authors. Data curation: All authors. Writing–original draft: **Elena Vigliar**, **Pasquale Pisapia**, **Filippo Dello Iacovo** and **Giancarlo Troncone**. Writing–review and editing: All authors. Visualization: All authors. Supervision: **Elena Vigliar**, **William C. Faquin**, **Martha Bishop Pitman**, and **Giancarlo Troncone**. Project administration: **Elena Vigliar**, **William C. Faquin**, **Martha Bishop Pitman**, and **Giancarlo Troncone**. Funding acquisition: **Giancarlo Troncone**.

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