



Cross-sectional Study

## Cellular pathology practice in the era of COVID-19 pandemic-related lockdowns - Experience from a tertiary hospital: A retrospective observational study

Mohammed Alorjani<sup>a,\*</sup>, Ismail Matalka<sup>a</sup>, Shaden Abu Baker<sup>b</sup>, Sohaib Al-Khatib<sup>a</sup>, Samir Al Bashir<sup>a</sup>, Mohammad Al-Qudah<sup>a</sup>

<sup>a</sup> Department of Pathology and Microbiology, Faculty of Medicine, Jordan University of Science and Technology, Irbid, 22110, Jordan

<sup>b</sup> Department of Pathology and Laboratory Medicine, King Abdullah University Hospital, Irbid, 22110, Jordan



## ARTICLE INFO

## Keywords:

Coronavirus  
COVID-19  
Lockdown  
Cellular pathology

## ABSTRACT

**Background:** The COVID-19 pandemic had many implications on healthcare services, including cellular pathology. The pandemic-related lockdown was applied in Jordan from March to May 2020. King Abdullah University Hospital (KAUH) was chosen to provide care for COVID-19 patients during that period. Since there was no experience in dealing with COVID-19 patients, the hospital maintained some essential services but canceled elective surgeries and procedures. The rationale was to prioritize care for COVID-19 patients and to provide better adherence to infection control policies and protect non-infected patients and healthcare workers. The purpose of the present study is to investigate the impact of COVID-19 pandemic restrictions on cellular pathology practice patterns at KAUH.

**Methods:** This is a retrospective observational study conducted at KAUH. All cellular pathology reports during the 2020 national lockdown were retrieved. The total numbers of specimens including types and procedures were recorded. Data were compared with the corresponding data in 2019 when there was no pandemic and when hospital and laboratory services were run in full capacity.

**Results:** 2020 lockdown period showed a 57.9% reduction in the total number of specimens received at the cellular pathology laboratory as compared to the corresponding period of 2019 (1400 versus 3322). Emergency procedures have represented 99.1% of the service during the lockdown with a remarkable diversity shift.

**Conclusion:** There was a significant drop in the number of specimens dealt with at KAUH cellular pathology laboratory during the COVID-19 pandemic-related national lockdown. We learned from this pandemic how to adapt to such circumstances by adjusting our way of working to reach the best level of staff safety while maintaining highly productive work. Implementing digital pathology platforms, working from home strategies and alternative training methodologies have emerged as an essential need.

### 1. Introduction

At the end of 2019, China reported for the first time a group of patients with pneumonia which warranted attention. Viral genomic sequencing analysis revealed that the patients were infected with a novel coronavirus [1]. This virus was then officially named SARS-CoV-2 causing the disease which the World Health Organization (WHO) named COVID-19 [2,3]. Late in January 2020, the WHO issued a Public Health Emergency of International Concern (PHEIC) alarm on the seriousness of this disease and urged health authorities all over the world to work

together in an attempt to control the rapid spread of COVID-19 which became a pandemic and difficult to control [4].

By the time of writing this manuscript, the number of confirmed cases of COVID-19 disease worldwide exceeded 83 million, with over 1.8 million deaths and the number is increasing on a daily basis [5]. In Jordan, until the December 31, 2020, the number of confirmed COVID-19 cases approached 300,000 and the number of deaths exceeded 3800 [6]. The March 2, 2020 was the date of first case of COVID-19 disease to be diagnosed in Jordan, to a Jordanian male who came from Italy [7]. In March 2020, the officials in Jordan, similar to many other

\* Corresponding author.

E-mail address: [Msalorjani@just.edu.jo](mailto:Msalorjani@just.edu.jo) (M. Alorjani).

<https://doi.org/10.1016/j.amsu.2021.02.001>

Received 17 January 2021; Received in revised form 31 January 2021; Accepted 2 February 2021

Available online 11 February 2021

2049-0801/© 2021 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

countries, were observing the spread of COVID-19 in the world and discussing options to control its entry and spread in Jordan. On the 18th of March, the Jordanian government progressively started to lockdown the country, suspended study in schools and universities, stopped praying in mosques and churches, closed its borders, and suspended all incoming and outgoing flights. Moreover, and as a precautionary step, the Jordanian government requested that all the arriving passengers from Queen Alia International Airport (the main international airport in the country) during that period to be placed in hotel quarantine for 14 days.

There are many governmental and private hospitals all over Jordan; nevertheless, the Jordanian health authorities in collaboration with the National Center for Security and Crisis Management decided, as a safety precaution for better containment of the spread of the disease, to admit all COVID-19 patients to two hospitals only; King Abdullah University Hospital (KAUH) in the North and Prince Hamza Hospital in the Capital Amman. Internationally adopted safety measures [8] along with local staff protection guidelines have been applied in the two hospitals and protection protocols have been assigned in order to prevent the spread of COVID-19 among hospital staff.

During the national lockdown period which lasted for nearly 2.5 months, KAUH set several strategies in order to minimize the workload in an attempt to prioritize tasks and for optimal utilization of resources. Such strategies included the postponement of elective surgeries and procedures, and outpatients' clinics until the end of the lockdown; dealing only with urgent surgeries and procedures, along with emergency cases during the lockdown period, as well as limiting aerosol generation procedures to negative pressure rooms [9]. Moreover, Healthcare workers (HCWs) with chronic medical illnesses like diabetes mellitus, hypertension and chronic respiratory diseases as well as pregnant ladies were exempted from work during this period [7].

HCWs have the potential for direct or indirect exposure to patients or infectious materials; therefore, it is critical to ensure the health and safety of them, both at work and in the community in order to minimize the risk of contracting communicable diseases, including respiratory viruses. Therefore, KAUH hospital applied strictly the internationally adopted WHO, Centers for Disease Control and Prevention (CDC) and Royal College of Pathologists (RCPATH)'s safety precautionary measures in dealing with potentially infectious specimens [8,10,11]. These included wearing personal protective equipment (PPE; types of PPE used in KAUH were: gloves, N95 masks with tight seal around mouth and nose, face and eye protection including face shields and goggles, clothing which includes gowns, aprons, head covering, and shoe covers) and dealing with fresh specimens in a class II biological safety cabinet. Surfaces where specimens are collected and dealt with were disinfected with 62–71% ethanol, 0.5% hydrogen peroxide, or 0.1% sodium hypochlorite application to the surfaces. According to recommendations, this step was expected to inactivate the SARS-CoV-2 virus within 1 min similar to the effect that was discovered before on other members of the coronavirus family. Formalin-fixed and paraffin embedded tissues are generally considered safe to deal with, since the process of fixation and embedding generally applied in histopathology laboratories should inactivate SARS-CoV-2 [12].

Digital pathology or whole slide imaging (WSI) service has emerged in recent years as part of modern trends in pathology practice that allows pathologists to work from remote places, e.g., from home. It is growing very fast and has long been recognized as an important healthcare education and research tool. It has also been recently deployed by diagnosticians, starting in Europe and Canada, where a number of WSI devices have been marketed for primary diagnosis [13]. Digital pathology offers a number of potential benefits as it enables electronic transfer of slides from the laboratory to the pathologist. This improves workflow in the laboratory and allows work to be shared across sites. Eventually, these measures could help in solving issues like shortages of pathologists or certain service needs and in improving turnaround times [14]. In response to the COVID-19 pandemic, the RCPATH has further

recommended recently that during periods of service need and clinical necessity, pathologists may request, or be requested, to work remotely. Its guidance concluded that digital slide reporting may help expedite assessment of urgent cases and help maintain pathology services [15].

The purpose of the present study is to investigate the impact of COVID-19 pandemic restrictions on cellular pathology practice pattern at KAUH.

## 2. Methods

This study was approved by the Deanship of Research and the Institutional Review Board at Jordan University of Science and Technology (IRB decision number: 57/137/2021). The study was registered with the Research Registry (researchregistry6507) in accordance with the declaration of Helsinki. The study was conducted according to the guidelines of Strengthening the reporting of cohort studies in surgery (STROCSS) 2019 [16].

It is a retrospective observational study conducted at KAUH. The cellular pathology service at KAUH is the only facility serving North of Jordan with a population of about three million [17]. Reports of all specimens received at the cellular pathology laboratory at KAUH in March, April and May of 2020, including histopathology, cytology and bone marrow specimens were retrieved from our Health Information System and were categorized according to the diagnosis into different groups related to their priority level. All gathered data were entered into excel sheets. Total numbers of specimens received in each group during the studied period were recorded along with classification of types of procedures into emergency and elective mandatory or elective procedures. Such data were then compared with equivalent data for the corresponding season of the preceding year 2019 when there was no COVID-19 pandemic and when hospital and laboratory services were run in full capacity.

## 3. Results

During the three-month study period of March–May 2020, a total number of 1400 specimens of different types were received in KAUH cellular pathology laboratory. In regard to the types of specimens, 1075 were histopathology specimens, 258 were cytology specimens and 67 were bone marrow specimens. Out of total number of 1075 histopathology specimens, 694 were for patients treated at KAUH, and 381 were external specimens, i.e., delivered to our laboratory from one of the many hospitals which provide patient service in North Jordan and do not have cellular pathology laboratory. Cytology service was also divided into KAUH and external (239 and 19 specimens, respectively). As for the bone marrow service, 55 specimens belonged to KAUH

**Table 1**  
KAUH cellular pathology laboratory practice during the COVID-19 national lockdown in Jordan (March–May 2020).

Specimen type	March–May 2020	% of service
All specimens received in KAUH cellular pathology laboratory	1400	
Histopathology specimens (All)	1075	76.8%
Cytology specimens (All)	258	18.4%
Bone marrow specimens (All)	67	4.8%
Histopathology specimens	1075	
KAUH histopathology	694	64.6%
External histopathology	381	35.4%
Cytology specimens	258	
KAUH cytology	239	92.6%
External cytology	19	7.4%
Bone marrow specimens	67	
KAUH bone marrow	55	82%
External bone marrow	12	18%

patients and 12 were external (Table 1).

During the comparison period of March–May 2019, when there was no COVID-19 pandemic, a total number of 3322 specimens of different types were received in our laboratory. Of these, 2621 were histopathology specimens, 603 were cytology specimens and 98 were bone marrow specimens. When compared with numbers from the lockdown period March–May 2020 (Fig. 1), the latter period showed a significant drop of 57.9% in overall specimen count (1400 versus 3322) and in the different types of specimens too (with reduction rates of 59%, 57.2% and 31.6% in counts of histopathology, cytology and bone marrow specimens, respectively). The only exception of this reduction was external bone marrow specimens which increased by 33.3% during the lockdown period compared to the equivalent period of 2019. However, these contributed a little to the practice in our laboratory.

Upon reviewing patient reports and medical records with a focus on histopathology practice at the laboratory during the study period of March–May 2020, emergency procedures were the source of 99.1% (1065 of 1075 specimens) with a remarkable diversity shift. The remaining 10 specimens belonged to elective procedures (Table 2). However, the records revealed that 8 of the latter group were sleeve gastrectomy surgeries performed prior to the lockdown date (18/03/2020), and only 2 were truly performed after the lockdown began.

#### 4. Discussion

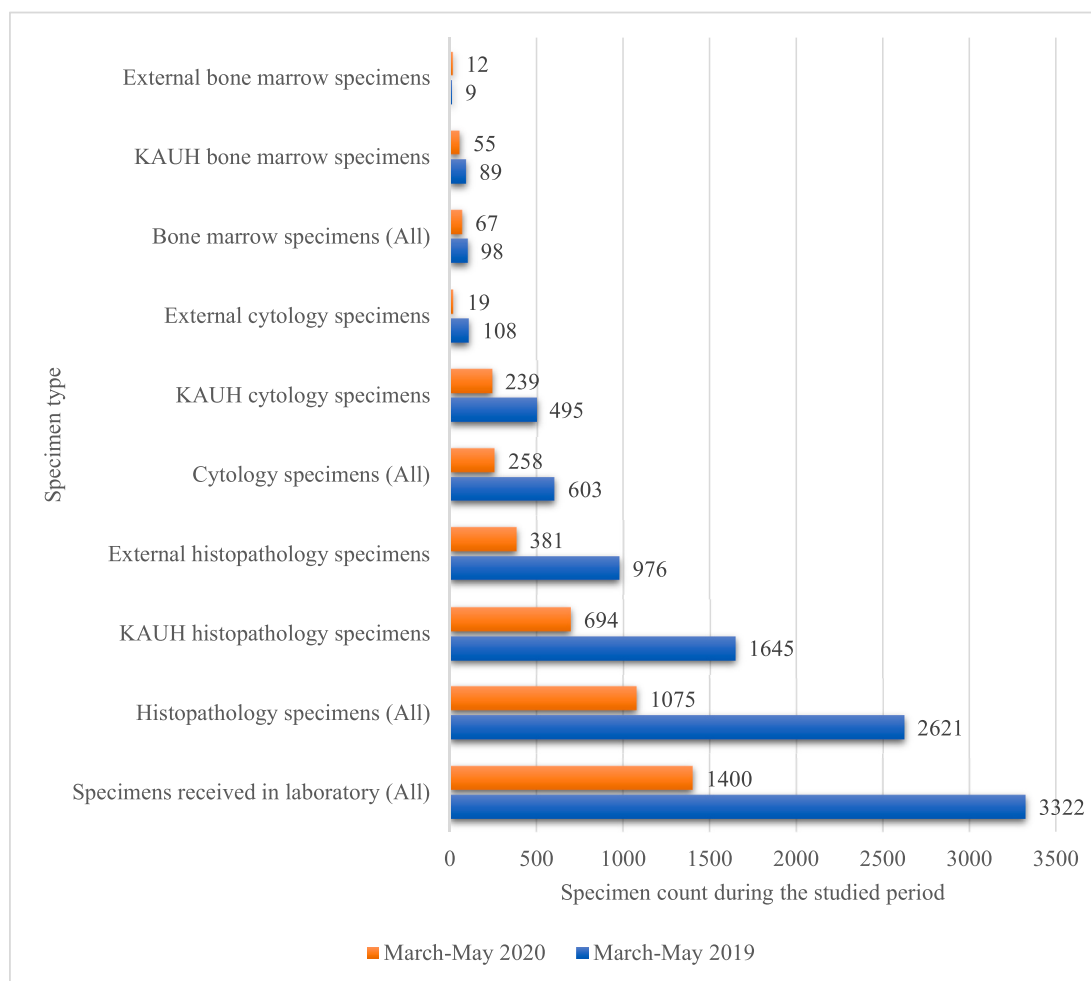
KAUH is a large tertiary teaching hospital that provides health

**Table 2**

Emergency versus elective Histopathology specimen distribution during March–May 2020 (Lockdown period).

Histopathology specimens	March–May 2020
Elective cases (All)	10
KAUH cases	10
External cases	0
Emergency cases (All)	1065
KAUH cases	684
External cases	381

services for the North of Jordan with a population of approximately 3 million [17]. The COVID-19 pandemic has had many implications on health services, both globally and locally. The COVID-19 related lockdown was initiated in Jordan on 18/03/2020. A special impact on the healthcare system in Jordan was witnessed at KAUH, because of its selection as one of the two only caring centers for COVID-19 patients during the lockdown period. This led to the decision of discontinuing routine medical practice and unnecessary elective surgical procedures during that period. As a consequence of this situation, volume, diversity and pattern of cellular pathology practice has been affected. The current data highlight important and different impacts on sustainability and quality of healthcare services in a tertiary center where cellular pathology practice is a real reflection of the extent and diversity of other clinical practices which dropped down for the reason mentioned earlier. Other important issue is related to the standards and adequacy of



**Fig. 1.** This chart shows the trend of change in counts of specimens received at KAUH cellular pathology laboratory between the two studied periods (March–May 2020 COVID-19 pandemic-related lockdown period and the equivalent period of 2019). A significant drop is noticed during the lockdown period for all types of specimens together and for different types of specimens (histopathology, cytology and bone marrow specimens).

training of residents in cellular pathology and other specialties and potential alternatives should this situation arise again.

The current study demonstrates the presence of a significant drop in the number of cellular pathology specimens at KAUH laboratory during the COVID-19 pandemic-related lockdown period (March–May 2020). This is well illustrated in [Table 1](#) by the 57.9% reduction rate in the total number of cellular pathology specimens of all types received in the laboratory (and nearly all sources, except for bone marrow specimens received from outside hospitals) as compared to the similar season of 2019 when there was no pandemic, and the healthcare services were run routinely in full capacity. The results reveal also that 99.1% of the cellular pathology practice during the lockdown period was related to emergency and non-delayable elective procedures like cesarian sections. Such findings reflect the hospital decision to give priority for such services over elective procedures during the national lockdown period when the hospital was involved in care for COVID-19 patients. Of important observation is that all fallopian tube ligation procedures during the lockdown period were performed during cesarian section surgeries and not as isolated procedures; hence they are best exempted from being considered pure elective surgeries. Moreover, all the reported elective procedures during the study period of 2020 which were performed at KAUH ([Table 2](#)) and included 8 sleeve gastrectomy surgeries, where performed prior to the actual lockdown date (18/03/2020).

To cope with the reduced patient service volume in the hospital and in an effort to minimize the risk of exposure of our staff, the work in the pathology laboratory was restructured during the lockdown period. The service rota before that period distributed the services in the laboratory among the consultant pathologists and residents in a way that necessitated all consultant pathologists and residents be available on-site during the five days of work a week. However, the lockdown rota schedule limited the on-site presence each working day to one consultant dealing with reporting different types of pathology specimens that day, and two residents (one junior and one senior); one of them for surgical cutup (under supervision of the attending consultant) and the other resident for microscopic reporting with the attending consultant. All possible efforts were made to get reports signed out on the same day. The only two exceptions for this were if ancillary studies are requested on the specimen or a second opinion is needed, then the case gets delayed to the following working day. The whole process has limited availability of the consultants in the hospital and the laboratory to almost one day per week. The relevant advices of the RCPATH while at work were also followed, including frequent hand washing and cleaning of work surfaces, along with wearing of a face mask and the use of multiheaded microscopes with avoidance of double-headed microscopes while resident doctors were reporting cases with consultants to maintain adequate social distancing requirements [18].

In addition, multidisciplinary meetings were scaled down to the minimum possible frequency without negatively influencing patient care. As per the technical biomedical staff, they followed also a similar way of work rotations. The application of such strategy for work style, along with the strict application of safety measures and protocols in hospital premises and in dealing with specimens received in the laboratory have contributed to maintaining COVID-19 disease acquisition among physicians and laboratory staff at low rate as we reported no proven infected staff in our laboratory, like other KAUH HCWs who kept working in the hospital during the lockdown period [7]. The traditional cellular pathology reporting sessions using multiheaded microscopes was replaced by using personal microscopes and connected monitors to avoid close contact or cross infection.

Up to the best of our knowledge, there is no published literature reporting the influence of COVID-19 related measures on the level of service in pathology laboratories in terms of numbers of specimens dealt with during pandemic lockdowns. However, Stathonikos et al. wrote a comprehensive review on their modified way of working in their laboratory during the COVID-19 pandemic; where they adopted a way

somehow similar to ours, in adapting to the pandemic restrictions [19]. They reduced the number of on-the-premises staff team present in the laboratory to the minimum each working day. For example, resident doctors were divided into groups of junior and senior residents and followed the week-on/week-off principle, and the week-off team was involved in work and learning remotely from home. As for the on-the-premises staff team, they followed the ‘need to be there’ principle; i.e., when the on-site work was finished, they returned home to work remotely. Moreover, social distancing on the premises was strictly maintained. They also followed the same WHO safety precautions in dealing with patient samples, as was practiced in our laboratory. Furthermore, Stathonikos et al. described in their review how they utilized beautifully digital home pathology diagnostic services and video-conferencing which replaced plenary staff meetings and diagnostic multidisciplinary meetings in many instances. Their staff had generally a positive feedback about this experience in which productivity was maintained and the staff was protected against COVID-19 infection (they reported 0 proven infected individual). Although we have not yet entertained the luxury of working from home, we reported no proven infected staff in our laboratory during the lockdown period; thanks to the measures that we followed. Digital pathology service has not yet been implemented in our laboratory but is underway and hopefully it will be present in the near future, adding a great value to improving our pathology workflow and quality.

Training opportunity and exposure for our residents has been affected by the reduced number of specimens. Limited literature is available on this important issue. Lo et al. studied the impact of COVID-19 pandemic on emergency medicine residency training. They noticed a reduced emergency department volume and decreased residents’ clinical exposure and advised to adjust the training programs and utilize ancillary methods of learning to ensure adequate training [20]. In pathology, Stathonikos et al. discussed in their review some measures that they followed to improve this, including utilization of digital pathology in training [19]. We have adopted several strategies to compensate for this shortcoming by asking the residents to review archived interesting cases, slide collections and ‘black box’ cases, and to register in the different virtual pathology activities taking place during that time. One of the unique and very helpful Continuing Professional Development (CPD) online platforms was the read and test Interactive Pathology Quiz (IPQ) activity which is organized by one of the pathologists in the region. We encouraged our residents to join this platform which provides a reading list of lead articles and then answering the monthly quizzes.

## 5. Conclusion

There was a significant drop in the number of specimens dealt with at KAUH pathology laboratory during the COVID-19 pandemic-related national lockdown. We learned from this pandemic how to adapt to such circumstances by adjusting our way of working to reach the best level of staff safety while maintaining highly productive work. Implementing digital pathology platforms, working from home strategies and alternative training methodologies have emerged as an essential need.

## Sources of funding

No funding.

## Ethical approval

Institutional approval was obtained from the Institutional Review Board at Jordan University of Science and Technology (Decision No. 57/137/2021).

## Consent

Not required due to the retrospective observational nature of the

study which does not involve human participants.

### Author contribution

All authors contributed significantly to this study. Mohammed Alorjani and Ismail Matalaka were involved in study design and manuscript writing. Mohammed Alorjani and Shaden Abu Baker were involved in data collection and literature review. All authors were involved in data interpretation and revision of the manuscript. All authors approved the final version to be submitted.

### Trial registry number

Name of the registry: Research Registry.

Unique Identifying number or registration ID: researchregistry6507.

Hyperlink to your specific registration: <https://www.researchregistry.com/browse-the-registry#home/>

### Guarantor

Mohammed Alorjani.

### Provenance and peer review

Not commissioned, externally peer reviewed.

### Declaration of competing interest

All authors declare that they have no conflicts of interest.

### Acknowledgements

Many thanks to KAUH Health Information System Staff who provided us with requested data for this study.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2021.02.001>.

### References

- [1] The State Council of the People's Republic of China, English.gov.cn, 2020 [cited 31 December 2020]. Available from: <http://english.www.gov.cn/>.
- [2] A. Gorbalenya, S. Baker, R. Baric, et al., The species *Severe acute respiratory syndrome-related coronavirus*: classifying 2019-nCoV and naming it SARS-CoV-2. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses, Nat. Microbiol. 5 (2020) 536–544, <https://doi.org/10.1038/s41564-020-0695-z>.
- [3] J. Guarner, Three emerging coronaviruses in two decades, Am. J. Clin. Pathol. 153 (4) (2020) 420–421, <https://doi.org/10.1093/AJCP/AQAA029>.
- [4] F. Ye, S. Xu, Z. Rong, et al., Delivery of infection from asymptomatic carriers of COVID-19 in a familial cluster, Int. J. Infect. Dis. 94 (2020) 133–138, <https://doi.org/10.1016/j.ijid.2020.03.042>.
- [5] World Health Organization Coronavirus Disease (COVID-19) Dashboard, Covid19.who.int., 2020 [cited 31 December 2020]. Available from: <https://covid19.who.int>.
- [6] Ministry of Health, The Official Website of the Jordanian Ministry of Health | Coronavirus Disease. Corona, moh.gov.jo., 2020 [cited 31 December 2020]. Available from: <https://corona.moh.gov.jo/en>.
- [7] N. Al-zoubi, B. Obeidat, M. Al-Ghazo, et al., Prevalence of positive COVID-19 among asymptomatic health care workers who care patients infected with the novel coronavirus: a retrospective study, Ann. Med. Surg. (Lond) 57 (2020) 14–16, <https://doi.org/10.1016/j.amsu.2020.06.038>.
- [8] World Health Organization, Infection Prevention and Control during Health Care when Novel Coronavirus (nCoV) Infection Is Suspected: Interim Guidance, 25 January 2020, Apps.who.int., 2020 [cited 31 December 2020]. Available from: <https://apps.who.int/iris/handle/10665/330674>.
- [9] T. Mazahreh, A. Aleshawi, N. Al-Zoubi, M. Hatamleh, A. Hmedat, The impact of COVID-19 on the surgical operations, Ann. Med. Surg. (Lond) 57 (2020) 49–51, <https://doi.org/10.1016/j.amsu.2020.06.042>.
- [10] Coronavirus Disease 2019 (COVID-19), Centers for Disease Control and Prevention, 2020 [cited 31 December 2020]. Available from: <https://www.cdc.gov/coronavirus/2019-nCoV/lab/lab-biosafety-guidelines.html>.
- [11] RCPATH advice on the opening of fresh or unfixed histopathological specimens during infectious disease outbreaks [cited 05 January 2021]. Available from: <https://www.rcpath.org/uploads/assets/4556f1b9-3a6d-4132-b7d0d7c22dfc0a5c/7b8a6470-ac7c-4fe1-876ae3b2f051a258/RCPATH-advice-on-the-opening-of-unfixed-histopathological-specimens-during-infectious-disease-outbreaks.pdf>.
- [12] A. Henwood, Coronavirus disinfection in histopathology, J. Histotechnol. 43 (2) (2020) 102–104, <https://doi.org/10.1080/01478885.2020.1734718>.
- [13] B.J. Williams, D. Bottoms, D. Treanor, Future-proofing pathology: the case for clinical adoption of digital pathology, J. Clin. Pathol. 70 (2017) 1010–1018, <https://doi.org/10.1136/jclinpath-2017-204644>.
- [14] RCPATH Best practice recommendations for implementing digital pathology [cited 27 January 2021]. Available from: <https://www.rcpath.org/uploads/assets/f465d1b3-797b-4297-b7fedc00b4d77e51/Best-practice-recommendations-for-implementing-digital-pathology.pdf>.
- [15] RCPATH Guidance for remote reporting of digital pathology slides during periods of exceptional service pressure [cited 27 January 2021]. Available from: <https://www.rcpath.org/uploads/assets/626ead77-d7dd-42e1-949988e43dc84c97/RCPATH-guidance-for-remote-digital-pathology.pdf>.
- [16] R. Agha, A. Abdall-Razak, E. Crossley, N. Dowlut, C. Iosifidis, G. Mathew, The STROCSS 2019 guideline: strengthening the reporting of cohort studies in surgery, Int. J. Surg. 72 (2019) 156–165, <https://doi.org/10.1016/j.ijsu.2019.11.002>.
- [17] Population – Jordan Department of Statistics, Dosweb.dos.gov.jo, 2020 [cited 31 December 2020]. Available from: <http://dosweb.dos.gov.jo/population/population-2/>.
- [18] RCPATH advice on the use of double-headed or multi-headed microscopes during infectious disease outbreaks [cited 05 January 2021]. Available from: <https://www.rcpath.org/uploads/assets/7f18934a-a8a5-493a-aced181bf9aea606/G231-RCPATH-advice-double-headed-multi-headed-microscopes-infectious-disease-outbreaks.pdf>.
- [19] N. Stathonikos, N. van Varsseveld, A. Vink, et al., Digital pathology in the time of corona, J. Clin. Pathol. 73 (11) (2020) 706–712, <https://doi.org/10.1136/jclinpath-2020-206845>.
- [20] H. Lo, S. Lin, C. Chaou, Y. Chang, C. Ng, S. Chen, What is the impact of the COVID-19 pandemic on emergency medicine residency training: an observational study, BMC Med. Educ. 20 (1) (2020) 348–355, <https://doi.org/10.1186/s12909-020-02267-2>.