Effect of Covid-19 Pandemic on Surgical Pathology and Cytopathology referrals for Detection of Malignancy

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ABSTRACT

Objective: This study aims to investigate the effect of the pandemic on the detection of diseases through the materials sent to the pathology laboratory, especially the malignant patient group.

Material and Methods: According to official data, the first Covid-19 patient was detected in our country on March 11 2020. All materials that came to the pathology laboratory between 11 March-10 April 2020 and 11 March-10 April 2019 were included into the study. The age, gender, material and diagnoses of the patients were recorded. The pre-pandemic period and post-pandemic period were analyzed statistically.

Results: Cases divided into five diagnostic groups as benign(92.9%), malignant(2.8%), pre-malignant(2%), atypia of uncertain significance(1.4%) and inadequate(0.9%). Although a numerical decrease was detected in all groups, statistically significant decrease was detected in the benign(p=0.001), malignant(p=0.001), and atypia of uncertain significance(p=0.047). According to the types of materials, the first five materials most frequently sent before the pandemic are smears(31.3%), gastric biopsy(18%), curettage(9%), gallbladder resections(5.2%), and skin biopsies(4.5%). After the pandemic, smears(29.8%), stomach biopsies(17.6%), curettage(10.2%), gallbladder(5.2%) and appendectomies(5.2%) are respectively. Materials with statistically significant reductions were skin biopsies(p=0.006), thyroid fine needle aspiration biopsies(p=0.018), and abortions(p=0.025).

Conclusion: It can be argued that the unknown and devastating effect of the pandemic is felt intensely, especially in malignant group, where early diagnosis and treatment are important. We would like to emphasize the necessity of putting B plans in global events such as pandemics to prevent any disruption in cancer screening programs in these special groups.

Keywords: covid19, pandemic, pathology, cytopathology

INTRODUCTION

Since December 2019, the world has been dealing with the pandemic that has delayed other health problems (1). With the Covid-19 pandemic, governments have taken precautions such as social distance, travel restrictions and quarantine (2). It was thought that these precautions taken to protect public health caused other problems by interrupting cancer screening programs along with the recommendation of non-emergency patients to delay their admission to the hospital. It is predicted that delays in diagnosis cause patients to be caught at more advanced stages and lead to the worse clinical outcome (3). There are some differences in cancer screening programs between countries. In our country, there are approaches for early detection of breast, cervical, and colorectal cancers in the cancer screening program published by the Cancer Department of the Ministry of Health, General Director of Public Health. For breast cancer, it is recommended that the individual physical examination monthly, annual clinical examination, and a mammogram every two years between the ages of 40-69.
For the detection of colorectal cancer, in addition to fecal occult blood test every two years for individuals aged 50-70, colonoscopy is performed every ten years for the same age group. In cervical cancer screening, it is recommended to take a smear every five years from women between the ages of 30-65 and to have an HPV-DNA test. These approaches are reflected in the pathology laboratory by sending tru-cut biopsies, lumpectomy and mastectomies, colon biopsy, colon resection materials and smears. It is thought that with the pandemic, disruptions in these screening programs are also experienced.

The aim of this study is to investigate the effect of the pandemic on the detection of diseases through the materials sent to the pathology laboratory, especially the malignant patient group.

MATERIAL and METHODS

Ethics committee decision was taken for the study (No: 2022/4-4). According to official data, based on the date of March 11 2020, when the first Covid-19 patient was detected in our country, all of the patients’ material which came to the pathology laboratory between 11 March-10 April 2020 and 11 March-10 April 2019 were included in the study. The patients’ age, gender, material type and diagnoses were found and recorded. Diagnoses were divided into five categories as benign, pre-malignant, malignant, atypia of undetermined significance and inadequate. Diagnosis of atypia of undetermined significance used in the presence of atypical squamous cells of undetermined significance (ASC-US) in smears, and in the presence of atypical cells of undetermined significance/follicular lesion of uncertain significance in thyroid fine-needle aspiration biopsies. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 25.0 software (SPSS Inc., Chicago, IL, USA). The compatibility of numerical variables to normal distribution was assessed using Kolmogorov-Smirnov test. Results were presented as frequencies and percentages for categorical variables, and as medians and interquartile ranges for numerical data. The Mann-Whitney U test was used to compare numerical variables, while the Chi-square or Fisher’s Exact test was used for comparing categorical data. A p-value of <0.05 was considered acceptable for statistical significance.

RESULTS

While the number of cases in our laboratory was 1359 before the pandemic, it decreased to 363 after the pandemic. Materials of female patients are three times more common than men. Groups were most frequently diagnosed as benign (92.9%), followed by malignant (2.8%), pre-malignant (2%), atypia of undetermined significance (1.4%), and inadequate (0.9%) (Table I).

Table 1: Descriptive features of the cases

| Diagnosis       | Before pandemic | %  | After pandemic | %  | χ² | p     |
|-----------------|-----------------|----|----------------|----|----|-------|
| Sex            |                 |    |                |    |    |       |
| Male           | 424             | 24.9| 363            | 21.1|    |       |
| Female         | 1294            | 75.1| 304            | 28.9|    |       |
| Period          |                 |    |                |    |    |       |
| Before pandemic | 1359            | 78.9| 363            | 21.1|    |       |
| After pandemic  | 363             | 21.1| 1294           | 78.9|    |       |
| Diagnosis       |                 |    |                |    |    |       |
| Benign          | 1294            | 75.1| 363            | 21.1|    |       |
| Malign          | 1300            | 78.9| 363            | 21.1|    |       |
| Pre-malign      | 48              | 2.8 | 363            | 21.1|    |       |
| Undetermined    | 34              | 2.0 | 363            | 21.1|    |       |

While 1277 cases were diagnosed as benign before the pandemic, this number decreased to 323 after the pandemic, and a statistically significant decrease was detected (p=0.001). While 29 patients (2.1%) were diagnosed as malignant before the pandemic, the number decreased to 19 (5.2%) after the pandemic, and a statistically significant decrease was detected (p=0.001).

While the cases diagnosed as pre-malignant were 24 (1.8%) before the pandemic, they decreased to 10 (2.8%) after the pandemic, but there was no statistically significant decrease (p=0.229). Patients diagnosed with atypia of undetermined significance showed a statistically significant decrease (p=0.047) from 15 (1.1%) before the pandemic to 9 (2.5%) after the pandemic (Table II).

According to the types of materials, the first five materials most frequently sent before the pandemic are smears (31.3%), gastric biopsies (18%), curettages (9%), gallbladders (5.2%) and skin biopsies (4.5%). After the pandemic, smears (29.8%), stomach biopsies (17.6%), curettages (10.2%), gallbladders (5.2%), and appendectomies (5.2%) are respectively. Materials in which statistically significant reductions were observed at skin biopsies (p=0.006), thyroid fine needle aspiration biopsies (p=0.018) and abortions (p=0.025) (Table III).

Table 2: Comparison of pre- and post-pandemic tumor type

| Diagnosis       | Pre-pandemic | Period | Post-pandemic | χ² | p     |
|-----------------|--------------|--------|---------------|----|-------|
|                 | n            | %      | n             | %  |       |
| Benign          | 82           | 6.0    | 40            | 11.0| 10.816| 0.001|
| Malign          | 1330         | 97.9   | 344           | 94.8| 10.161| 0.001|
| Pre-malign      | 29           | 2.1    | 19            | 5.2 | 5.2   | 0.229|
| Undetermined    | 1335         | 98.2   | 353           | 97.2| 1.447 | 0.229|
| Insufficient    | 1344         | 98.9   | 354           | 97.5| 3.944 | 0.047|

χ²: Chi-Square test.*: Fisher’s Exact test
In the study conducted by Rosas et al. in Latin America, they compared the pathology materials in the 2.5-month period when the pandemic started and the same period of 2019 and found that the number of samples decreased (1).

In this study, numerical decreases were observed in each material type, and a statistically significant decrease was found only in skin biopsies, thyroid fine-needle aspiration biopsies and abortions.

Kaufman et al. compared the change in the number of newly diagnosed cancer patients before and during the pandemic. In their study, 75% of the patients were women, and they found a significant decrease in six common cancer types (breast, colorectal, lung, pancreas, stomach and esophagus). They suggested that the delay in diagnosis may lead to a lower life expectancy by catching patients at a later stage (3). In our study, 75.1% of the patients were women, and a statistically significant decrease was found in patients diagnosed with atypia of undetermined significance and malignant. Before the pandemic, the most frequently encountered cancers were bladder (10 cases), skin (6 cases), stomach (3 cases), and lymph nodes (3 cases), while after the pandemic, bladder (6 cases), colon (4 cases) and breast (4 cases) changed too. While there were fourteen colon biopsies diagnosed as pre-malignant before the pandemic, this number decreased to four after the pandemic. The cases diagnosed as pre-malignant in the smears performed for cervical cancer screening were four before, and three after the pandemic. Before the pandemic, twelve of the fifteen cases were smeared and three of them were thyroid fine-needle aspirations in the atypia of

**DISCUSSION**

Covid-19, caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), first appeared in Wuhan, China, in December 2019 and turned into a pandemic by spreading all over the world (4). According to official data, the first Covid-19 case in Turkey occurred on March 11, 2020, and the first death occurred on March 15, 2020. On April 1, 2020, it was announced that the coronavirus had spread all over Turkey. The scientific committee recommended some measures such as quarantine, postponement of non-emergency elective surgeries, and restriction of hospital admission for health problems that could be postponed to reduce the hospital burden. Because of the fear, panic, and scientific committee recommendations, patients’ hospital admissions, surgeries, and materials sent to the pathology laboratory have also decreased.

Pelsemaeker et al. compared the workload of the pathology laboratory with the pre-pandemic period, taking into account the number of preparations, the number of blocks, the type of materials sent based on pathology and molecular tests. In March, they found that the total number of samples in January and February of the same year decreased by 35% and 40–45% compared to March of the previous three years. Responsible personnel observed a numerical decrease in each type of material that came to the laboratory. Still, they found that this decrease was not statistically significant in prostate biopsies, appendectomies, lower gastrointestinal resection materials, bone marrow biopsies, and central nervous system samples (2).

In the study conducted by Rosas et al. in Latin America, they compared the pathology materials in the 2.5-month period when the pandemic started and the same period of 2019 and found that the number of samples decreased (1).

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undetermined significance group. No fine-needle aspiration biopsy has been sent after the pandemic, and it all consists of smears.

Miller et al. also investigated the effect of the pandemic on cervical cancer screening according to age group and ethnicity, and found a decrease in the pandemic period compared to the pre-pandemic period, regardless of age group and ethnicity (5). In our study, although a numerical decrease was observed in the smear material, no statistically significant (p=0.560) decrease was detected. This suggests that our cervical cancer screening program has not been statistically interrupted despite the pandemic.

**CONCLUSION**

There was a statistically significant decrease in the number of patients diagnosed with malignant and atypia of undetermined significance compared to the pre-pandemic period. In these groups, especially malignant, where early diagnosis and treatment are of vital, the pandemic’s unknown and devastating effect is felt intensely, and the pandemic has delayed the patients’ admission to the hospital, causing the patients to be diagnosed at a later stage. We would like to emphasize the necessity of putting B plans into action in global events such as pandemics that affect the whole world, so as not to disrupt cancer screening programs in these special groups.

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**REFERENCES**

1. Vázquez Rosas T, Cazap E, Delgado L, Ismael J, Bejarano S, Castro C, et al. Social Distancing and Economic Crisis During COVID-19 Pandemic Reduced Cancer Control in Latin America and Will Result in Increased Late-Stage Diagnoses and Expense. JCO Glob Oncol. 2021;(7):694–703.

2. De Pelsemaeker MC, Guiot Y, Vanderveken J, Galant C, Van Bockstal MR. The Impact of the COVID-19 Pandemic and the Associated Belgian Governmental Measures on Cancer Screening, Surgical Pathology and Cytopathology. Pathobiology. 2021;88(1):46–55.

3. Kaufman HW, Chen Z, Niles J, Fesko Y. Changes in the Number of US Patients with Newly Identified Cancer before and during the Coronavirus Disease 2019 (COVID-19) Pandemic. JAMA Netw Open. 2020;2019(8):2019–21.

4. Rana C, Kumar S, Babu S, Kushwaha R, Singh US, Ramakant P, et al. Impact of ongoing COVID-19 pandemic on cytology: An institutional experience. Diagn Cytopathol. 2021;49(2):311–5.

5. Miller MJ, Xu L, Qin J, Hahn EE, Ngo-Metzger Q, Mittman B, et al. Impact of COVID-19 on Cervical Cancer Screening Rates Among Women Aged 21–65 Years in a Large Integrated Health Care System Southern California, January 1–September 30, 2019, and January 1–September 30, 2020. MMWR Morb Mortal Wkly Rep. 2021;70(4):109–13.

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