

Original Research Article

Thyroid cytology during the COVID-19 pandemic: a single centre experience

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ABSTRACT

Background: In our study, thyroid fine-needle aspiration biopsy (FNAB) data in the same calendar period of 1 year before and after the COVID-19 pandemic were compared.

Methods: Thyroid FNAB data for the same calendar period of 1 year before and after the COVID-19 pandemic were included in the study. The patients were grouped according to age, gender and thyroid FNABs according to the Bethesda system for reporting thyroid cytopathology, and the data of both groups were compared considering the diagnoses of the patients who underwent thyroid surgery afterwards.

Results: In the post-pandemic period, the number of thyroid FNABs and the number of patients over the age of 40 decreased (all $p < 0.001$). In the post-pandemic period, the rates of atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS), follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN), suspicious for malignancy, and malignant cytology increased despite the decrease in the number of patients ($p = 0.001$). Furthermore, the malignant tumour rate was 1.4% before the pandemic in patients who underwent surgical thyroidectomy and/or lobectomy; this rate was 3.5% in the post-pandemic period ($p = 0.045$).

Conclusions: We found an increase in the percentage of AUS/FLUS, FN/SFN, suspicious for malignancy, and malignant cases during the period when there were restrictions, such as pandemics, and the sampling was reduced. This finding is valuable in terms of detecting an increased malignancy rate by performing less thyroid FNAB by carefully determining the indications for thyroid aspiration biopsy regarding the latest guidelines.

Keywords: Thyroid pathology, FNAB, COVID-19 pandemic, Malignant thyroid nodules, Benign thyroid nodules

INTRODUCTION

Coronavirus disease (COVID-19), first detected in Wuhan (Hubei region, China) at the end of 2019.¹ It rapidly spread to several countries. On 13 March 2020, the world health organization declared COVID-19 a pandemic. In April, it was announced that the cases of COVID-19 had spread all over Turkey. This situation has led to the restriction of non-emergency medical procedures in the country, which aims to use health resources carefully and to protect them at the highest possible level during the pandemic period. Thyroid fine-

needle aspiration biopsy (FNAB) is a routinely used and highly reliable method in the initial screening of patients with thyroid nodules in our institution before the COVID-19 outbreak. Thyroid FNAB plays an important role in our daily cytology practice; however, it has been numerically affected by these restrictions. The number of thyroid FNABs, which was 966 in 1 year in the pre-COVID-19 pandemic period, decreased to 427 after the restrictions in the post-pandemic period. Our hospital, with its 1,550-bed capacity, is the most important centre in the region where thyroid FNABs and thyroid surgeries are widely performed; our hospital also plays a major role in the fight against the COVID-19 pandemic. Our study

focuses on how patients who underwent thyroid FNAB before and after the pandemic and who underwent thyroid surgery afterward were affected cyto-pathologically and histo-pathologically.

In this study, thyroid FNAB data for the same 1-year dates before and after the pandemic were compared.

METHODS

Ethics committee approval of Health Sciences University Adana City Training and Research Hospital was obtained for this study (Decision no: 1447). To compare how the pandemic affected thyroid aspiration biopsy results, the sample size was determined as the same calendar period of one year before and after the pandemic. The pathology reports of patients who underwent thyroid FNAB between April 1, 2019- March 31, 2020 before the COVID-19 pandemic and between April 1, 2020- March 31, 2021 after the pandemic were scanned in the Adana City Training and Research Hospital automation system. The study was done retrospectively by examining the data. Only patients who underwent thyroid FNAB were included in the study. However, patients who had undergone thyroid surgery before thyroid FNAB, received radioactive iodine treatment, chemotherapy and radiotherapy were not included in the study. The following parameters were compared by grouping the patients as pre-and post-pandemic periods. Age, gender and thyroid FNABs were classified according to the Bethesda system for reporting thyroid cytopathology (TBSRTC), and the data of both groups were compared according to the diagnosis of patients who underwent thyroid surgery afterwards. Age was grouped as under and over 40 years old. All thyroid FNAB results were classified according to TBSRTC terminology as follows. They were grouped as nondiagnostic or unsatisfactory, benign, atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS), follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN) suspected malignancy, and malignant cytology.² Among these patients, those who did not undergo thyroidectomy or lobectomy after thyroid FNAB were classified as non-operable, and those who underwent the surgery were classified as benign or malignant according to the results of the pathology report. According to the TBSRTC, malignancy risks were determined according to the thyroid FNAB and surgical results of the patients before and after the pandemic. How the restrictions during the pandemic process affected the results of thyroid FNAB and subsequent thyroid surgery was investigated.

The SPSS 19 package software (SPSS Inc., Chicago, Illinois, USA) was used for statistical analysis. Categorical variables, such as thyroid FNAB number, gender, TBSRTC and surgical operation, were summarized as numbers (n) and percentage (%). Descriptive statistics for the age variable, which is a continuous variable, were summarized as mean. Chi-

square test, Fisher's exact test or likelihood ratio test were used in the analysis of categorical variables. A $p < 0.05$ value was taken as statistical significance level.

RESULTS

The numbers of patients who underwent thyroid FNAB before and during the COVID-19 pandemic were 966 (81.6% female) and 427 (79.2% female), respectively. Thyroid FNAB count was reduced by more than half. The mean ages before and after the pandemic were 51 and 48, respectively. Furthermore, the rates of patients over 40 years of age who underwent thyroid FNAB in the pre- and post-pandemic periods were 82% and 73.8%, respectively. When we assess the distribution of patients according to TBSRTC, the most common category is benign, with rates of 77.1% and 70.4% in the pre- and post-pandemic periods, respectively.

When the thyroid FNAB numbers of 966 pre-pandemic patients and 427 post-pandemic patients were compared, the results were statistically significant ($p < 0.001$). When the thyroid FNAB numbers of patients under and over 40 years old in the pre- and post-pandemic periods were compared, a statistically significant relationship was found ($p < 0.001$). While the applications of patients over 40 years old were 82% in the pre-pandemic period, it decreased to 73.8% in the post-pandemic period. The applications of patients under the age of 40 increased from 18% to 26.2%.

When the TBSRTC data of patients during the pre- and post-pandemic periods were compared, the results were statistically significant ($p = 0.001$). The rates of FN/SFN were 1.3% and 3.3% in the pre- and post-pandemic periods, respectively, whereas those of malignant cytology were 1.4% and 4.4% in the pre- and post-pandemic periods, respectively. In the post-pandemic period, the rates of AUS/FLUS, FN/SFN, suspicious for malignancy, and malignant cytology increased despite the decrease in the number of patients.

When the results of the patients who underwent surgery after cytology during the pre- and post-pandemic periods were compared, the results were statistically significant ($p = 0.045$). The rate of malignant tumours in patients who underwent thyroidectomy and/or lobectomy before the pandemic was 1.4%, and this rate was 3.5% in the post-pandemic period. Data on patients before and after the pandemic are summarized in Table 1.

In our study, the malignancy risks in the pre- and post-COVID-19 pandemic periods for TBSRTC categories in patients who underwent surgical lobectomy and/or thyroidectomy after thyroid FNAB are shown in the table below. In the pre-pandemic period, malignancy risk ratios were found to be close to the recommended values in the categories in the Bethesda classification.² In the post-pandemic period, malignancy risk rates were found to be high in the nondiagnostic or unsatisfactory and benign

categories. No malignant case was found in the AUS/FLUS category. The rates of thyroid FNAB malignancy risk according to TBSRTC before and after the COVID-19 pandemic are shown in Table 2.

A graphical summary of patients according to TBSRTC before and after the pandemic is shown in Figure 1.

The cytological and histopathological microscopic images of follicular carcinoma and papillary thyroid carcinoma are shown in Figure 2.

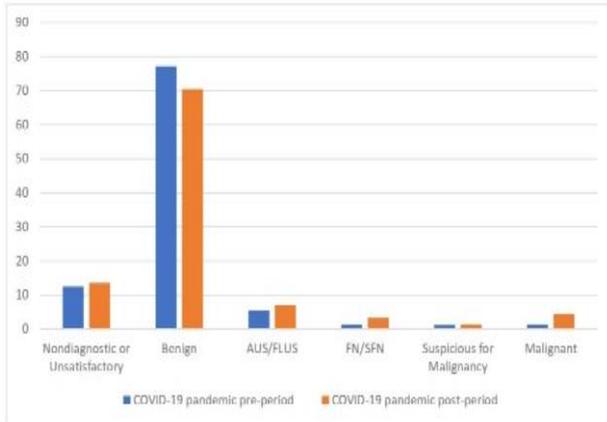


Figure 1: Distribution of patients by TBSRTC before and after the COVID-19 pandemic.

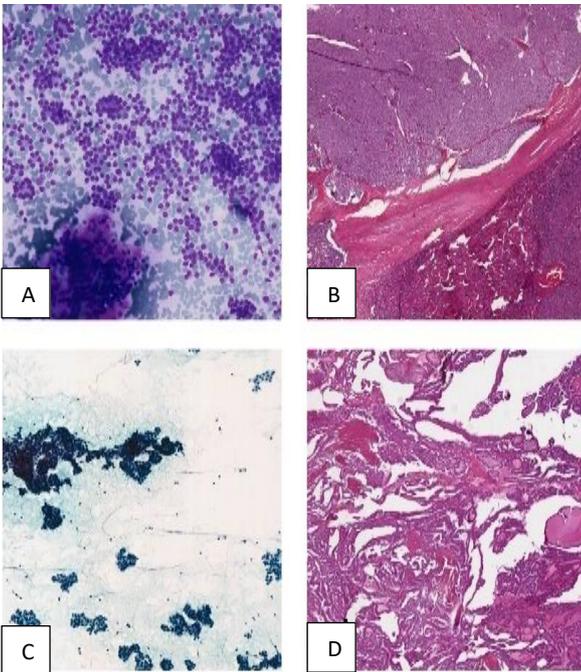


Figure 2 (A-D): FN/SFN in thyroid FNAB (May Grunwald / Giemsa staining 200x); follicular carcinoma on histopathological sections (Hematoxylin and eosin staining 100x); malignant, papillary thyroid carcinoma in thyroid FNAB (Papanicolaou staining 50x); papillary thyroid carcinoma in histopathological sections (Hematoxylin and eosin staining 20x).

Table 1: Data before and after the COVID-19 pandemic.

Variables	COVID-19 pandemic pre-period, N (%)	COVID-19 pandemic post-period, N (%)	P value
Thyroid FNAB	966 (69.3)	427 (30.7)	<0.001
Age range (Years)	15-91	8-81	
Age (Years)			
<40	174 (18)	112 (26.2)	<0.001
>40	792 (82)	315 (73.8)	
Gender			
Female	788 (81.6)	338 (79.2)	0.291
Male	188 (18.4)	89 (20.8)	
TBSRTC			
Nondiagnostic or unsatisfactory	130 (13.4)	57 (13.5)	0.001
Benign	745 (77.1)	301 (70.4)	
AUS/FLUS	53 (5.5)	30 (7)	
FN/SFN	13 (1.3)	14 (3.3)	
Suspicious for malignancy	12 (1.2)	6 (1.4)	
Malignant	13 (1.3)	19 (4.4)	
Surgical operation			
Non-operable	910 (94.2)	393 (92)	0.045
Benign	42 (4.3)	19 (4.4)	
Malignant	14 (1.4)	15 (3.5)	

Table 2: Thyroid FNAB malignancy risk rates according to TBSRTC before and after the COVID-19 pandemic.

Variables	COVID-19 pandemic pre-period risk of malignancy (%)	COVID-19 pandemic post-period risk of malignancy (%)
Nondiagnostic or unsatisfactory	12.5	33.3
Benign	4.7	22
AUS/FLUS	14.2	0
FN/SFN	20	40
Suspicious for malignancy	100	66
Malignant	100	100

DISCUSSION

The incidence of thyroid cancer has increased by 4.5% per year over the past 10 years, with no change in mortality; this rate is faster than that of other cancers. In general, patients with thyroid cancer follow a calm course and show good results after follow-up. Whether the early detection and treatment of thyroid cancers can

significantly alter disease outcomes lacks evidence. The overall mortality rate remained less than 0.5% despite the improvement of imaging modalities and the increase in tumour incidence.³ When a thyroid nodule is diagnosed, thyroid FNAB performed by evaluating its clinical and radiological findings is the most important diagnostic method to rule out the presence of cancer. However, the diagnostic accuracy of thyroid FNAB depends on the indication for performing FNAB combined with aspiration procedure and cytological evaluation. In regions where thyroid nodules are prevalent, accurate results may not be obtained by indiscriminately performing thyroid FNAB to the whole population. This strategy may reduce diagnostic accuracy and cause unsatisfactory results.⁴

After the world health organization declared SARS-Cov-2 a pandemic on 13 March 2020, although it changed from time to time in our country, it led to the restriction and postponement of non-emergency elective medical and surgical procedures. Opinions supporting the postponement of thyroid FNAB during the pandemic period are common. Both the European clinical guidelines on the management of thyroid nodules during the COVID-19 period and the US endocrinology recommendations suggest that most thyroid aspiration biopsies can be performed at later dates.⁵ Guidelines on thyroid nodules have recently changed the recommendations for FNAB to reduce the demands for thyroid aspiration biopsy, especially in non-high-risk patients on ultrasonography.⁶

Most thyroid nodules are low risk. Safely deferring most thyroid FNABs during the pandemic period can be considered, as even the malignant ones can be treated with delay. At the same time, no clear evidence has been found that SARS-CoV-2 directly affects thyroid disease.⁷

During the COVID-19 pandemic, the indication for thyroid FNAB must be carefully evaluated for the following reasons. The first reason is that most thyroid FNABs can be delayed, and the other is the risk of COVID-19 transmission to healthcare personnel during thyroid aspiration biopsy, transport, dissemination and staining.^{5,8} In this difficult period of the pandemic, we had two main goals that determined our approach to cytological materials covering all biopsies and thyroid FNABs. These goals ensured the safety of all health personnel and provided the highest contributions to patient treatment by giving the correct diagnoses. During this period, all pathologists and pathology technicians in our department wore personal protective surgical masks and face shields in their working areas.

Our study is consistent with the results of other studies, which show a decrease in thyroid FNAB during the COVID-19 pandemic period.⁹⁻¹¹ The number of thyroid FNABs, which was 966 in the same calendar period before the COVID-19 pandemic in our institution, has decreased by 55.8% to 427 due to the restriction of non-

emergency medical procedures. Some psychological factors, especially fear of being infected with a virus, in thyroid FNAB reduction suggest that many patients are anxious about coming to the hospital and undergoing any medical procedures.¹⁰ In our study, the decrease in the applications of patients over the age of 40 for thyroid FNAB during the COVID-19 pandemic period also supports this idea.

A study in the literature shows that the benign category has decreased proportionally in the thyroid FNAB during the period when the restrictions were most stringent in Italy during the COVID-19 period, whereas that in suspected malignancy and malignant categories has increased proportionally.¹⁰ In our study, while the benign category decreased proportionally according to TBSRTC after the COVID-19 pandemic, the AUS/FLUS, FN/SFN, suspected malignancy and malignant categories has increased proportionally. This situation shows that clinicians avoid unnecessary thyroid FNAB during the pandemic period with the latest guidelines and reflect the number of high-risk nodules.

As in other studies, the number of thyroid surgeries has decreased in our study during the pandemic period.⁹ While the rate of benign results did not change in the pathology reports of patients who underwent surgery in our study, the rate of malignancy has increased approximately 2.5 times after COVID-19 pandemic. This finding shows that although the number of thyroid FNAB and thyroid surgeries has decreased, cases reported as malignant cytology can be operated on successfully by taking necessary preventive measures and arrangements.

In our study, the rates of malignancy risk in the pre-pandemic period in patients who underwent thyroid FNAB and subsequent surgery are close to the range of values recommended in the categories in TBSRTC.² We believe that the concern created by the assignment of pathologists in the COVID-19 pandemic services, pandemic test sampling areas and filtration teams is effective in high-malignancy risk in the nondiagnostic and benign categories in the post-pandemic period.

Our study had some limitations. These are the assignments of pathologists from time to time to COVID-19 services, pandemic test sampling areas, and filtration teams during the COVID-19 pandemic period, and the psychological factors created by the pandemic. At the time of the evaluation of the data of this study, especially for the post-COVID-19 pandemic period, the fact that the patients did not have a long time to undergo surgery according to the thyroid FNAB results was a limiting factor in determining the risk of malignancy.

CONCLUSION

The COVID-19 pandemic has led to the restriction of non-emergency medical procedures in healthcare. Although the number of thyroid FNAB samples

decreased by more than half, we found a significant increase in the percentage of AUS/FLUS, FN/SFN, suspicious for malignancy and malignant cases. This shows that a higher malignancy rate can be detected by performing fewer thyroid FNABs by carefully determining the indications for thyroid aspiration biopsy in the light of the latest guidelines. Our study is significant in that it demonstrates that it can continue to give the most accurate diagnosis to high-risk thyroid nodules by strictly applying safety protocols to prevent disease transmission, with the policy of accurate sampling in times of health crisis during the pandemic.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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