Histopathological profile of ovarian tumors in a tertiary care centre and impact of recent WHO 2020 classification

Authors

1) **Sheenam Azad, Professor, Dept of Pathology, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.**
2) **Neelima Bahal, Associate Professor, Dept of Pathology, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.**
3) **Trisha Sharma, Junior Resident, Dept of Pathology, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.**
4) **Nidhi Kumari, Assistant Professor, Dept of Gynae & Obs, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.**
5) **Seema Acharya, Professor and Head, Dept of Pathology, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.**

Corresponding Author: Dr. Neelima Bahal, Associate Professor, Dept of Pathology, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India;
Email: drneelimasuri@gmail.com

Manuscript submitted – 13th December 2021
Peer review completed – 11th June 2022
Accepted for Epub – 13th April 2023

Abstract:

Background: Ovarian tumors are amongst the common neoplasms affecting the Indian women. The grave nature of these tumors is proved by the highest mortality rates attributed by lack of symptoms in most patients and inaccessible site. The WHO 2014 classification was modified in 2020, keeping in consideration the probable tissue of origin and associated molecular basis. **Objectives**: This study was conducted to see the histopathological profile of ovarian tumors and impact of recent WHO 2020 classification. **Methods:** This study was a retrospective study conducted in the pathology department at SGRRIM & HS, Dehradun. Hysterectomies, oophorectomies and ovarian cystectomy specimens received in the pathology department over a period of four years were included in the study. Ovarian tumors classified according to the WHO 2014 classification were reclassified according to WHO 2020 classification and a comparison was made between the two. There were 114 cases of ovarian tumors, received in the department of pathology during this duration. All the relevant history, clinical findings and investigations were recorded. **Results**: Benign tumors were the commonest (76.9% cases) followed by malignant tumors which accounted for 20.14% of all the ovarian tumors. Borderline tumors were the least common tumors constituting only 2.87% cases. The surface epithelial tumors were the most commonly diagnosed ovarian tumors comprising 64.02% cases followed by germ cell tumors, which constituted 28.77% cases. Serous cystadenoma was the commonest primary benign tumors followed by benign teratoma. Serous carcinoma was the commonest primary malignant tumor followed by adult granulosa cell tumors. Serous carcinoma was further categorized into high grade serous carcinoma and low grade serous carcinoma which are distinct entities according to WHO 2020 classification. Endometriotic cysts which were mentioned along with endometrioid cystadenoma in benign endometrioid tumors in the 2014 classification are no longer placed in this category. **Conclusion**: The benign ovarian tumors are more common than the malignant tumors in all the age groups and histologically, epithelial tumors are the most common. The WHO classification 2014 and 2020 stresses upon the combined use of histopathology, immunohistochemistry and molecular pathology for better reproducibility and accurate diagnosis. There were no major changes except the terminology and categorization of certain entities especially the surface epithelial tumors.

Keywords: Menorrhagia, fibromyoma, perimenopausal woman.

Azad S, Bahal N, Sharma T, Kumari N, Acharya S. Histopathological profile of ovarian tumors in a tertiary care centre and impact of recent WHO 2020 classification. The New Indian Journal of OBGYN. 14th April 2023. Epub Ahead of Print.

Ovarian tumors are amongst the common neoplasms afflicting the Indian women after breast and cervical neoplasms. They are the seventh leading cause of cancer deaths among women worldwide and in India it comprises 8.7% of the cancers in different parts of the country [1,2]. The grave nature of these tumors is further proved by the highest mortality rates associated with them. This may be attributed to the lack of symptoms in most patients in early stage of the disease, inaccessible site and limited use of newer diagnostic techniques. Approximately 70% of the patients of ovarian tumors have the tumor spread outside the pelvis at the initial presentation. Diversity of ovarian tumor types poses a challenge for surgical pathology. To add to this challenge, the ovary is also a common site of metastatic deposits from other abdominal cancers.

The WHO classification forms the histopathological basis for classification of ovarian tumors. It was modified in 2014 and incorporated some changes in the category of surface epithelial tumors based on the most probable tissue of origin and molecular basis. It sharpened the dividing line between adenomas and SBOTs. The newer classification of 2020 is largely unchanged [3]. It has emphasized upon the use of modern diagnostic techniques comprising of immunohistochemistry and molecular methods. Despite all these modifications in the newer classification of ovarian tumors, morphology still remains the backbone of the diagnosis. Both tumor stage (according to the FIGO classification) and tumor type (according to WHO classification) are important for planning the treatment. This study was conducted to see the histopathological profile of ovarian tumors and impact of recent 2020 WHO classification on the profile.

Materials and methods

The present study was a retrospective study conducted in the department of pathology at a tertiary care hospital and medical college in Dehradun after approval by institutional ethical committee. There were 114 cases of ovarian tumors, received in the department of pathology between January 2016 to December 2019. Non-neoplastic lesions and tumor like conditions were not included in the study. The relevant clinical details and investigations were recorded. All the slides of cases of diagnosed histopathologically as ovarian tumors, were retrieved from the records and reexamined.

Histopathological findings were recorded and the tumors were then recategorized according to WHO classification 2020. A comparison was done between the two classifications to see the impact on the histopathological profile.

The WHO 2020 classification of ovarian tumors differs from 2014 classification only in terms of categories and terminologies especially of surface epithelial tumors. The previous 2014 classification divided the ovarian serous carcinoma into low grade and high grade. However WHO 2020 considered them to be entirely different tumors, rather than different grades of the same tumor on the basis of different sites of origin of these tumors. Seromucinous carcinoma included in the previous classification has been removed and is considered as a subtype of endometrioid carcinoma. The classification of ovarian sex cord stromal tumors, germ cell tumors, miscellaneous and tumor like lesions has not been changed. The broad classification of ovarian tumors, according to the updated 2020 WHO guidelines is as under [3] -

(A) Epithelial tumors
  - Serous tumors
  - Mucinous tumors
  - Endometrioid tumors
  - Clear cell tumors
  - Seromucinous tumors
  - Brenner tumors
(B) Mesenchymal Tumors
(C) Mixed epithelial and mesenchymal tumors
(D) Sex cord stromal tumors
(E) Germ cell tumors
(F) Miscellaneous tumors
(G) Tumor like lesions
(H) Metastasis to the ovary.

Results

A total of 114 cases of ovarian tumors were received during the study period. Amongst these, 78.7% (n=89) cases were unilateral and 21.0% (n=25) cases were bilateral. In certain cases, the types of tumors were different in the two ovaries. Therefore the bilateral tumors were counted separately making the total number as 139 (n=139).

Grossly 76.2% of the tumors were cystic, 15.8% cases were solid and 7.9% cases were partly solid and partly cystic. Amongst the bilateral tumors, serous cystadenoma was the most common bilateral benign tumor and serous carcinoma was the most common bilateral malignant tumor. Benign tumors were the commonest comprising 76.9% cases followed by malignant tumors which accounted for 20.14% of all the ovarian tumors. Borderline tumors were the least common tumors constituting only 2.87% cases. Females during the reproductive age were commonly affected as shown in table 1.

Table 1: Comparative frequency of different ovarian tumors in different age groups

Age in years	Surface epithelial tumors n (%)	Germ cell tumors n (%)	Sex cord stromal tumors n (%)	Secondary tumors n (%)	Miscellaneous tumors n (%)
0-19	4/89(4.5)	6/40(15.0)	-	-	-
20-50	61/89(68.5)	25/40(62.5)	2/4(50)	4/4(100)	-
>50	24/89(26.9)	9/40(22.5)	2/4(50)	-	2/2(100)
Total	89	40	4	4	2

Table 2: Comparative analysis of broad histological types of ovarian neoplasms

Tumor types	2014 n (%)	2020 n (%)	Benign n (%)	Borderline n (%)	Malignant n (%)
Epithelial tumors	89(64.02)	79(61.2)	67(62.6)	04(100)	18(64.28)
Sex cord stromal tumors	04(2.87)	04(3.1)	01(0.93)	00	03(10.71)
Germ cell tumors	40(28.7)	40(31.0)	39(36.44)	00	01(3.57)
Secondary tumors	04(2.87)	04(3.1)	00	00	04(14.28)
Miscellaneous tumors	02(1.43)	02(1.5)	00	00	02(7.14)
Total	139	129	107(76.9)	04(2.8)	28(20.14)

Table 3: Comparative distribution of surface epithelial tumors

Types of tumors	2014 n (%)	2020 n (%)
Serous tumors		
Serous cystadenoma	32/89(35.95)	32/79(40.5)
Serous adenofibroma	04/89(4.5)	04/79(5.1)
Serous borderline tumor	03/89(3.37)	03/79(3.8)
Low grade serous carcinoma	02/89(2.24)	02/79(2.5)
High grade serous carcinoma	08/89(8.98)	08/79(10.1)
Mucinous tumors		
Mucinous cystadenoma	16/89(17.9)	16/79(20.25)
Mucinous borderline tumor	01/89(1.12)	01/79(1.2)
Mucinous carcinoma	01/89(1.12)	01/79(1.2)
Endometrioid tumors		
Endometriotic cysts	10/89(11.2)	-
Endometrioid cystadenoma	04/89(4.5)	04/79(5.1)
Seomucinous tumors		
Seromucinous cystadenoma	01/89(1.12)	01/79(1.26)
Total	89	79

Based on the histopathological classification, surface epithelial tumors were the most commonly diagnosed ovarian tumors comprising 64.02% cases (89/139) followed by germ cell tumors, which constituted 28.77% cases (40/139). Sex cord stromal tumors and secondary tumors were very less and each comprised 2.8% (4/139) of all the cases (table 2). Epithelial tumors formed the commonest group in all the benign (62.6%), borderline (100%) and malignant (64.28%) tumors (table 2). Germ cell tumors were the second most common group, whereas sex cord stromal tumors were the second commonest group of primary ovarian malignant neoplasm. The histopathological profile of ovarian tumors and subcategorisation of surface epithelial tumors based on WHO 2020 classification is shown in table 2 and table 3.

Amongst the germ cell tumors, most common was benign teratoma (39/40 tumors; 97.5%). There was only one case of yolk sac tumor (1/40; 2.5%). Majority of the tumors were malignant in the category of sex cord stromal tumors (i.e. adult granulosa cell tumor; 75%). Fibroma was the only benign sex cord stromal tumor diagnosed during the study period. In the category of miscellaneous tumors, there were two cases of small cell carcinoma (1.83%). The secondary tumors included four cases of Krukenberg's tumor (2.87%).

Discussion

Ovarian tumors arise from different cell lineages and have varied clinical behavior and malignant potential. The present study compares the histopathological profile of ovarian tumors based on the previous and updated 2020 WHO classification. Benign tumors were three times more common than the malignant neoplasms in both systems of classification in the present study and a few other studies by Gupta et al, Pilli et al, Shoail et al and Kuldeepa et al, who have all reported almost similar percentage of benign and malignant tumors [4,5,7,8]. The unilateral tumors were found to be more common than bilateral tumors in this study as well as studies by Pilli et al, Kuldeepa et al and Jha et al [4 - 6].

The surface epithelial tumors were the most common followed by germ cell tumors in the present study and few other studies [2,6,9,10]. Most of the cases were seen in the younger age group (21-40 years) in the present study and a few other [10 - 13].

Serous tumors comprise about one - third of all the ovarian tumors. Serous cystadenoma was the most common benign surface epithelial tumor followed by mucinous cystadenoma in the present study. Similar findings have been observed by Shah & Hishikar and Thanikasalam K et al [14,15]. However, Mankar and Jain reported mucinous cystadenoma to be more common than serous cystadenoma [16].

As per the previous WHO classification 2014, serous borderline tumors were divided into two categories, namely serous borderline tumor/atypical proliferative serous tumor and serous borderline tumor - micropapillary variant/non invasive low grade serous carcinoma. But in the updated classification of 2020, a broader term 'serous borderline tumor of ovary' is recommended for borderline tumors encompassing both the categories of borderline tumors of WHO 2014 classification. The use of terminology 'Non invasive low grade serous carcinoma/Atypical proliferative serous tumors' is now no longer recommended in the updated classification. In the present study, 3 cases of serous borderline tumors were diagnosed. Priya et al also reported serous borderline tumors to be more common than mucinous borderline tumors but Li et al found a higher incidence of mucinous borderline tumors [17,18].

Serous carcinomas are the most common malignant ovarian tumors and account for approximately 40% of all cancers of the ovary. According to molecular alterations involved in serous carcinogenesis, the new WHO classification categorizes serous carcinomas into low grade and high grade carcinomas, which are now considered as distinct tumors and not the same tumors having low and high grade. This is because they have different origin, morphology, molecular and genetic nature. Low grade serous carcinomas arise within the ovary from benign and borderline serous tumors and high grade serous carcinomas arise from distal fimbrial end of the fallopian tube from a precursor lesion known as serous intraepithelial carcinoma. The low grade tumors are invasive serous tumors with low grade malignant potential which were historically classified as grade I serous carcinoma. On the other hand, high grade tumors included were historically classified as grade 2 or grade 3 serous carcinomas. Necrosis is not observed in low grade serous carcinoma and mitosis is also low (<2-3 mitotic figures per 10 HPF). Serous carcinoma was more common than mucinous carcinoma in the present

study. These comprised eight cases of high grade serous carcinoma (10.1%) and two low grade serous carcinoma (2.5%). These results were in concordance with studies by Mankar and Jain & Jha et al [6,16].

The WHO 2014 classification placed the endometriotic cysts in the same category as benign endometrioid cystadenoma due to similar ARDIA 1 mutations but the recent 2020 classification does not mention them. However, it is important to look for endometriosis because of potential malignant transformation. Endometriosis is implicated in the development of endometrioid, seromucinous and clear cell tumors . Four cases of endometrioid cystadenoma were diagnosed during the study period.

Seromucinous group of tumors was a newly added entity in the 2014 WHO classification. Seromucinous cystadenoma is mullerian cystadenoma of mixed cell types. In the present study, only one case of seromucinous cystadenoma (1.26%,1/79) was diagnosed in the epithelial ovarian tumors. The recent classification has removed seromucinous carcinoma as a separate entity because of significant overlap with endometrioid carcinoma based on immunohistochemical and molecular studies. No case of seromucinous carcinoma was observed during the study period.

Germ cell tumors constitute 20% of all ovarian neoplasms and most of them are seen in children and young adults. Approximately 95% of these tumors are benign teratomas as seen in the previous studies as well as present study [19,20]. Sex cord stromal tumors are predominantly malignant. Adult granulosa cell tumor was observed to be the most common malignant germ cell tumor as seen in the present study and another study by Haroon et al [21].

Miscellaneous tumors are rare and include rete ovarii, wolffian tumor, small cell carcinoma, hypercalcemic type, small cell carcinoma, pulmonary type, Wilm's tumor, paraganglioma and solid pseudopapillary neoplasm. Secondary tumors to the ovary are the neoplasms which spread from the extraovarian sites. In the present study also, there were four cases of secondary ovarian tumors (Kruckenberg's tumor) and only two cases of small cell carcinoma were reported comprising 2.87% and 1.43% cases respectively.

Conclusion

In all age groups benign tumors were common than malignant tumors. Serous epithelial tumors remain the commonest tumors followed by germ cell tumors. Serous cystadenomas are the commonest primary benign tumors followed by benign teratomas. Serous carcinoma are the commonest primary malignant tumors followed by adult granulosa cell tumors. The WHO classification defines the actual type of tumor which serves as a guide for clinical management and also provides a framework for organizing the diseases that helps in further scientific investigation. The WHO classification 2020 of ovarian tumors stresses upon the combined use of histopathology, immunohistochemistry and molecular pathology, however, histopathology remains the gold standard for making the diagnosis. There were no major changes in the recent WHO 2020 classification except the terminology and categorization of certain entities especially the surface epithelial tumors without much impact on the major common broad categories in the histopathological profile of ovarian tumors.

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Conflict of interest: None. **Disclaimer:** Nil.