A RETROSPECTIVE CLINICOPATHOLOGICAL STUDY OF MALIGNANT OVARIAN TUMORS: A 3 YEAR EXPERIENCE IN A TERTIARY HEALTH CARE CENTER OF DHAKA, BANGLADESH

SAHA S[1], SIDDIQUE S[2], AKTER S[3], QUADER MA[4], PRASAD I[5], SIDDIQUE S[6], ALAM S[7], MEHZABIN S[8]

Abstract:

Background: *Ovarian tumors are a heterogeneous group of neoplasm that have become increasingly important now-a-days because of their large variety of neoplastic entities and gradually increased rate of mortality due to female genital cancers.*

Objectives: *The aim of this study was to analyze the histopathological pattern and clinical presentation of malignant ovarian tumors-according to the WHO classification of ovarian tumors [2003] in a tertiary care center of Dhaka, Bangladesh.*

Materials and Methods: *This retrospective study included and studied a total of 54 cases of malignant ovarian tumors at the Department of Obstetrics and Gynecology, Popular Medical College Hospital, Dhaka, Bangladesh over a period of 3 years from Jan 2015 to Dec 2017.*

Results: *The mean age was 47.44±14.24 years old (age ranged from 20-70 years). Of the 54 malignant ovarian tumors studied, the commonest histological pattern observed in the study was serous cyst adenocarcinoma constituting 26 cases (48.15%) followed by adenocarcinoma of ovary (25.9%), mucinous cyst adenocarcinoma (14.8%), endometriod adenocarcinoma (3.7%), dysgerminoma (3.7%) and ovarian choriocarcinoma (3.7%). High level of serum CA125 was found in most of the cases (n=48; 88.89%). The chief complaints were abdominal pain (n=38; 70.37%) and abdominal distension (n=29; 53.70%). Majority were admitted with less than one month duration of symptoms. The size of the tumor varied from 2.2 to 20 cm. All the patients were admitted in III and IV stage.*

Conclusions: *Serous cyst adenocarcinoma was the common finding of this study. The prognosis and varying therapeutic strategies of malignant ovarian tumors necessitate an accurate histopathological evaluation.*

Key words: *Malignant ovarian tumors, serous cyst adenocarcinoma, mucinous cyst adenocarcinoma, dysgerminoma.*

Introduction:

Ovarian cancer is the most serious disease of the female genital tract. The high mortality reflects both the frequency of the disease and the late stage at which most women with ovarian cancer present. A woman with an enlarging ovarian cancer will not be aware of its presence; only when there is noticeable abdominal distension, pain or interference with bowel or urinary function will it apparent that the tumor is present and, by that time, it is unlikely to be confined to the ovary.

Ovarian cancer represents one of the most frequently seen malignancies in women and it is the fifth most common cause of cancer-related death in women.[1] The total number of ovarian cancer cases worldwide has been estimated to

1. Dr. Joysree Saha, Associate Professor, Department of Obstetrics and Gynecology, Popular Medical College, Dhanmondi -2, Dhaka, Bangladesh.
2. Dr. Sohana Siddique, Associate Professor & Head of Department of Obstetrics and Gynecology, International Medical College, Gushulia, Gazipur, Bangladesh.
3. Dr. Sumaya Akter, Assistant Professor, Department of Obstetrics and Gynecology, Popular Medical College, Dhanmondi -2, Dhaka, Bangladesh.
4. Dr. Md. Abdul Quader, Associate Professor, Department of Transfusion Medicine, Popular Medical College, Dhanmondi -2, Dhaka, Bangladesh.
5. Dr. Indrajit Prasad, Associate Professor, Department of Endocrine and Metabolism, Dhaka Medical College, Dhaka.
6. Dr. Sharmina Siddique, Consultant, Obs & Gynae, DMCH, Dhaka
7. Dr. Saleha Alam, Registrar, Obs & Gynae, DMCH, Dhaka
8. Dr. Shafinaz Mehzabin, Medical Officer, Sheikh Hasina National Institute of Burn and Plastic Surgery, Dhaka

Correspondence: Dr. Joysree Saha, Associate Professor, Department of Obstetrics and Gynecology, Popular Medical College, Dhanmondi -2,Dhaka, Bangladesh.

be 1, 92,000 per year in 2000 and representing 4% of all cancers in women and the sixth leading site of malignancy.[2]

Many ovarian tumors are asymptomatic in the early stages and are unfortunately diagnosed in the advanced stages. The high mortality rate of ovarian cancer is due to its late detection, thus earning itself the term "Silent Killer".[3]

The ovarian tumors present wide variation in the clinical and histopathological patterns. As there are no screening tests for ovarian tumors and these tumors cannot be confidently distinguished from one another on the basis of their clinical, radiological or gross characteristics, it is important to determine the histological pattern of ovarian tumor to achieve the optimum treatment response as prognosis depends on the degree of differentiation.[4,5]

Ovarian tumors are one of the major health problems representing 30% of cancers of female genital tract.[6] It is the most complex tumor of women in terms of histiogenesis, clinical behaviour and malignant potentiality and represents the sixth most common female cancer and the fourth leading cause of death due to cancers in women.[7]

Of all the gynecological cancers, ovarian tumors represent the greatest challenge to clinicians because it is very difficult to diagnose it in early stage due to its nonspecific symptoms and even asymptomatic nature in many cases. On the other hand, ovarian tumors at an advanced stage are easy to diagnose but associated with poor prognosis despite advances in surgery, chemotherapy, and more recently, targeted therapy. Ovarian tumors are also a constant source of confusion to the pathologists because of the wide spectrum of clinical and morphological features.[8]

Ovarian cancer is the sixth most common cancer and seventh most common cause of death among women world-wide, Japan and Asian countries have rates of 2–6.5 new cases per 100,000 women per year.[9,10]

An ovarian neoplasm affects a significant number of female populations and has the worst prognosis among all gynecological malignancies. These tumors behave in a diverse way and generally escape detection until they attain a larger size.[11]

Ovarian tumors are notorious for poor prognosis owing to the late detection of disease. The histogenesis of many tumors is interrelated and accurate histopathological diagnosis is needed for effective treatment.[12] Due to the fatal outcome of this disease, early and accurate diagnosis of ovarian tumor is needed. The early detection and assessment of ovarian malignancy are an important part of gynaecological practice.[13]

Thus present study was undertaken to analyze clinical presentation, histopathological patterns and tumor markers of patients with malignant ovarian cancers as per the World Health Organization (WHO) classification 2003 (14) in a tertiary care hospital in Dhaka, Bangladesh.

Materials and Methods:

In this retrospective study, 54 cases of malignant ovarian tumors were studied from January 2015 to December 2013 in the Department of Obstetrics and Gynecology, Popular Medical College Hospital, Dhaka, Bangladesh. All the materials such as blocks and slides available in the department were studied.

Detailed case history was taken with clinical examination data from the histology requisition forms and wherever required from the medical record section. Data regarding patient's age, symptoms, size of tumors, stage of tumors, tumor markers, histopathology and follow up where ever possible was recorded and analyzed.

Formalin fixed, paraffin embedded tissue block were used. H and E stained tissue sections were examined and classified as per the WHO classification of ovarian tumors (14).

Inclusion criteria
- Clinically diagnosed patients of malignant ovarian cancer who underwent surgery in the Department of Obstetrics and Gynecology at Popular Medical College Hospital, Dhaka, Bangladesh.

Exclusion criteria
- Non-neoplastic lesions of ovary (Polycystic ovary, follicular cyst, corpus luteal cyst, endometrioma) and benign ovarian tumors

- Specimens without the complete information
- Ovarian tumors managed conservatively.

Results:

Among the 54 cases, age of the patient was ranged from 20-70 years. The mean age was 47.44±14.24 years old [Table-1 and Figure 1.].

Table-I

Age distribution

Age (years)	Number of patients (%)
20-29	8 (14.81%)
30-39	12 (22.22%)
40-49	9 (16.66%)
50-59	14 (25.92%)
60-70	11 (20.37%)
Total	54 (100%)
Mean ± SD	47.44 ± 14.24

All patients (n=54) were admitted to the hospital
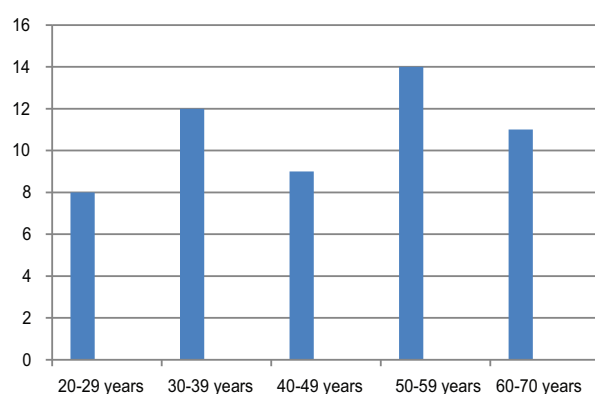
Fig.-1: *Showing age distribution in graphical manner.*

with either stage III disease (n=30; 55.56%) or with stage IV disease (n=24; 44.44%) [Table-II].

Table-II

Stage of malignant ovarian cancer.

Stage	Number of patients (%)
Stage III	30 (55.56%)
Stage IV	24 (44.44%)
Total	54 (100%)

The chief complaints were abdominal pain and abdominal distension. 38 patients (70.37%) came to the hospital with abdominal pain, 29 (53.70%) patients presented with abdominal distension, 18 patients (33.33%) with lower abdominal discomfort and other symptoms. Duration of symptoms was 1 month or less in majority of patients (64.96%) with malignant ovarian tumors. [Table-III and Figure 2]

Of the 54 malignant ovarian tumors studied, the commonest histological pattern observed in the study was serous cyst adenocarcinoma (n=26; 48.15%) followed by adenocarcinoma of ovary (n=14; 25.9%), mucinous cyst adenocarcinoma (n=8; 14.8%), endometriod adenocarcinoma (n=2; 3.7%), dysgerminoma (n=2; 3.7%) and ovarian choriocarcinoma (n=2; 3.7%). [Table-4 and Figure 3]

High level of serum CA125 was found in most of the cases (n=48; 88.89%) [Table-5].

The size of the tumor varied from 2.2 to 20 cm [Table-6].

Table-III

Distribution of symptoms with duration

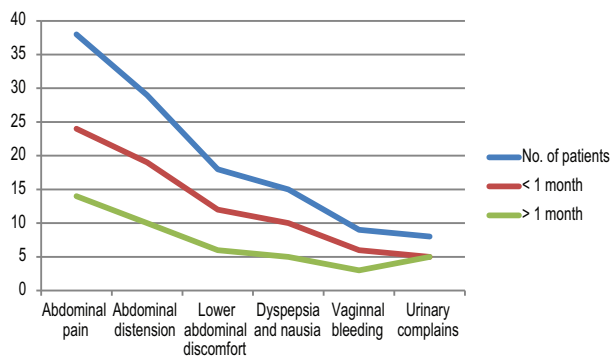|	Number of patients (%)	Duration of symptoms	
		< 1 month	> 1 month
Abdominal pain	38 (32.48%)	24 (20.51%)	14 (11.97%)
Abdominal distension	29 (24.79%)	19 (16.24%)	10 (8.55%)
Lower abdominal discomfort	18 (15.38%)	12 (10.26%)	6 (5.12%)
Dyspepsia and nausea	15 (12.82%)	10 (8.55%)	5 (4.27%)
Vaginal bleeding	9 (7.69%)	6 (5.13%)	3 (2.56%)
Urinary complains	8 (6.84%)	5 (4.27%)	3 (2.57%)
Total (multiple response)	117 (100.00%)	76 (64.96%)	41 (35.04%)

Fig.-2: *Distribution of symptoms with duration.*

Table-IV

Histopathology of tumors

Types	Number of patients (%)
Serous cyst adenocarcinoma	26 (48.15%)
Adenocarcinoma of ovary	14 (25.9%)
Mucinous cyst adenocarcinoma	8 (14.8%)
Endometriod adenocarcinoma	2 (3.7%)
Dysgerminoma	2 (3.7%)
Ovarian choriocarcinoma	2 (3.7%)
Total	54 (100%)

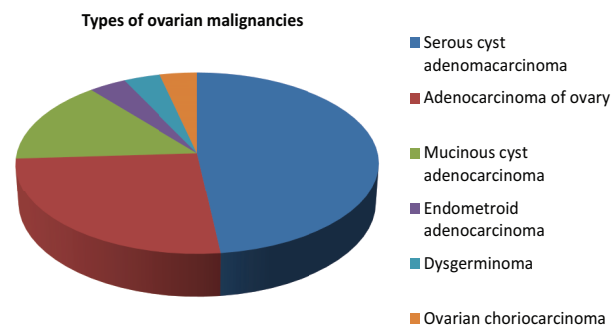**Fig. 3.** *Distribution of types of ovarian malignancies.*

Table-V

Distribution of serum CA-125.

Serum CA-125	Number of patients (%)
Raised	48 (88.89%)
Normal	6 (11.11%)
Total	54 (100%)

Table-VI

Distribution of tumor size.

Size of tumor	Number of patients (%)
1-5 cm	4 (7.4%)
5.1-10 cm	32 (59.26%)
10-20 cm	18 (33.33%)
>20 cm	0 (0%)
Total	54 (100%)

Discussion:

Ovarian cancer is the most lethal gynecologic malignancy. Ovarian tumors are fairly common in gynaecological practice. In this present study the mean age of the study subjects were 47.44 ± 14.24 years. Age group 40-59 years showed the highest ovarian tumors (42.58%). Pradhan HK et al. (15) showed that 41-60 years old had suffered much in ovarian malignancies (61.10%). Jha et al. (16) noted most malignant tumors above 40 years (73.10%). Study done by Chowdhury S et al. (17) in Bangladesh showed 77.77% ovarian tumors in age group 41-59 years. All the studies above were higher than the present study. In a study done by Deeba F et al (13) showed that mean age of the patients were 40.60 ± 12.5 years and 50.00% of them showed ovarian malignancies which is similar to the present study.

In this study all the patients were admitted to the hospital with stage III diseases (n=30; 55.56%) and stage IV diseases (n=24; 44.33%). Basu et al (18) reported 80% patients in stage III/IV at diagnosis but Saini et al (19) described 20.8% cases were in stage II, 47.85% in stage III and 16.56% in stage IV. In a study by Mondal et al (20) had 20% cases in stage II and 60% in stage III while Doufekas et al (21) reported 60% cases were diagnosed in stage III and IV. In Krishnaswamy P et al. (22) study 59 (55.6%) patients presented in the last stages III and IV (stage III: n=49, 46.2%, stage IV: n=10, 9.4%). The variations may be due to age and sample size of the study subjects.

The commonest symptom in the present study was abdominal pain noticed in 38 patients (32.48%) followed by abdominal distension and lower abdominal discomfort (24.79% & 15.38%). Abdominal pain as main complaints was similar

to study by Rashid et al (23), Pradhan HK et al. (15), Chowdhury S et al. (17) and Krishnaswamy P (22) et al. studies. Other complaints were variable with the present study.

Deeba F et al. (13) found abdominal lump (71.40%) and weight loss (60.70%) as main symptoms which differ from the present study.

The commonest histological pattern observed in the study was serous cystadenocarcinoma (48.15%) followed by adenocarcinoma of ovary (25.9%), mucinous cystadenocarcinoma (14.8%), endometriod adenocarcinoma (3.7%), dysgerminoma (3.7%) and ovarian chorio-carcinoma (3.7%). This observations are comparable to the previous published data of a multicenter study conducted at different Tertiary Health Care Centers of Dhaka, Bangladesh (13) and Badge SA et al. (24) study. This study differs with the findings of Pradhan HK et al. (15), Chowdhury S et al. (17) and Krishnaswamy P (22) et al.

It was observed that 11.11% patients had normal serum CA-125. Raised serum CA-125 was found in 88.89% cases. Raised serum CA 125 were observed in malignant ovarian tumors by Kondoh et al. (25) 77.60% and Deeba F et al. (13) 78.60% which is comparable to the present study. Of the 22 malignant ovarian cancers, 20 cases (90.91%) showed raised CA 125 by Agarwal P et al. (8) and in 88.89% cases of Chowdhury S (17) which was much higher than the present study.

Size range was 2-2 to 20 cm in the present study. It was observed that 7.4% cases had 1-5 cm, 59.26% cases had 5.1-10 cm and 33.33% cases had more than 10 cm tumor size. Maximum of the tumors were observed in 5.1-10 cm size group, which correlates with study of Deeba F (13) and Sarangan A (25). More than 20 cm size tumors which differ from present study were seen by Agarwal P et al. (8) and Muzaffar M et al. (26).

Since most of the ovarian cancer remain asymptomatic for prolong period so measure should be taken for early diagnosis for better outcome. Although histopathological study is still the gold standard in diagnosing most of the ovarian tumors, may be supplemented by the newer techniques such as immuno-histochemistry, morphometric analysis, and flow cytometric analysis of ploidy status, to resolve the difficult, dilemmatic cases and also to predict the prognosis.

Conclusion:

Ovarian neoplasm is one of the most common and lethal malignancy in female reproductive tract in older age group but now a days more no. of cases also seen in younger age group. The observations from this study warrant us to screen women at an earlier age and also think of this lethal malignancy in women who present with abdominal pain, distention and other vague symptoms. Early diagnosis is crucial to help in decreasing morbidity and mortality among these patients. It is therefore suggested that efforts must be made to identify the risk factors for malignancy. So, assessment of each regions of statistical information reflecting its own profile may be important for calculation of risk for development of ovarian cancer and so helpful for preventive measure.

References:

1.   Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics 2007. CA Cancer J Clin. 2007;57(1):43-66.

2.   Parkin DM, Bray F, Ferlay J et al.: Estimating the world cancer burden: GLOBOCAN 2000. Int J Cancer. 2001;94:153-6.

3.   Khushpreet K, Rama G, Arvinder K et al.: A Retrospective Clinicopathological Study of Ovarian Tumours. International Journal of Medical Science and Clinical Inventions 2017; 4(10): 3222-3225.

4.   Vaddatti T, Reddy ES, Vahini G. Study of morphological patterns of ovarian neoplasms. IOSR Journal of Dental and Medical Sciences. 2013; 10(6):11-16.

5.   Sohail I, Hayat Z, Saeed S. A comparative analysis of frequency and patterns of ovarian tumours at a tertiary care hospital between two different study periods 2002-2009. J Postgrad Med Inst. 2012; 26(2):196-200.

6.   Tavassoli FA, Devilee P. Classification of Tumours. Pathology and Genetics of Tumours of the Breast and Female Genital Organs. IARC Press. 2003.

7.   Tortolero L, Mictchell FM, Rhodes HE. Epidemiology and screening of ovarian cancer. Obstet Gynecol Clin North Am. 1994; 21:63-75.

8. Agrawal P, Kulkarni D G, Chakrabarti P R, Chourasia S, Dixit M, Gupta K. Clinicopathological spectrum of ovarian tumors: A 5- year experience in a tertiary care center. Journal of Basic and Clinical Reproductive Sciences · July - December 2015; Vol 4 · Issue 2: 90-96.

9. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005; 55:74-108.

10. Murad A. Ovulation induction and ovarian tumours: the debate continues. J Pak Med Assoc. 1998; 48:353-6.

11. Nishal AJ, Naik KS, Modi J. Analysis of spectrum of ovarian tumours: a study of 55 cases. Int J Res Med Sci. 2015 Oct; 3(10):2714-2717.

12. Priya V. Clinicopathological profile of ovarian tumors in the age group 10-20 years. Int J Reprod Contracept Obstet Gynecol. 2017 Mar;6(3):877-880.

13. Deeba F, Alam ABMM, Banu J. Clinlcopathological Study of Ovarian Cancer: A Multi Centered Study. J Shaheed Suhrawardy Med Coll June 2013; 5(1):3-6.

14. Fox H, Wells M. Haines and Taylor Obstetrical and Gynecological Pathology. 5th ed, vol. 1. London: Churchill Livingstone Pvt. Ltd.; 2003. P. 693-879.

15. Pradhan HK, Singh P, Ravikumar MS, Gothwal M. Study risk factors and tumor markers in ovarian malignancy in western part of Odisha: a prospective observational study. Int J Reprod Contracept Obstet gyecol. 2018 Apr; 7(4): 1571-1578.

16. Jha R, Karki S. Histological pattern of ovarian tumors and their age distribution. Nepal Med Coll J. 2008;10:81-5.

17. Chowdhury S, Jahan R, Hossain DL, Sharmin F, Rahman S, Dewan F. J Shaheed Suhrawardy Med Coll 2017; 9(2): 69-73.

18. Basu P, De P, Mandal S, Ray K, Biswas J. Study of 'patterns of care' of ovarian cancer patients in a specialized cancer institute in Kolkata, Eastern India. Indian J Cancer. 2009;46:28-33.

19. Saini SK, Shrivastava S, Singh Y, Dixit AK, Prasad SN. Epidemiology of epithelial ovarian cancer, a single institution-based study in India. Clin Cancer Investig J. 2016; 5:20-4.

20. Mondal SK, Banyopadhyay R, Nag DR, Roychowdhury S, Mondal PK, Sinha SK. Histologic pattern, bilaterality and clinical evaluation of 957 ovarian neoplasms: a 10-year study in a tertiary hospital of eastern India. J Can Res Ther. 2011;7:433-7.

21. Doufekas K, Olaitan A. Clinical epidemiology of epithelial ovarian cancer in the UK. Int J Women's Health, 2014;6:537-45.

22. Krishnaswamy P, Nayak A, Shivananjiah C. Int J Community Med Public Health. 2016 Jan;3(1):86-89

23. Rashid S, Sarwar G, Ali A. A clinicopathological Study of ovarian cancer. Departments of Radiotherapy and oncology Sir Ganga Ram Hospital and Mayo Hospital Lahore. J Pak Med Assoc. 1998;36;117-25.

24. Badge SA, Gosavi AV, Sulhyan KR. Histopathological study of ovarian tumors. Indian Medical Gazette September 2013; 345-351.

25. Kondo E, Ogura M, Kagami Y, Taji H, Miura K, Takeuchi T, Maeda S, Asakura S, Suzuki R, Nakamura S, Morishima Y. Assessment Of Prognostic Factors In Follicular Lymphoma Patients. Int J Hematol. 2001; 73: 363-368.

26. Muzaffar M, Malik IA, Ashraf S. A clinicopathological study of 107 ovarian tumors. J Pak Med Assoc. 1987; 37: 194-197.