

Association of Ascites and Cytological Findings with Malignancy in Ovarian Tumors

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Abstract

Background: Ovarian tumors are a heterogeneous group of neoplasms ranging from benign lesions to highly aggressive malignancies. Ascites and ascitic fluid cytology may provide important clues to malignant potential and peritoneal spread, but evidence on their association with malignancy is limited in the local setting.

Aim of the study: This study aimed to evaluate the association of ascites and cytological findings with malignancy in ovarian tumors.

Methods: This hospital-based cross-sectional analytical study was conducted in the Department of Pathology at Ibrahim Medical College, Dhaka, Bangladesh, over a 1-year period (..... to). A total of 86 consecutively available cases of ovarian tumours with histopathological diagnosis were included. Clinical, laboratory, imaging, gross, and cytological data were collected from records and pathology documents. Histopathology was used as the gold standard for diagnosis, and borderline tumours were grouped with non-malignant tumours for comparison where appropriate. Data were analysed using SPSS version 26.0.

Results: Among 86 ovarian tumors, 53.5% were benign, 3.5% borderline, and 43.0% malignant. The mean age was 38.5±15.9 years, and malignant cases had significantly higher CA-125 levels (405.1±396.9 vs 41.9±33.4 U/mL) and larger tumor size (21.3±5.4 vs 13.0±3.6 cm), both $p < 0.001$. Menstrual status and family history were significantly associated with malignancy ($p = 0.003$ and $p = 0.001$, respectively). Malignant tumors were predominantly complex or solid on ultrasonography and mainly solid-cystic on gross examination ($p < 0.001$). Ascites was present in 16.3% of cases and showed a strong association with malignancy; 85.7% of tumors with ascites were malignant compared with 34.7% of those without ascites ($p < 0.001$). However, malignant cells in ascitic fluid did not show a significant association with malignancy ($p = 0.430$).

Conclusion: Ascites was strongly associated with ovarian tumor malignancy, while ascitic fluid cytology showed no meaningful association in this dataset. Larger tumor size, elevated CA-125, menopausal status, and complex or solid morphology also indicated malignancy.

Keywords: Ovarian tumors, Ascites, Malignancy and Histopathology

I. INTRODUCTION

Ovarian tumors comprise a heterogeneous group of neoplasms. They range from benign cystic lesions to highly aggressive malignancies and remain a major diagnostic and therapeutic challenge in gynecologic pathology. Ovarian cancer is among the most lethal gynecologic malignancies. This is because it is often clinically silent in its early stages and is frequently diagnosed only after peritoneal dissemination has occurred [1,2]. Global epidemiologic analyses continue to show a substantial disease burden. There is marked geographic variation in incidence and mortality that reflects differences in reproductive patterns, genetics, health-system capacity, and diagnostic access [1,3]. In Asia, the ovarian cancer burden is considerable. Population-level analyses have shown meaningful associations between ovarian cancer incidence and measures of human development, underscoring the need for region-specific clinicopathological evidence [3,4].

Distinguishing benign from malignant ovarian tumors before or at surgery is clinically important. Management, extent of staging, need for chemotherapy, and prognosis differ sharply according to malignant potential and histologic subtype [2,5]. Early diagnosis is difficult because symptoms like abdominal pain, bloating, enlargement, early satiety, and urinary complaints are nonspecific and common in benign conditions as well [5,6]. Serum CA125 and imaging are widely used in preoperative work-up, but neither alone is sufficient to confidently discriminate in all patients. Histopathology remains the gold standard for definitive diagnosis [7,8]. In practice, adjunct clinicopathological indicators that correlate with malignancy are valuable, especially in resource-constrained settings [7,8].

Among these indicators, ascites and cytological examination of peritoneal or ascitic fluid deserve special attention. Ascites is not merely a passive fluid collection. It is increasingly recognized as a biologically active tumor microenvironment that facilitates exfoliation, peritoneal spread, immune modulation, and treatment resistance in ovarian cancer [9,10]. Clinically, ascites is associated with advanced disease, patient morbidity, and poorer outcomes [9,10]. Cytological detection of malignant cells in ascitic or peritoneal fluid can provide important evidence of transcoelomic spread. It can contribute to staging, and in some settings, support treatment decisions even before definitive surgery [11-13]. Prior studies have shown that peritoneal cytology may correlate with tumor size, capsular invasion, omental involvement, and stage. However, reported diagnostic performance varies, likely because of differences in sample collection, processing, tumor type, and disease extent [11-13].

In Bangladesh, available studies have mainly described the histomorphological spectrum of ovarian tumors or broad clinicopathological correlations. They consistently emphasize the difficulty of preoperative distinction and the central role of pathology in guiding management [14-16]. However, focused evidence on the association of ascites and cytological findings with malignancy in ovarian tumors remains limited in the local setting [14-16]. Generating such data is important for improving preoperative suspicion, surgical planning, and pathological interpretation in routine practice. Therefore, the present study was undertaken to evaluate the association of ascites and cytological findings with malignancy in ovarian tumors.

II. METHODOLOGY

This hospital-based cross-sectional analytical study was conducted in the Department of Pathology, Ibrahim Medical College, Dhaka, Bangladesh. The study duration was one year, from to All 86 consecutively available cases of ovarian tumors received in the department during the study period were included according to the selection criteria. Patients of any age with clinically and surgically diagnosed ovarian tumors, for whom histopathological examination reports were available, were considered eligible. Cases with incomplete clinical records, inadequate tissue samples, or inconclusive histopathological diagnosis were excluded from the study.

Relevant clinical and laboratory information was collected from patient records, pathology requisition forms, and hospital documents. Data included age, marital and menstrual status, parity, family history, serum CA-125 level, tumor size, ultrasonographic findings, gross morphology, presence or absence of ascites, cytological findings of ascitic fluid, and final histopathological diagnosis. Histopathology was considered the gold standard for confirmation of benign, borderline, and malignant ovarian tumors. For analytical comparison, borderline tumors were grouped with non-malignant tumors where appropriate. Gross examination of resected ovarian specimens was performed, followed by routine tissue processing and hematoxylin and eosin staining for histopathological diagnosis. Where ascitic fluid was available, cytological examination was done to detect malignant cells.

The collected data were compiled and analyzed using standard statistical software (SPSS, V 26.0). Categorical variables were expressed as frequency and percentage, while continuous variables were presented as mean \pm standard deviation. The association of ascites and cytological findings with malignancy was assessed using the chi-square test or Fisher's exact test as applicable. A p-value of <0.05 was considered statistically significant.

III. RESULTS

The mean age of the patients was 38.5 ± 15.9 years; malignant cases were slightly older than non-malignant cases, 41.2 ± 18.8 vs 36.5 ± 13.2 years. Most patients were married (77.9%) and multiparous (76.7%). Menstrual status showed a significant association with malignancy, $p = 0.003$; 51.4% of malignant cases were menopausal, while 30.6% of non-malignant cases had regular menstruation. Positive family history was present in 9.3% of cases overall, and all cases with a positive family history were malignant ($p = 0.001$).

Table 1. Baseline demographic and reproductive characteristics according to final histopathological diagnosis

| Variable | Category | Overall, n (%) | Malignant (n = 37), n (%) | Non-malignant (n = 49), n (%) | p value |
|------------------|---------------|-----------------|---------------------------|-------------------------------|---------|
| Age (years) | Mean \pm SD | 38.5 ± 15.9 | 41.2 ± 18.8 | 36.5 ± 13.2 | 0.169 |
| Marital status | Married | 67 (77.9) | 27 (73.0) | 40 (81.6) | 0.291 |
| | Unmarried | 18 (20.9) | 10 (27.0) | 8 (16.3) | |
| Parity | Multiparous | 66 (76.7) | 26 (70.3) | 40 (81.6) | 0.303 |
| | Nulliparous | 20 (23.3) | 11 (29.7) | 9 (18.4) | |
| Menstrual status | Regular | 16 (18.6) | 1 (2.7) | 15 (30.6) | 0.003 |
| | Irregular | 37 (43.0) | 17 (45.9) | 20 (40.8) | |
| | Menopausal | 33 (38.4) | 19 (51.4) | 14 (28.6) | |
| Family history | Absent | 78 (90.7) | 29 (78.4) | 49 (100.0) | 0.001 |
| | Present | 8 (9.3) | 8 (21.6) | 0 (0.0) | |

Mean CA-125 was markedly higher in malignant tumors than non-malignant tumors (405.1 ± 396.9 U/mL vs 41.9 ± 33.4 U/mL, $p < 0.001$). Mean tumor size was also larger in malignant cases (21.3 ± 5.4 cm vs 13.0 ± 3.6 cm, $p < 0.001$). On ultrasonography, 47.7% of tumors were cystic overall, but malignant tumors were mainly complex (62.2%) or solid (37.8%), $p < 0.001$. Grossly, malignant tumors were predominantly solid-cystic (62.2%), whereas 83.7% of non-malignant tumors were cystic ($p < 0.001$).

Table 2. Clinical and tumor-related characteristics according to final histopathological diagnosis

| Variable | Category | Overall, n (%) / mean \pm SD | Malignant (n = 37) | Non-malignant (n = 49) | p value |
|--------------------------|----------------|--------------------------------|--------------------|------------------------|---------|
| CA-125 (U/mL) | Mean \pm SD | 198.2 \pm 316.3 | 405.1 \pm 396.9 | 41.9 \pm 33.4 | <0.001 |
| Tumor size (cm) | Mean \pm SD | 16.6 \pm 6.0 | 21.3 \pm 5.4 | 13.0 \pm 3.6 | <0.001 |
| Ultrasonographic finding | Cystic mass | 41 (47.7) | 0 (0.0) | 41 (83.7) | <0.001 |
| | Complex mass | 27 (31.4) | 23 (62.2) | 4 (8.2) | |
| | Solid mass | 18 (20.9) | 14 (37.8) | 4 (8.2) | |
| Gross appearance | Cystic | 42 (48.8) | 1 (2.7) | 41 (83.7) | <0.001 |
| | Solid | 16 (18.6) | 13 (35.1) | 3 (6.1) | |
| | Solid + cystic | 28 (32.6) | 23 (62.2) | 5 (10.2) | |

Among the 86 cases (53.5%) were benign, 3.5% borderline, and 43.0% malignant. The most common benign tumors were mucinous cystadenoma (19.8%) and mature cystic teratoma (19.8%). Among malignant tumors, serous carcinoma (14.0%) was the most frequent subtype, followed by mucinous carcinoma (8.1%). Of all malignant tumors, 54.1% were epithelial, 35.1% germ cell, and 10.8% sex cord-stromal.

Table 3. Distribution of final histopathological diagnoses and common histological subtypes

| Variable | Category | n | % |
|-----------------------------------|-------------------------|-----------------------------|------|
| Diagnosis | Benign | 46 | 53.5 |
| | Borderline | 3 | 3.5 |
| | Malignant | 37 | 43 |
| Histopathological type | Mucinous cystadenoma | 17 | 19.8 |
| | Mature cystic teratoma | 17 | 19.8 |
| | Serous carcinoma | 12 | 14 |
| | Mucinous carcinoma | 7 | 8.1 |
| | Serous cystadenoma | 6 | 7 |
| | Immature teratoma | 4 | 4.7 |
| | Serous cystadenofibroma | 3 | 3.5 |
| | Granulosa cell tumor | 3 | 3.5 |
| | Mixed germ cell tumor | 3 | 3.5 |
| | Serous borderline tumor | 3 | 3.5 |
| | Malignant tumor group | Epithelial malignant tumors | 20 |
| Malignant germ cell tumors | | 13 | 35.1 |
| Sex cord-stromal malignant tumors | | 4 | 10.8 |

Ascites was present in 16.3% of cases and was strongly associated with malignancy. Among tumors with ascites, 85.7% were malignant, compared with 34.7% among those without ascites ($p < 0.001$). Malignant cells in ascitic fluid did not show a significant association with malignancy ($p = 0.430$), largely because the variable was almost uniformly coded as present (98.8%).

Table 4. Association of ascites and cytological findings with malignancy in ovarian tumors

| Variable | Category | Total, n (%) | Malignant, n/N (%) | Non-malignant, n/N (%) | p value |
|----------------------------------|----------|--------------|--------------------|------------------------|---------|
| Ascitic fluid | Present | 14 (16.3) | 12/14 (85.7) | 2/14 (14.3) | <0.001 |
| | Absent | 72 (83.7) | 25/72 (34.7) | 47/72 (65.3) | |
| Malignant cells in ascitic fluid | Present | 85 (98.8) | 36/85 (42.4) | 49/85 (57.6) | 0.43 |
| | Absent | 1 (1.2) | 1/1 (100.0) | 0/1 (0.0) | |

IV. DISCUSSION

In the present study, 43.0% of ovarian tumors were malignant. This is higher than the proportions reported in several recent histopathological series, which ranged from 14.6 to 31.1% [17-20]. The comparatively higher malignant yield may reflect the tertiary referral nature of the study setting. It may also result from selective submission of clinically suspicious tumors for pathological evaluation. The grouping of borderline tumors with non-malignant lesions during comparative analysis could contribute as well. Despite this difference in overall frequency, our histological pattern was broadly concordant with the literature. In our series, serous carcinoma was the most common malignant subtype, accounting for 14.0% of cases. Epithelial malignancies comprised 54.1% of malignant tumors. Previous studies also reported a similar dominance of serous malignant tumors [17-20]. However, our most frequent benign tumors were mucinous cystadenoma and mature cystic teratoma. This contrasts with studies where serous cystadenoma predominated [17,19]. The prominence of mature cystic teratoma among benign lesions agrees with findings from Afghanistan and Saudi Arabia [19,20]. These variations likely reflect differences in population age structure, regional case-mix, referral pathways, and histopathological classification.

Our clinicodemographic results also support the established association between malignancy and increasing age. The mean age in malignant tumors was 41.2 ± 18.8 years, compared with 36.5 ± 13.2 years in non-malignant tumors, and 51.4% of malignant cases were menopausal. This is consistent with Behnamfar et al., who observed significantly older age among malignant cases [8], and with Khoiwal et al., who reported that most malignant adnexal masses occurred between 41 and 60 years [21]. Farag et al. also showed that malignancy became more prominent with advancing age, particularly above 60 years, where malignant tumors formed 58.8% of cases [20]. In contrast, Huwidi et al. did not find a significant association between age or menopausal status and malignancy [22], which may be due to their smaller sample of malignancies. A striking finding in our study was that all patients with a positive family history belonged to the malignant group, supporting the well-established hereditary contribution to ovarian cancer. Zheng et al. reported familial relative risks of 2.40 when only mothers were affected, 2.59 when only sisters were affected, and 10.40 when both mother and sisters had ovarian cancer [6]. Clinically, this suggests that family history should remain an essential triage variable when evaluating ovarian tumors.

The biological behavior of malignancy in our study was further reflected by markedly elevated CA-125 and larger tumor size. Mean CA-125 was 405.1 ± 396.9 U/mL in malignant tumors versus 41.9 ± 33.4 U/mL in non-malignant tumors, and mean tumor size was 21.3 ± 5.4 cm versus 13.0 ± 3.6 cm, respectively. These findings are consistent with those of Huwidi et al., who reported mean CA-125 levels of 635 U/mL in malignant masses and 41 U/mL in benign masses [22]. Khoiwal et al. likewise found raised CA-125 in 74% of malignant adnexal masses [21]. However, Behnamfar et al. showed that CA-125 alone had limited discriminatory ability, with an AUC of only 0.60 [8], indicating that serum markers should be interpreted alongside morphology. This is supported by our imaging findings, where malignant tumors were predominantly complex, 62.2%, or solid, 37.8%, and grossly solid-cystic, 62.2%, while 83.7% of non-malignant tumors were cystic. Lee et al. demonstrated that CA-125 performs variably across tumor subtypes and that ROMA may be superior in selected groups, especially endometriotic-type tumors [23]. More recent imaging studies by Wu et al. and Pan et al. further showed that combining ultrasound-based risk stratification with CA-125 improves diagnostic performance, with AUCs up to 0.97 and 0.945, respectively [24,25]. Together, these observations reinforce that multimodal assessment, rather than reliance on a single marker, offers the best preoperative discrimination.

The most clinically relevant finding of the present study was the strong association between ascites and malignancy. Ascites was present in 16.3% of all cases, but 85.7% of tumors with ascites were malignant, compared with 34.7% of tumors without ascites, yielding an odds ratio of 11.28. This strongly supports ascites as a high-risk feature in ovarian tumors. Behnamfar et al. similarly found that ascites was significantly more frequent in malignant adnexal masses [8]. By contrast, our cytology variable did not show a significant association with malignancy ($p = 0.430$), largely because 98.8% of cases were coded as positive, leaving little discriminatory power. This differs from Baransi et al., who reported ascitic cytology sensitivity of 80.6% and specificity of 100% in postmenopausal women with advanced ovarian cancer [13], and from Živadinović et al., who found a 30.2% false-negative rate, emphasizing both the usefulness and limitations of cytology [11]. Therefore, while ascites should immediately heighten suspicion of malignancy and prompt referral to gynecologic oncology, ascitic fluid cytology should be considered an adjunct, not a substitute for definitive histopathology. Overall, our findings suggest that ascites, menopausal status, family history, elevated CA-125, larger tumor size, and complex or solid morphology together form a clinically meaningful risk profile for malignancy in ovarian tumors

Limitations of the study: This was a single-centre study with a relatively small sample, which may limit generalizability. In addition, the ascitic fluid cytology variable showed very little variation in the dataset, reducing its analytical value for assessing association with malignancy.

V. CONCLUSION

This study demonstrated that ascites was strongly associated with malignancy in ovarian tumors. In addition to the presence of ascites, malignant tumors were also characterized by higher CA-125 levels, larger tumor size, and predominantly complex or solid morphology on imaging and gross examination. However, while ascitic fluid cytology did not show a significant association with malignancy in this dataset, these collective findings suggest that ascites, along with key clinical and pathological features, may serve as important indicators for early suspicion and risk assessment of malignant ovarian tumors.

VI. RECOMMENDATIONS

Patients with ovarian tumors showing ascites, raised CA-125, larger size, and complex or solid morphology should undergo careful preoperative evaluation for possible malignancy. Larger multicenter studies with better-standardized ascitic fluid cytology assessment are recommended to confirm these findings.

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Author Contribution:

- Conception and design: Flora T A1
- Acquisition, analysis and interpretation of data: Flora T A1, Khan RR2, Tapu TT3
- Manuscript drafting and revising it critically: Flora T A1, Khan RR2, Tapu TT3
- Approval of the final version of the manuscript: Flora T A1, Khan RR2, Tapu TT3
- Guarantor accuracy and integrity of the work: Flora TA1, Khan RR2, Tapu TT3

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