Original Article

Clinicopathological patterns and outcomes of ovarian borderline tumors: a tertiary center experience

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ABSTRACT

Objectives: to study clinical/ morphological parameters of ovarian borderline tumors (OBT) and outcomes at a major national center.

Design: Retrospective study**.**

Setting: Jordan University Hospital, Amman, Jordan

Subjects & Methods: we studied 42 OBTs meeting inclusion criteria from 2009 to 2019. Data from medical and histopathology sources were collected.

Main outcome measures: Clinicopathological parameters and predictors of recurrence/ death were explored using descriptive statistics and correlations.

Results: Mean age = 38.5 years. 5^{th} decade was commonest age group (38.1%). 21.4 % were menopausal. Mean follow up = 46 months. Surgery included fertility sparing (27; 64.3%) and non-fertility sparing procedures (15; 35.7%). Commonest presentation was pain (17; 40.5%). 81% were unilateral. Mean tumor diameter =10.54 cm. Serum CA125 was elevated in 15 (35.7%). CA19.9 was elevated in 3 (7.1%). 28 were serous (66.7%); and 14 (33.3%) mucinous. FIGO stage included I (34; 81%); II (1; 2.4%), and III (7; 16.7%). Recurrence occurred in 6 (14.2%). Successful pregnancy was documented in 8 (19%). Death occurred in 4 (9.5%). Recurrences and deaths respectively were significantly correlated to higher stage (Pearson chi^2 0.000; 0.000); positive peritoneal washings (0.002; 0.000); omental metastasis (0.000; 0.000); and residual mass post op (0.002; 0.013). Other studied parameters didn't reveal significance including age, histotype, surgery type, diameter, CA125, CA19.9, lymph node status, ovarian surface involvement, lymphovascular invasion, micropapillary architecture, microinvasion, and intraepithelial carcinoma.

Conclusion: OBTs have excellent prognosis with low rates of recurrences and death. Conservative surgery for desired fertility preservation balanced by long-term follow-up is recommended.

KEYWORDS: Ovarian borderline tumors; serous tumors; mucinous tumors

INTRODUCTION

Ovarian tumors are a common gynecological problem that can occur at any time during a woman's life[1]. The prevalence of an ovarian tumor on ultrasound examination varies broadly among different studies with is higher in reproductive-age women than in postmenopausal women[2]. The etiology varies from benign in some individuals to aggressive malignant conditions in others.

Ovarian borderline tumors (OBT) are an intermediate category of ovarian neoplasms, first described in 1929, and then World Health Organization (WHO) made further characterization and designations over the past 2 decades. OBT represent about a fourth of epithelial ovarian tumors, with an annual incidence rate of 1.8 to 4.8 cases per 100000 females[2]. Although they may affect any age, pre-menopausal women are predominantly affected. OBT are said to have excellent prognosis [2]. The key difference between OBT and malignant tumors is histopathological confirmation of ovarian stromal invasion in the latter.

The aim of the current study was to examine the clinicopathological features and predictors of recurrence in ovarian borderline tumors at a major national tertiary care center.

MATERIAL AND METHODS

The Faculty of Medicine and Scientific Research Deanship's Research Ethics Committee, and hospital IRB committee approved the current study. We conducted this retrospective study at the University Hospital and it covered the period from January 2009 to December 2019. Inclusion criteria in the study incorporated patients who were diagnosed with OBTs, and underwent diagnostic/ therapeutic surgical procedures at our institution (including both fertility-sparing and non-fertility-sparing procedures), and had documented follow up data from gynecology clinic visits and follow up radiological imaging studies. Cases were included regardless of patient age, fertility, co-morbidities.

The patients' medical records were used to obtain clinical data, including age at diagnosis, presenting symptoms, fertility, follow up periods, pelvic washings, staging results, residual mass, treatment regimens, pregnancy post therapy, recurrences, final outcome, and death due to disease. The hospital database was used to retrieve biochemical test results for tumor markers CA125, CA19.9, from blood samples taken around the time of diagnosis .

Morphometric features of the tumors were obtained from histopathology reports of Pathology Department at our institute for all specimens. These included maximum diameter, bilaterality, histotype, extra-adnexal masses, stage at presentation, ascites, surface involvement, presence of micropapillary pattern, microinvasion, implant type, and residual disease. Corresponding formalin-fixed, paraffin- embedded tissue blocks for the surgical specimens were retrieved with representative Hematoxylin & Eosin-stained microscopic slides for each specimen were reviewed by 2 pathologists.

Statistical analysis was performed using the Statistical Package for Social Sciences software version 20 (IBM Corp., Armonk, NY, USA). Descriptive frequency statistics and correlations were performed using Pearson Chi square with $p< 0.05$ considered significant.

RESULTS

42 ovarian borderline tumors were studied, including 28 serous OBTs (66.7%) and14 mucinous OBT (33.3%). Patient age ranged from 20 to 71 years, and the mean patient age was 39.2 years for serous OBT, and 37.4 years for mucinous OBT. 33 patients (78.6%) were in reproductive years, and nine (21.4%) were menopausal. Follow up periods ranged from 6 months to 130 months. The mean FUP in order for all cases; S-OBT; and M-OBT was 46.02; 39.4; and 65 months, respectively.

According to standardized laboratory measures, the normal CA125 serum values are ≤ 35 U/ml. CA125 serum levels in the study cases ranged from 5 to 1000 (Mean =69.6 U/ml). Serum CA125 was elevated in 15 cases (3.7%), including 11 S-OBT (39.3%), and 4 M-OBT (28.6%). Similarly, normal CA 19.9 serum levels are ≤ 37 U/ml. CA19.9 serum levels ranged from one to 6407.7 U/ml (mean= 148.91± 728.38 SD). CA19.9 was elevated in three cases (7.1%) all were M-OBTs, and none of S-OBT.

Tumors were unilateral in 34 (81%). They were bilateral in seven S-OBT cases (25%), and unilateral in all M-OBT (100%). Cases were initially divided into groups according to the patient's age (refer to Table 1). Were group one includes ages 20 to 30; group two (31-40); group three (41-50); group four (51-60); group five (61-70); and group six (≥71). S-OBT were more frequent in all age groups, with the highest frequency in age group 3 (41-50 years old) with 11 out of 16 cases (68.8%). M-OBT were most frequent in age group 1, with 6 out of 14 cases (42.9%).

Primary surgery included both 27 fertility-sparing procedures (including cystectomy in 13 (31%); oophorectomy in 14 (33.3%)); as well as 15 non-fertility sparing procedures (including TAH & BSO in 10 (23.8%); and debulking in five (11.9%)). Commonest presentation was abdominal pain in 17 (40.5%). Tumor diameters ranged from two to 32 cm (mean = 10.54 cm). Pelvic lymph node involvement was detected in 2/42 (4.8%). 34 (81%) of cases were FIGO stage I; one (2.4%) in stage 2, and 7 (16.7%) stage 3. Recurrence/metastasis were documented in six cases (14.2%). Residual mass post-surgery was diagnosed in five cases.

Successful pregnancy post-treatment was documented in eight cases (19%). Death due to disease occurred in four cases (9.5%); 2 patients with S-OBT (7.1%) and 2 cases with M-OBT (14.3%). Ovarian endometriosis was identified in two cases (4.8%). Ovarian endosalpingeosis in five cases (11.9%). Microinvasion in four cases (9.5%). Lymphovascular invasion (LVI) in one case (2.4%). Ovarian surface involvement in five cases (11.9%). Micropapillary morphology was detected in eight

(28.5%) S-OBT; Intraepithelial carcinoma was detected in 6 (42.9%) M-OBT. Clinicopathological characteristics are summarized in Table 2.

Statistical correlations between each of disease recurrence and death with various clinical and morphological parameters were explored using Pearson chi$^{2.}$ The statistical results are summarized in Table 3.

Characteristics of S-OBT. Patient age ranged from 20 to 71, and the mean patient age was 39 years. 22 (78.6%) were in reproductive years, and six were menopausal. Commonest presentation was abdominal pain (50%). Other presenting symptoms included abdominal mass in four (14.3%); ascites in one (3.6%); abnormal cycles or vaginal bleeding in five (17.9%); and four described other symptoms. Mean tumor diameter was 7.5 cm, and ranged from two to 18 cm. The mass was unilateral in 21 case (75%) and bilateral in seven (25%). Serum CA125 was elevated in 11 cases (39. 3%).The values ranged from 6 and 1000 IU/ml (mean = 86.8 IU/ml). Serum CA19.9 was not elevated in any of S-OBTs (0%), the values ranged from one to 19.81 U/ml (mean = 7.9 IU/ml).

Primary surgical procedure was cystectomy in six (21.4%); oophorectomy/ salpingectomy in 11 (39.3%); TAH & BSO in nine (32.1%); debulking (TAH, BSO, omentectomy) in two (7.1%). Appendectomy was performed adjunct to primary surgery in four cases (14.3%). Peritoneal washings were positive in two cases (7.1%) and negative in the remaining 26 cases. Omental metastasis was diagnosed in three cases (10.7%). Residual mass post primary surgery was identified in one case (3.5%). Recurrence was diagnosed in two cases (7.1%). Pregnancy post op was successful in six cases (21.4%). FUP ranged from six to 127 months, with a mean value of 39.4 months. Lymph node involvement by tumor was detected in two cases (7.1%). Secondary surgery was performed in 19 cases (67.9%). Chemotherapy was given to one Patients (3.6%). Death due to disease complications was documented in 2 patients (7.1%).

Histopathological slide review revealed the following: Endometriosis was diagnosed in one case (3.6%). Micropapillary architecture was detected in eight cases (28.6%) (Figure 1a). Endosalpingeosis was diagnosed in three cases (10.7%) (Figure 1b). Microinvasion was found in one case (3.6%). Ovarian surface involvement was detected in 4 cases (14.3%). LVI was not identified in any of the cases (0%).

Characteristics of M-OBT. 14 cases of M-OBT were studied. Patient age ranged from 20 to 63 (mean =37.4 years). Eleven (78.6%) were in reproductive years, and three were menopausal. Commonest presentation was abdominal mass (57.1%). Other presenting symptoms included pain in four (28.6%); ascites in one (7.1%); abnormal cycles or vaginal bleeding in one (7.1%). Mean tumor diameter was 16.4 cm, and ranged from three to 32 cm. the mass was unilateral in all 14 cases (100%). Serum CA125 was elevated in 4 cases (28.6%) the values ranged from five and 103 IU/ml, with a mean value of 35.9 IU/ml. Serum CA19.9 was elevated in three cases (21.4%) the values ranged from one to 4607.7 U/ml, with a mean value of 431.7 IU/ml.

Primary surgical procedure was cystectomy in seven (50%); oophorectomy/ salpingectomy in three (21.4%); TAH & BSO in one (7.1%); and debulking (TAH, BSO, omentectomy) in three (21.4%). Appendectomy as adjunct to surgical procedure was performed in three cases (21.4%). Peritoneal washings were positive in two cases (14.3%) and negative in the remaining 12 cases. Omental mass was diagnosed in two cases (14.3%). Residual mass post primary surgery was identified in four cases (28.6%). Recurrence was diagnosed in three cases (21.4%). Pregnancy post op was successful in two cases (14.3%). FUP ranged from six to 134 months, with a mean value of 65 months. Lymph node metastasis was not detected in any of the cases. Secondary surgery was performed in seven cases (50%). Chemotherapy was given in one case (7.1%). Death due to disease complications occurred in two cases (14.3%; 2/14).

Histopathological slide review revealed the following: Endometriosis was diagnosed in one case (3.6%). Endosalpingeosis was diagnosed in two cases (14.3%). Microinvasion was identified in three cases (21.4%) (Figure 2a). Ovarian surface involvement was identified in one case (7.1%). LVI was identified in one case (7.1%) (Figure 2b). Intraepithelial carcinoma was seen in 6 cases (42.9%).

DISCUSSION

OBTs. OBT are epithelial neoplasms characterized by proliferation with nuclear atypia but lacking stromal invasion or destructive growth pattern[3], that frequently affect reproductive aged- women. The terminology "borderline" derives from the intermediate biological behavior of these tumors that is somewhere in between benign and malignant counterparts, despite the potential occurrence of peritoneal involvement[4].

OBT were first described in 1929 by Taylor and designated as semi-malignant [5]. Further characterization and designation of OBT was serially made by WHO over the past 2 decades [2].

OBTs represent about a fourth of epithelial ovarian tumors in different series, with an annual incidence rate of 1.8 to 4.8 cases per 100000 females[2]. Although they may affect any age, pre-menopausal women are predominantly affected. OBT are said to have excellent prognosis [2]. The key difference between OBT and malignant tumors is histopathological confirmation of ovarian stromal invasion in the latter.

Symptoms are non specific including abdominal mass, abdominopelvic pain, abnormal vaginal bleeding or menstrual abnormalities [6]. Some cases are even completely asymptomatic and the diagnosis is purely incidental, during, for instance, routine ultrasound examination[7]. Ultrasound [8] as well as Magnetic Resonance Imaging [9] findings are not highly sensitive to predict accurate diagnosis. In addition, preoperative evaluation of OBTs is still a controversial issue. Currently, specific serum tumor markers for OBTs do not exist. Relevant data are available for the broader spectrum ovarian tumor markers such as CA125 and CA19.9. Since serum CA125 levels increase in both OBTs as well as benign and malignant epithelial ovarian tumors, the use of this parameter in preoperative evaluation

would not be suitable [10]. On the other hand, other research groups reveal CA125 levels were noted in 40% of patients in stage I OBT and 83% of those with advanced-stage OBT [10]. Large-scale studies on other serum tumor markers including CA19-9, CA15-3 and CEA in OBTs are still needed**.**

Thus, it is difficult to diagnose OBT clinically, radiologically and serologically [11]. The mainstay in diagnosis of OBT is still histopathological examination of resected tumors [6].

Intraoperative frozen section (FS) has a controversial role in OBT. Many papers including large meta-analysis indicate that FS analysis of OBTs has low accuracy, sensitivity, and positive predictive value. In addition, it may lead to under-diagnosis and over-diagnosis, or even worse, misdiagnosis [12]. Conversely, other researchers believe that FS analysis plays an important role in selected situations and is associated to a high sensitivity and specificity in cases of ovarian and endometrial tumors [13], and increase the possibility of obtaining an optimal surgical treatment at first surgical approach.

According to the current World Health Organization (2014 WHO) Classification[2], these tumors are also called atypical proliferative tumors. Six histologic subtypes are distinguished on the base of the epithelial cell type they derive from: serous OBT (S-OBT), that represent around 50% of all cases, mucinous (M-OBT) around 45% and other rare subtypes (endometrioid, clear cell and Brenner) that account for the remaining 5% of the cases. Most of the knowledge about the prognosis of OBT derive from the serous subtype that represents the most common type [2]. As the histologic types display conspicuous differences in clinical presentation and behavior, determination of the histological type is critical in the assessment of OBTs, and the different types should be assessed distinctly.

Compared to their frankly malignant counterparts, OBTs have a notable favorable prognosis, with early-stage disease (FIGO stage I and II) exhibiting a five‐year and 10-year overall survival rate of almost 98% and 95%; and with more advanced disease (FIGO stage III and IV) demonstrating a rate of 92% and 86%, respectively [14, 15]. Many research papers tried to explore clinical and morphological factors that may play a role in outlining the prognosis of OBTs.

Lymph node involvement was reported in up to 25% of patients with advanced stage OBTs (FIGO stages III and IV). Many studies, however, have failed to demonstrate that lymph node involvement in patients with OBT did exert an adverse effect on survival [16].

Decisions for surgical treatment in patients with OBTs include fertility-sparing procedures (like simple cystectomy; unilateral oophorectomy/salpingo-oophorectomy with contralateral ovarian biopsy to assess the opposite ovary) along with non-fertility-sparing procedures (i.e. hysterectomy with bilateral salpingo-oophorectomy; with or without multiple peritoneal biopsies, and fluid samples from peritoneal washing for cytological evaluation). The first option is usually used for young, fertility-desiring patients; and considered generally safe approaches. In some studies, recurrence rates ranged from 12% to 58% in patients with OBT who had conservative surgery (cystectomy), whereas patients treated by non-fertility-sparing surgery recurrence rates ranged between 0 and 20% [14].

Appendectomy and lymphadenectomy are currently non-compulsory surgical managements for OBT, because it has been shown that even in cases with lymph node involvement, survival and recurrence rates have not changed [17]. Studies validating advantageous effects of adjuvant treatments like chemotherapy and radiotherapy in patients with advanced stage OBT are lacking. Despite that, some patients with advanced stage OBT respond well to cisplatin-based adjuvant chemotherapeutic regimens; still, there is no promising effect on long-term survival [14].

S-OBT. S-OBT subtype comprise 43% to 53% of all OBTs [18]. Literature review reveals the peak age at presentation to be 40- 50 years [16]. Roughly 30% of S-OBTs are bilateral and frequently extra ovarian invasion in the form of non- invasive peritoneal implants is detected [19]. Peritoneal implants in the current WHO criteria are noninvasive by definition. The incidence of bilaterality and extra ovarian spread is well known to be higher in S-OBT than that in M-OBTs [15].

S-OBTs usually spread through peritoneal metastases rather than lymphatic or hematogenous pathway[16]. These peritoneal metastases histologically exhibit epithelial or desmoplastic features. Prognosis is similar in both types. The mean survival of patients with these peritoneal implants is adversely affected with a mortality rates of about 4% had been reported [16]

Macroscopically, S-OBT are usually cystic masses with thin fluid and intra-cystic papillary projections; however, gross examination is not dependable to differentiate benign, borderline and malignant serous tumors. Histologically, a diagnosis of S-OBT is confirmed when at least 10% of the tumor exhibits a hierarchical, branching architecture lined by cuboidal to columnar epithelium, including ciliated cells, with mild cytological atypia. Some tumors display variable number of polygonal and hobnail cells containing eosinophilic cytoplasm and moderately enlarged, hyperchromatic nuclei and sometimes nucleoli.
Micropapillary growth pattern is another important morphological characteristic of S-OBTs. Whether its presence may affect prognosis adversely is still controversial, however, the increased rates of invasive recurrence in patients with micropapillary structure had been proved in various studies.[20] In one study [17], it was demonstrated that during follow-up, the rates of invasive recurrences were higher and disease-free survival rates were significantly lower in patients with versus without micropapillary structures (75.9% vs. 94.3%).[17]

Stromal microinvasion in S-OBT has become an arguable issue. It is defined as of invasion of less than 3 mm or 10 mm^2 in one or more than one focus [21]. According to the current WHO criteria [2], the extension of these foci of stromal microinvasion must not exceed 5 mm in linear extent. The main source of debate is whether the risk of recurrences increases in cases with microinvasion. Still, literature indicates that microinvasion should be regarded as a prognostic factor for S-OBT[17]. Five patterns of stromal microinvasion [22] have been described: “classic” microinvasion (single eosinophilic cells/ cell clusters), single and non-complex branching papillae, inverted macropapillae, cribriform glands and micropapillae. The last three may be linked to higher threat of evolution [14].

In addition, morphometric parameters were evaluated looking for potential prognostic markers in OBT. Those parameters included bilaterality, surface involvement, capsular rupture [23], presence of micropapillary pattern, and microinvasion [22]. Advanced stage at presentation [24], peritoneal implants[14], and residual disease are reportedly associated with more aggressive disease in S-OBT.

M-OBT. M-OBTs comprise 42%-52% of all BOTs among different geographical populations [18]; and account for around 10 % of all primary ovarian mucinous tumors [2]. Geographical variation in incidence is interestingly seen in M-OBT; while they rank second to serous OBT in frequency [25] in Western and Middle Eastern populations, they appear to be the most common histotype in Asian communities, with about 70% of all OBT [18].

First described by Fisher in 1955 [26], since then the entity had gone through many controversies and nomenclature arguments till 2004 where national cancer institute declared that "M-OBT", "atypical proliferative tumor", and "low malignant potential" are interchangeable terms [15], and hence adopted by WHO 2014 tumor classification [2].
M-OBT are famous for being of enormous size, and masses reaching more than 50 cm in diameter had been reported [16]. Several tumor markers had been said to be elevated, especially CA19.9 and CEA [16]. Even CA125 may be elevated in some cases as well [10]. M-OBT are frequently unilateral adnexal masses, with ≤10% of cases are said to be bilateral [19]. Most of these tumors tend to be confined to the ovary at the time of first diagnosis.
Macroscopically, M-OBT displays a cystic mass with smooth outer-surface and a multiloculated inner aspect, and variable amounts of solid component on cut section. The cysts contain thick viscous mucoid material. Histologically, the epithelium may look like gastric or intestinal-type epithelium admixed with inconstant numbers of goblet cells. A diagnosis of M-OBT is confirmed when at least 10% of the cyst epithelium display areas of stratified, tufted and villiform growth [19]. Cytological examination shows columnar epithelial cells with abundant eosinophilic cytoplasm. Nuclear crowding, hyperchromasia, and mild nuclear atypia with scattered mitoses are accepted, but by definition, it should lack stromal invasion [2].
If the lining epithelial cells display pronounced nuclear pseudo stratification and high-grade cytological atypia associated with high mitotic activity, a diagnosis of M-OBT with intraepithelial carcinoma is made; regardless of the degree of architectural complexity [27].
Using immunohistochemcial staining, M-OBTs tend to express a similar pattern to that of mucinous gastrointestinal tract tumors. They are regularly CK7 positive, variably positive to CK20, carcinoembryonic antigen, CA19-9, and less so to CDX2, as well as for MUC5AC, MUC1, MUC2, and MUC6. PAX8 positivity is present in two thirds of tumors. Typically, M-OBT lack expression of Mullerian markers such as Estrogen Receptor, Progesterone Receptor, and Vimentin. They can also show patchy p16 staining [28]. Most common genetic alterations in M-OBT are Kras mutations, occurring in 80%. Similar Kras mutations in benign, borderline, and malignant components within the same tumor had been detected, suggesting a potential role of these aberrations as an early event in the biologic progression of mucinous neoplasms [29].

The most significant issue, obviously, is to distinguish M-OBT from metastatic mucinous tumors spreading to ovaries. As in both tumors, histological features and even histochemical profiles can be very similar. The differential will favor M-OBT in cases lacking bilateral ovarian involvement, pseudomyxoma peritonei, and/or extra-ovarian disease.

The prognostic value of intra-epithelial carcinoma in M-OBT is a matter of controversy; however, it is a general guideline that M- OBTs with intraepithelial carcinoma should be sampled comprehensively to exclude any invasive focus [15]. Some studies claimed that intraepithelial carcinoma is associated with higher recurrence rates [30].
Stromal microinvasion as defined for S-OBTs also holds accurate for M-OBTs. However, in M-OBTs was not associated with increment in disease recurrences or worse prognosis [21]. The current WHO guideline is to regard any focus of stromal invasion measuring < 5 mm in greatest linear scope as microinvasion [2]. Four different morphologic patterns of microinvasion had been described, including isolated individual cells/ clusters within tissue spaces; irregular glands with reactive stroma/ chronic inflammatory infiltrate; foci of confluent glandular/ cribriform growth; and gutters/ nests of tumor cells within extracellular mucin [2].

Overall survival in patients with M-OBT with intraepithelial carcinoma is about 95% in early stage disease [16]**.** Ancient literature sources may reveal worse survival patterns (40-50%), but this could be because some of previous reported cases were actually metastatic mucinous tumors involving ovary, especially from appendix, rather than true primary M-OBT. Prognosis of M-OBT with intra-epithelial carcinoma is comparable to that of conventional ones [30]. It is not known if the prognosis is different in cases with microinvasion in M-OBT, due to the limited number of available studied cases [30].

Recurrences of M-OBT are described, and could be either in the form of OBT or invasive mucinous carcinoma. Possible attributes include regrowth of tumor following simple management by cystectomy; missed micro invasive foci of the primary tumor; incomplete surgical staging; tumor rupture before or during surgery; or inadequate sampling of the tumor.

To recap, the main dispute concerning treatment choices in OBTs is the critical balance between fertility-sparing desire and risk of disease recurrence. According to some studies, histological subtyping seems to have implications on this choice [17], which proposed that the risk maybe higher in M-OBTs, compared to S-OBTs [17]. Some researchers even suggested that salpingo-oophorectomy is favored over cystectomy during conservative surgery for patients with M-OBT [15]. Similarly, in a large-scale meta-analysis, higher recurrence rates were observed for patients who undergone bilateral salpingo-oophorectomy when compared to those with hysterectomy with bilateral salpingo-oophorectomy. As mentioned earlier, noteworthy variance in recurrence rates were suggested by other papers between OBTs treated by conservative surgery (cystectomy alone) and those treated by extensive surgery (bilateral salpingo-oophorectomy) [17]. Conversely, it was not proved that these recurrences deduce an adverse outcome on survival rates [16].

The results of the current study explore the clinicopathological features and outcomes in patients with OBTs at a major tertiary canter in our country. Three fourths of the patients were in reproductive years. Peri-menopausal years were the most frequent age at presentation. The majority of OBTs were in FIGO stage I. Two thirds were serous subtype. Serum CA 125 was elevated in a third of cases (both S-OBT and M-OBTs). CA 19.9 was elevated in a minority of cases and all were M-OBT. Two thirds had fertility-sparing surgical procedures, with eight successful gestations afterwards. Long-term follow up was the protocol used in management. Excellent survival rates are found with recurrences occurring in only 14% of cases, and deaths in 9.5%, both of which were directly linked to initial staging and disease extent including stage at diagnosis, peritoneal washings, peritoneal implants, residual mass post-op.

Other parameters failed to show such statistical significance, including Clinical and morphological correlates like age, menopausal status, laterality, type of surgical procedure, serum CA 125, tumor diameter, histotype, pelvic lymph node involvement, ovarian surface involvement, LVI, intraepithelial carcinoma, micropapillary morphology in S-OBT, stromal microinvasion, endometriosis, and endosalpingiosis.

CONCLUSIONS

Our results are in agreement with literature from other parts of the word that OBTs have an excellent prognosis. Conservative surgery is to be considered for patients of reproductive age who desire preservation of fertility. A long-term follow-up, however, is highly recommended for these tumors.

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Table 1. OBT distribution among age groups. S-OBT: serous ovarian borderline tumor. M-OBT: mucinous ovarian borderline tumor.

Age groups	Group by years	Total	%	S-OBT no.(%)	M-OBT no. (%)
1	20-30	14	33.3	8 (57.1)	6 (42.9)
2	31-40	7	16.7	6 (85.7)	1 (14.3)
3	41-50	16	38.1	11(68.8)	5 (31.3)
4	51-60	3	7.1	2 (66.7)	1 (33.3)
5	61-70	1	2.4	1 (100)	0 (0)
6	≥ 71	1	2.4	1 (100)	0 (0)
Total		42	100.0	28	14

Table 2. Clinicopathological characteristics of OBTs. *(LVI) Lymphovascular invasion.

Characteristics	All cases	S-OBT	M-OBT
Mean age (range)	38.5 (20-71) years	39.2 (20-71)	37.4 (20-63)
Age no. (%)			
< 50 years' old	37 (88.1%)	25 (89.3)	12 (85.7)
> 50 years' old	5 (11.9%)	3 (10.7)	2 (14.3)
Menopause			
No	33 (78.6)	22 (78.6)	11 (78.6)
Yes	9 (21.4)	6 (21.4)	3 (21.4)
Serum CA125			
Mean (range) U/ml	69.6 (5- 1000)	86.8 (6-1000)	35.9 (5- 103)
Elevated [no. (%)]	16 (38.1)	11 (39.3)	4 (28.6)
Serum CA19.9			
Mean (range) U/ml	148.9 (1-6407.7)	7.9 (1-19.81)	431.7 (1-4607.7)
Elevated in [no. (%)]	3 (7.1)	0 (0)	3 (21.4)
Fertility-sparing procedure			
No	15 (35.7)	17 (60.7)	10 (71.4)
yes	27 (64.3)	11 (39.3)	4 (28.6)
FIGO stage			
I	34 (81)	24 (85.7)	10 (71.4)
II	1 (2.3)	0 (0)	1 (7.1)
III	7 (16.7)	3 (14.3)	3 (21.4)
IV	0 (0)	0 (0)	0 (0)
Histotype	42	28 (66.7)	14 (33.3)
Histopathology			
Mean Diameter (cm)	10.54 (2-32)	7.5 (2-18)	16.4 (3-32)
Bilateral tumor	7 (16.6%)	7 (25%)	0 (0%)
+ Microinvasion	4 (9.5%)	1 (3.6)	3 (21.4)
+ Peritoneal invasion	5 (35.7)	3 (10.7%)	2 (14.3)
+ Micropapillary	8 (28.6)	8 (28.6)	0 (0)
+ peritoneal washings	4 9.5)	2 (7.1%)	2 (14.3)
+ Ovarian surface	5 (11.9)	4 (14.3)	1 (7.1)
+ intraepithelial ca	6 (42.9)	0 (0)	6 (42.9)
+ LVI*	1 (2.4)	0 (0)	1 (7.1)
+ lymph nodes	2 (4.8)	2 (7.1)	0 (0)
Residual mass post-op	5 (11.9)	1 (3.5)	4 (28.6)

Pregnancy post-op	8 (19)	6 (21.4)	2 (14.3)
Recurrences	6 (14.2)	3 (10.7)	3 (21.4)
Outcome			
Alive without disease	36 (85.7)	26 (92.8)	11(78.5)
Alive with disease	3 (7.1%)	1 (3.6)	1 (7.1)
Dead	4 (9.5%)	2 (7.1)	2 (14.3)

Table 3. Statistical correlation of clinico-pathological parameters with recurrences and death. P values with * indicates significant Pearson chi^2.

Study Parameter	no.	Recurrences (p value)	Death (p value)
FIGO stage > I	8	5 (0.000)*	4 (0.000)*
Residual mass post-op	5	3 (0.002)*	2 (0.013)*
Omental metastasis	6	4 (0.000)*	4 (0.000)*
+ Peritoneal washings	5	3 (0.002)*	4 (0.000)*
Age (≥ 50 years)	5	1 (0.939)	1 (0.309)
Fertility-sparing procedure	27	3 (0.802)	3 (0.513)
Tumor diameter (≥ 15 cm)	9	3 (0.101)	2 (0.231)
CA 125 ≥ 35 U/ml	16	2 (0.302)	1 (0.302)
CA 19.9 ≥ 37 U/ml	3	1 (0.469)	1 (0.756)
S-OBT M-OBT	28 14	3 3 (0.350)	2 2 (0.457)
Positive lymph nodes	2	0 (0.554)	0 (0.638)
Positive ovarian surface	5	1 (0.697)	0 (0.440)
Lymphovascular invasion	1	0 (0.679)	0 (0.743)
Micropapillary pattern	8	0 (0.382)	0 (0.554)
Stromal microinvasion	4	1 (0.520)	0 (0.495)
Intraepithelial carcinoma	6	2 (0.352)	1 (0.733)

Fig 1. Histopathological findings in a case of S-OBT. Micropapillary configuration (a). Endosalpingiosis adjacent to tumor (b). (H&E stain 100×).

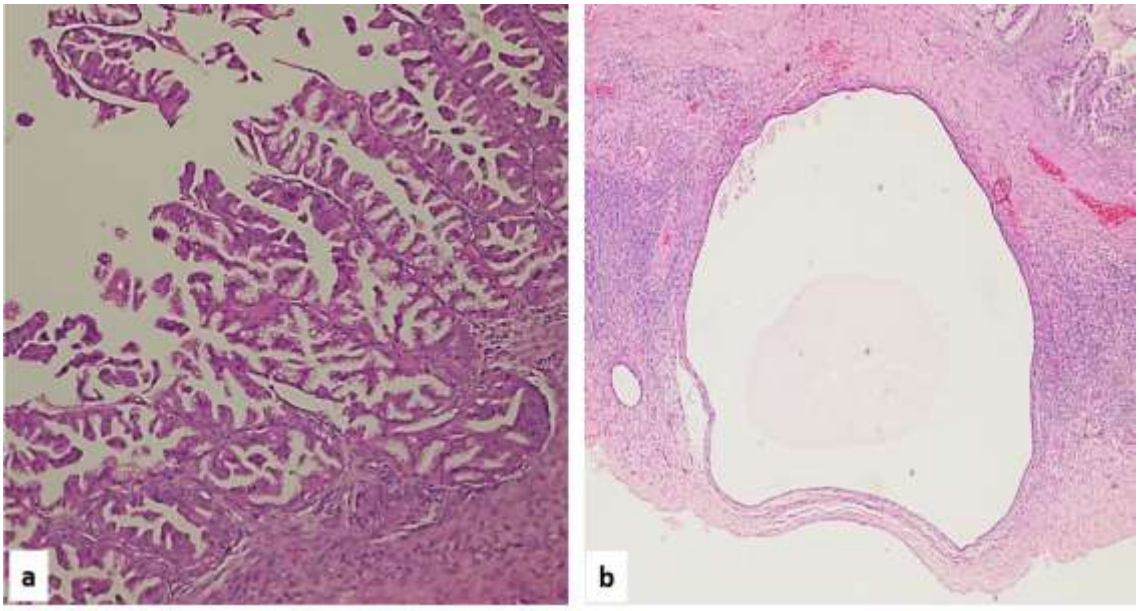

Fig 2. Histopathological findings in a case of M-OBT. Stromal microinvasion (a; black stars). Intraepithelial carcinoma (b; black arrows); lymphovascular invasion (b; arrowhead). (Original magnification 100 ×).