Original Article

Clinical Spectrum and Management of Ovarian Masses in Children and Adolescent up to 20 Years of Age

*Khatoon F[1], Begum SA[2], Choudhury N[3], Yeasmin S[4], Begum M[5]

Abstract

Pathological type as well as management of ovarian tumor in the pediatric population are different than adult women. We performed a retrospective analysis of clinical and diagnostic aspects of ovarian tumors and tumor-like lesions in girls in order to identify characteristics associated with malignancy and it's clinical management which is different from adult women. This is a descriptive type of cross sectional study was condunted among seventy nine female children and adolescent admitted in Bangabandhu Sheikh Mujib Medical University (BSMMU) with ovarian mass from January 2017 to December 2020. Secondary data were collected from hospital record review. The demographic data, diagnostic procedure, management and histopathological analysis of the ovarian tumor were recorded. Mean age of study population was 16.7±3.1 and age range was 8-20 Years. Benign and malignant ovarian tumor was 40.50% and 59.49% respectively. The main symptom and sign were abdominal pain and palpable mass were found in 51% and 50% cases respectively. Malignant lesion appeared as cystic in 22.44%, solid 44.89% and mixed in 32.65% cases. But benign ovarian tumor was found predominantly as cystic in 70% cases preoperatively. More than three fourth (75.51%) of malignant ovarian tumor showed one or more positive tumor marker whereas one third (33.33%) benign tumor had raised tumor marker. Large lesions in both benign and malignant cases were found in almost similar number of cases and these were 80% and 81% respectively. In the group of solid tumors, positive tumor marker results occurred more frequently in patients with malignant tumor (57.14%). Elevated serum alpha feto protein (AFP), Human Chorionic Gonadotrophin (HCG) and high Lactate Dehydrogenage (LDH) value associated more often with malignant tumor. Laparotomy was performed in all cases of study population. Among 49 malignant ovarian tumour 34 (69.3%) underwent ovary preserving surgery. All patient with benign ovarian tumor undergone conservative surgery. Predominantly solid structures noted on imaging studies, large dimension and positive tumor markers are clinical predictors of malignancy. Multicenter prospective studies are needed to improve and unify the ovarian preservation rates across the world.

Keywords: *Ovarian masses, alpha-feto protein, fertility preserving surgery*

1. *Dr. Farhana Khatoon, Assistant Professor, Department of Gynecologic oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka. Email: farhana shimu1977@gmail.com, Mobile number: 01934279313
2. Dr. Shirin Akter Begum, Professor, Department of Gynecologic Oncology, BSMMU, Shahbag, Dhaka.
3. Dr. Nazneen Choudhury, Assistant Professor, OSD, DGHS, BSMMU, Shahbag, Dhaka.
4. Dr. Sabiha Yeasmin, OSD, DGHS, BSMMU, Shahbag, Dhaka.
5. Dr. Monowara Begum, Consultant, BSMMU, Shahbag, Dhaka.

*For correspondence

INTRODUCTION

Ovarian masses in girls represent a wide pathological spectrum ranging from tumor-like conditions to highly aggressive malignant tumors. Malignant ovarian tumors (MOT) in children and adolescents are rare, accounting for 0.9% of all malignancies.[1,3,5] It is estimated that almost 10-30% of all the ovarian neoplasms occurring in girls up to 17 years of age are malignant.[2] In premenarchal girls, up to 40% of ovarian neoplasms are malignant.[3,4,5] However, the true incidence of MOT in the pediatric population is unknown, as only few studies, case reports and case series have been published. Germ cell tumors (GCT) are the most frequent malignant tumor of childhood, this contrasts with adults, in whom epithelial malignant tumors (EMT) account for most malignant ovarian neoplasm. Mature cystic teratoma is the most frequent neoplastic tumor of children and adolescents, accounts for more than one half of ovarian neoplasms in women younger than 20 years of age.[1,3,4] Females under the age of 20 years with ovarian masses are unique in terms of clinical symptoms, pathological subtypes and the treatment required.

Tumour markers, including CA 125, AFP, LDH, CEA, and beta hCG, are essential tools in the diagnosis and follow up of specific malignancies in childhood. In children and adolescents, the estimation of serum AFP and B-HCG levels is essential in the evaluation of adnexal

masses. LDH, inhibin, and CA 125 levels may also be useful markers for ovarian tumors that do not produce AFP or b-HCG [11, 8] Management of ovarian lesions varies with demographic, hospital, and physician factors. International treatment guidelines dedicated to children are still not established, causing a great difficulty in making appropriate therapeutic decisions (a search of PubMed: English language; 1966–2017; search terms: "ovarian neoplasms" and "child"/ "ovarian masses" and "child"). This in turn poses a threat to the patient's life and fertility in the future. Recently, efforts are being made to promote ovary-sparing surgery in the appropriate setting. [9,5,7] The rarity of this condition prompted us to conduct this study and share our experience on the clinical aspects and management of different ovarian tumors in girls up to 20 years of age operated at our instituition in last 3 years.

MATERIAL AND METHOD

We reviewed the records of 79 females of the age 20 and below with adnexal masses who were treated at the Gynaecological Oncology department of BSMMU from 2017 to 2020. Sampling was nonrandom purposive sampling. Patients demographics and clinical characteristics, results of laboratory and diagnostic studies especially ultrasound findings and tumor marker were extracted from the hospital database for each cases. Tumor markers, including serum alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (β-HCG), LDH, cancer antigen 125 (CA-125), carbohydrate antigen 19–9(CA 19–9) and carcino embryonic antigen (CEA) were tested in most cases. The stages of malignant ovarian tumors were done after histopathological report and classified according to FIGO staging. Operative procedure, and histopathology report of and clinical outcome (including preservation rate), of the patients were recorded. All clinical characteristics were reviewed to test their association with malignancy. Patients were followed-up for an average of 17 month (range: 1 to 6 months for benign masses; 1 month to 3 years for malignant neoplasms). Demographic and clinical characteristics of patients in our at-risk cohort were described with frequencies and percentages for categorical variables and medians and interquartile ranges for continuous variables. Descriptive statistics for prevalence and age-wise prevalence was done. Bivariate relationships between patient characteristics and malignancy were assessed using Chi-square, Fisher's exact, and Wilcoxon-Mann-Whitney U tests where appropriate.

The study group was divided into two subgroups of patients; girls with tumor-like lesions combined with benign tumors (non-malignant group) and malignant tumors. A p value of less than 0.05 was required to reject the null hypothesis. For statistical purposes, we included the non-neoplastic cases comprising of corpus luteal cyst, follicular cyst and endometriotic cyst in benign cases. The borderline surface epithelial tumours are included in the malignant category for the same reason. An ovarian lesion was described arbitrarily as large when its diameter was 10 cm or more. Such classification obtained from the previous experiences of other Authors. [9,10]

RESULT

This study was conducted among 270 patients of ovarian tumor by reviewing record of last 3 years period. Among them, 79 cases of girls up to 20 years of age were included for this study purpose.

Table I shows, 67.1% of the patient belong to >15 years age group, 30.4% were between 10-15 years and only 2.5% were from below 10 years age group.

Table-I: Distribution of respondents according to age (n=79)

Age Group (in Years)	Frequency	Percent
<10 Years	2	2.5
10-15 years	24	30.4
>15 years	53	67.1

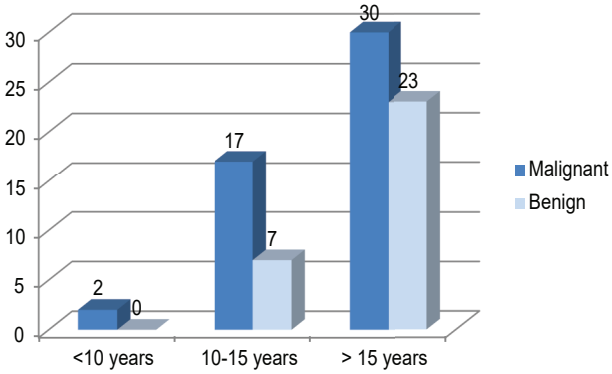
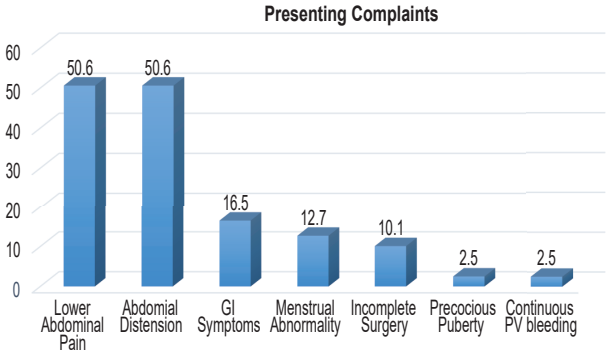


Figure 1: Bar diagram showing frequency of tumors type in different age group

Figure 1 shows, the distribution of types of ovarian tumor (OT) in different age group. Among 79 ovarian tumor, benign ovarian tumor (BOT) were 40.50% and MOT were 59.49%. BOT and MOT in >15 years age group

were 76.66% and 61.22% respectively .On the other hand , In 10-15 years age group BOT and MOT were 23.33% and 34.69%. All cases below 10 years were malignant.



**Multiple responses*

Figure 2: Bar diagram showing distribution of presenting complaints

Figure 2 shows, the most common presenting complain; here both abdominal pain and abdominal distension were 50.6%. GI symptom and menstrual abnormality were 16.5% and 12.7%. Incomplete surgery in MOT were 10.1%. Precocious puberty and P/V bleeding both were 2.5% in frequency.

Table II Shows the distribution of different histopathologic type ; distribution of GCT, epithelial tumor and sex cord stromal tumor were 35 (44.30%) ,28(35.44%) and 5(6.32%) respectively. Non-neoplastic lesion were 11(13.92%). Among GCT, dysgerminoma were 11 (23.40%), Endodermal Sinus tumor were 9 (19.14%) and immature teratoma were 8(17.02%). Among epithelial tumor, Mucinious cystadenocarcinoma were 9 (19.14%) and serous cystadenocarcinoma were 7 (14.89%). Benign Serous and Mucinious tumor were 9(11.39%) and 3(3.79%) respectively.

Table -II: Distribution of Histopathologic type of tumor and age group (n=79)

Histopathologic Type		Age Groups (in Years)			Total
		< 10 Years	10 to 15 years	>15 years	
Germ Cell Tumor(GCT)				35	
	Mature Teratoma	0	2	5	**7**
	Immature Teratoma	1	2	5	**8**
	Dysgerminoma	0	4	7	**11**
	Endodermal Sinus Tumor	1	4	4	**9**
Epithelial Tumor				28	
	Benign Mucinous Tumor	0	0	3	**3**
	Malignant Mucinous Tumor	0	3	6	**9**
	Benign Serous Tumor	0	2	7	**9**
	Malignant Serous Tumor	0	1	6	**7**
Sex Cord Stromal Tumor				5	
	Juvenile Granulosa Cell Tumor	0	3	2	**5**
Non Neoplastic Lesion				11	
	Corpus Luteal Cyst	0	1	0	**1**
	Endometriotic Cyst	0	2	5	**7**
	Paraovarian Cyst	0	0	2	**2**
	Functional Cyst	0	0	1	**1**
Total		**2**	**24**	**53**	**79**

Table III Shows the comparision of clinical and peroperative findings in BOT and MOT; sonographically 70 %, 23.33% and 6.66% BOT were cystic, mixed and solid in nature. In contarary MOT, were cystic, mixed and solid in 32.65%, 22.44%, and 44.89% cases. The mean ovarian tumor volume was 15.2 (+-8.1) cm (range 2 to 40 cm). Per-operatively 81.63% MOT (40/49) and 80% (24/30) BOT were >10 cm. Among MOT 67.2% were unilateral 33.3% were bilateral. Torsion was found in 14.3% of MOT and 30.0% of BOT. Metastasis were present in 38.8% of MOT. Age, size and laterility of tumor had no statistical significance with malignancy status of the patient (P=0.262,P=0.579,P=0.059). Only free fluid is statistically significant (p=0.00).

Table-III: Comparison of clinical data in benign and malignant tumor (N=79)

Variables		**Malignant Frequency (%)**	**Benign Frequency (%)**	**P value**
Age Groups (in Years)				
	< 10	2 (4.1)	0 (0.0)	p=0.262
	10 to 15	17 (4.7)	7 (23.3)	
	>15	30 (61.2)	23 (76.7)	
USG Findings				
	Cystic Mass	11 (22.44)	21 (70)	p=0.176
	Solid Mass	22 (44.89)	2 (6.66)	
	Mixed Mass	16 (32.65)	7 (23.33)	
Per-operative findings:				
Size of the tumor (in cm)				
	< 10	9 (18.4)	6 (20.0)	p=0.579
	10 to 15	18 (36.7)	14 (46.7)	
	>15	22 (44.9)	10 (33.3)	
Laterality				
	Unilateral	45(91.8)	23 (76.7)	p=0.059
	Bilateral	4 (8.2)	7 (23.3)	
Consistency				
Cystic		7 (14.28%)	19 (63.33)	P=0.456
Solid		25 (51.02)	0 (00)	
Mixed		17 (34.69%)	11 (36.66)	
Torsion				
	Yes	7 (14.3)	9 (30.0)	p=0.092
	No	42 (85.7)	21 (70.0)	
Free Fluid				
	Yes	22 (44.9)	4 (13.3)	p=0.004
	No	27 (55.1)	26 (86.7)	
Metastatic Deposit				
	Yes	19 (38.8)	6 (20.0)	p=0.082
	No	30 (61.2)	24 (80.0)	

Table IV Shows the various tumor marker status in both BOT and MOT; AFP and both LDH and B-HCG were raised in 15 and 14 cases of MOT. CA-125 were raised in 21 (80.8%) MOT and in 5 (19.2%) BOT. CA-19-9 and CEA were elevated in 14 (77.8%) and 6 (85.7%) MOT, 4(22.2%) and 1(14.3%) cases of BOT. Both large size and raised marker (any one) were found in 70% (28/40) of MOT 45.83% (11/24) of BOT. All solid tumor along with elevated marker 57.14% (8/14) were malignant.

Table V Shows the according to FIGO, Stage distribution of different Histological type; Among 11 cases of Dysgerminoma, 7 cases presented at stage I only 1 cases at stage IV. Among 9 Endodermal sinus tumor tumor 4 cases presented in advanced stage (stage III). 5 cases of Immature teratoma were found in stage I and 3 cases in stage III. All juvenile granulosa cell tumor found in stage I. Seven cases Malignant mucinious cystadenocarcinoma mostly found stage I. Only I cases is found in advanced stage. 4 cases of serous cystadenocarcinoma found in early stage and 2 cases in advanced stage. (Table-V)

Table-IV: Results of tumor marker (n=79)

Variables	Malignant f(%)	Benign f(%)
AFP	15 (100%)	00(00%)
LDH	14 (100%)	00 (00%)
B-HCG	14 (100%)	00 (00%)
CA 125	21(80.8%)	5 (19.2)
CA-19-9	14(77.8)	4 (22.2)
CEA	6 (85.7)	1 (14.3)
Large lesion with positive marker	28/40 (70%)	11/24 (45.83%)
Solid lesion (in USG) with positive marker	8/14(57.14%)	0/5(0%)

Table-V: Distribution of Histological type according to FIGO stage

Histologic type of tumor	Stage of tumor				Total
	Stage I	Stage II	Stage III	Stage IV	
Dysgerminoma	7	2	1	1	11
Endodermal Sinus Tumour	3	2	4	0	9
Immature Teratoma	5	0	3	0	8
Juvenile Granulosa Cell Tumour	5	0	0	0	5
Mucinous Cystadenocarcinoma	7	1	1	0	9
Serous cystadenocarcinoma	4	1	2	0	7

Table VI Shows the modalities of treatment offered in BOT and in MOT; 69.3% MOT and 100% of BOT had ovary preserving surgery. Cystectomy were done in 43.3% of BOT. Unilateral SO (salphingo-ophorectomy) and Unilateral SO with infracolic omentectomy were done in 57.1% and 12.2% cases of MOT and 50.0% and 3.3% cases of BOT . 29.6% MOT underwent radical surgery. Among radical surgery TAH with BLSO with infracolic omentectomy, PCS, SCS and ICS were done in 14.2%,10.2%,4.1% and 2% cases of MOT consecutively. Adjuvant Chemotherapy were given in 31 cases of malignant ovarian tumor. All patient with benign ovarian tumor undergone conservative surgery.

Among the 48 malignant cases we followed up 30 patient for 3 years. Among them 7 girls were found dead. Among them 2 cases were serous cystadenocarcinoma stage III, died at 8-month post-surgery. Two were mucinious cystadenocarcinoma, one died at 1 month and 18 month of follow up. One patient with stage IV dysgerminoma died at 6 month follow up. One yolk sac tumor of stage III and one immature teratoma of stage III died respectively at 19 month and 5 month follow up.

Table-VI: Distribution of respondents according to treatment given n=79

Type of Treatment	Malignant Frequency (%)	Benign Frequency (%)
Ovary Preserving Surgery	34 (69.3%)	30(100%)
Cystectomy (Unilateral / Bilateral)	0 (0.0)	13 (43.3)
Unilateral SO with Cystectomy	0 (0.0)	1 (3.3%)
Unilateral SO	28 (57.1)	15 (50.0)
Unilateral SO with Infracolic Omentectomy	6 (12.2)	1 (3.3)
Radical Surgery	15(29.6%)	00(00%)
TAH with BLSO with Infracolic Omentectomy	7 (14.3)	0 (0.0)
Primary Cytoreductive Surgery(PCS)	5 (10.2)	0 (0.0)
Secondary Cytoreductive Surgery(SCS)	2 (4.1)	0 (0.0)
Interval Cytoreductive Surgery(ICS)	1 (2.0)	0 (0.0)
Adjuvant CT	31 (63.3)	00 (00%)

DISCUSSION

In this study, patient ranged in age from 8 years to 20 years, with a mean age of 16.8(+-3.2) at the time of presentation. which is nearly similar with previous study.[12] Ovarian malignancy accounts for 1% of all the childhood tumors in previous studies but incidence is found as high as 6% and 11.2% in some other studies.[2,11,13] Another study reported 34.8% of all ovarian tumor were malignant, in contrast we found 59.49% were malignant ovarian tumor in paediatric and adolescent adnexal masses.[12] The high frequency of malignant ovarian tumour in our study may be due to our one is a referral hospital where suspected malignancy are reffered.

Regarding age distribution some contradictory observation was found among girls with malignant tumors in the literature.[14,15,16] One study in a large group of 1037 patients noted that most girls with malignant lesions were between 15 and 19 years of age, while another study in a group of 424 patients found the highest incidence of malignancy between 1 and 8 years of age.[10, 17] In our study we noted the mean age of malignant ovarian tumor 16.4 years (+-3.3) and the highest incidence was in the group aged 15 to 20 years. Mean age for benign ovarian tumor was 17.4 (+-2.6).

Germ cell tumor were seen to be three times more than epithelial tumours in younger age group in literature.[18] The frequency of germ cell tumor is reported to vary from 67% to 85% in previous studies.[19] In contrast we found germ cell tumor at a frequency of 44.30 . Second most common was epithelial ovarian tumor at a frequency of 35.44%. Similar frequency of surface epithelial tumor was seen in a study (12). But contrast result regarding surface epithelial was observed, about 15 – 20% [20]. This finding could possibly be explained by the fact that our study population included girls up to 20 years of age when a lot of girls have achieved menarche and are already going through the various hormonal surges giving rise to these tumours.

Dysgerminoma is commonest malignant tumour in our study, which is in accordance with other studies.[2,21]

Sex cord stromal tumor constitute 10-25% of all paediatric ovarian neoplasm.[22] In this study we reported only 6.32% sex cord stromal tumour ,all were Juvenile granulosa cell tumor, similar frequency (5.1%) were observed in previous study.[23]

As regards clinical presentation of ovarian pathology in children we noted another discrepancy between various clinical series in the literature. In our series of patient, Abdominal pain was in frequency of 50% which is in concordance with other study, which shows 45.5%[12] Palpable adnexal mass was 51% which is in contrast with other study , where adnexal mass was 24% in frequency. [22] At the time of initial examination, in this study malignant ovarian tumor was found to be large in 81.01% . Such clinical presentation may indicate significant delay in seeking of medical consultation by the patients and their

parents. Other symptoms, incidental diagnosis (2.53%) and precocious puberty was reported 2.5% in our study, but other study shows 4.6% and 6.2% respectively[22]. There is no strict correlation between the size of ovarian mass and its histology. But study reveals that a large ovarian mass should always raise a concern and should be treated as a risk factor for malignancy [10,24,25]

The gold standard for diagnosing ovarian masses is ultrasound (1). Sonographically we categorise the lesion as cystic, solid mixed. We observed that sonographically mixed masses (32.65%) had more tendency to being malignant .Most of the solid tumor (22/24) were malignant. although previous study did not show any specific relation with large or complex mass.[26,27]

USG continues to be the primary imaging modality used to identify and characterize adnexal masses. USG demonstration of a solid component within a cystic mass is the most important predictor of malignancy and conversely malignancy is very unlikely in the absence of a solid component.[27] but there is pitfall in USG finding which lead to diagnostic problem. Solid component can be seen with benign, as well as borderline and malignant tumor [3,26.]

Regarding gross feature in our study, Apart from the size, the structure of the tumor and its characteristics found very important in preoperative evaluation. Reviewing the data of other authors and our own series it may be concluded that a solid lesion must always be viewed as potentially malignant. But in our series we also found cystic lesion to be malignant, which is also reported by other authors [28]

Tumor marker is an important step in a preoperative assessment of a girl with a pelvic mass. Although many studies have confirmed association of their elevated levels with malignancy, there are some that highlight their limited diagnostic accuracy.[10,29, 30] AFP particularly are increased in patients with tumour with yolk sac components 29. Our results also revealed their positive role in predicting histology of ovarian lesions. We found , Among the elevated AFP, nine were Yolk sac tumor , 2 were immature teratoma, 2 dysgerminoma,1 juvenile granulosa cell tumor and one was serous cystadeno-carcinoma. Our results revealed all the tumor with elevated AFP were malignant. In a recent study, high serum AFP separated benign from malignant tumors in children and adolescents with a specificity of 89% and with sensitivity of 50% [29] In this study all yolk sac tumor except 2 exibit 2 or 3 marker elevation along with alpha fetoprotein either LDH or B HCG. One yolk sac tumor show very high level >20,000 iu/ml which was in FIGO stage IIB.

Similarly in our study Raised HCG (14 cases) were observed in three were yolk sac tumor (range from 1000 to 5000iu/), five immature teratoma (ranges 50-10,000 iu/l) and in five dysgerminoma. The same observation was made other study.[15] Our study shows neither CA-12 5, nor CA19-9, is very specific as these were the positive markers in non-malignant lesion too. But when positive markers are correlated with the size, structure and level of tumor marker, they provide very important diagnostic clue. Because tumor marker levels can be high in both benign and malignant tumors, it has been recommended to perform frozen-section analysis before radical surgery and not to rely solely on tumor marker levels in decision -making.[30,31]

In this study. Among malignant ovarian tumour (34/49) 69.3% underwent ovary preservation surgery. The preservation rate was reported in other series vary between the studies (24-82.9%) [32, 24, 33, 34] .There were some reviews indicating lower rates of Oophorectomy when a gynecologic surgeon was present [25,28, 32,33,34]. As fertility preserving procedure are a priority in the constant aging society, we had every attempt to do that. We were dealt with all suspected malignant ovarian tumor and all cases were undergone open laparotomy with frozen section facility. Therefore decision were taken according to the per-operative finding and frozen section report, that may explain the high rate of preservation surgery in our series. The ovarian-sparing technique has been widely adopted in pediatric surgical centers in girls with benign lesions. However,it requires verification based on a long-term follow-up review [9,28,33,31,15,17].Although ovary preserving surgery was done in majority of malignant tumor, adjuvant treatment was given regardless of extent of surgery rather on the basis of histopathological findings. 63.3% of patient got adjuvant chemotherapy. Many studies showed that oncologic treatment such as chemotherapy and radio-therapy increase infertility.[33,34] So it is crucial to diagnose these lesion in early stage.

In summery, We presented important descriptive data from a referral institution where suspected malignancies are referred. The incidence of ovarian tumor increased with age, being most common in patients older than 14 years of age. Abdominal pain is the most common presenting complaint of young adolescent girls with adnexal masses. So the index of suspicion should be kept high and prompt

investigations like ultrasound must be performed to rule out such adnexal masses. AFP is the most useful diagnostic marker for ovarian tumors in young females. Germ cell tumors are the most common ovarian neoplasms in adolescent girls, but fair no. of surface epithelial tumors was observed in our study. Which may be due to inclusion of adolescent up to 20 years.

CONCLUSIONS

The rate of malignant ovarian tumour in children and adolescent is high, 59.49% in this study. More than three fourth 75.51% ovarian tumour showed one or more positive tumour marker. Screening of ovarian tumour might serves girls from malignancy. Treatment guidelines for ovarian lesions in children should be established on the basis of multicenter prospective studies and introduced as soon as possible in order to improve and unify the ovarian preservation rates across all gynecologist. There is need for bigger population studies with larger sample size.

REFERENCES

1. Deligeoroglou E, Eleftheriades M, Shiadoes V,et al: Ovarian masses duringadolescence: clinical, ultrasonographic and pathological findings, serumtumor markers, and endocrinological profile. Gynaecol Endocrinol 2004,19:1–8
2. Bhattacharyya NK, De A, Bera P, Mongal S, Chakraborty S, Bandopadhyay R. Ovarian tumors in pediatric age group- A clinicopathologic study of 10 years' cases in West Bengal, India. Ind J Med Paed Oncol. 2010;31(2):54–7. http://dx.doi.org/10.4103/0971-5851.71656 PMid:21209765 PMCid:PMC2970935
3. Quint EH, Smith YR:Ovarian surgery in pre-menarchal girls.J PediatrAdolesc Gynecol1999, 12:27.
4. Kozlowski KJ. Ovarian masses. Adolesc Med. 1999; 10: 337-50.
5. Abbas PI, Dietrich JE, Francis JA, Brandt ML, Cass DL, Lopez ME. Ovarian-Sparing Surgery in Pediatric Benign Ovarian Tumors. J Pediatr Adolesc Gynecol. 2016;29(5):506–10. [PubMed: 27079914]
6. Aldrink JH, Gonzalez DO, Sales SP, Deans KJ, Besner GE, Hewitt GD. Using quality improvement methodology to improve ovarian salvage for benign ovarian masses. Journal of Pediatric Surgery. 2018;53(1):67–72.
7. Chabaud-Williamson M, Netchine I, Fasola S, Larroquet M, Lenoir M, Patte C, et al. Ovarian-sparing surgery for ovarian teratoma in children. Pediatric blood & cancer. 2011;57(3):429–34. [Pub Med: 21370434]
8. Granato T, Midulla C, Longo F, Colaprisca B, Frati L, Anastasi E. 2012. Role of HE4, CA72.4, and CA125 in monitoring ovarian cancer. Tumor Biology 33: 1335–1339.
9. Zhang M, Jiang W, Li G, Xu C. Ovarian masses in children and adolescents - an analysis of 521 clinical cases. J Pediatr Adolesc Gynecol. 2014;27(3):e73–7.
10. Oltmann SC, Garcia N, Barber R, Huang R, Hicks B, Fischer A. Can we preoperatively risk stratify ovarian masses for malignancy? J Pediatr Surg. 2010; 45(1): 130–4.
11. Oumachigui, Narasimhan KL, Reddy KS. et al. A clinicopathologic study of ovarian tumors in children. J Obstet Gynecol. 1991;140:441-5.
12. Rathore R, Sharma S, Arora D. Spectrum of Childhood and Adolescent Ovarian Tumors in India: 25 Years Experience at a Single Institution. Open Access Maced J Med Sci. 2016 Dec 15; 4(4):551-555. https://doi.org/10.3889/oamjms.2016.090
13. Sawai MM, Sirsat MV. Ovarian neoplasm in children and adolescents. Indian J Cancer. 1973;10:302-11. PMid:4362177
14. Andrés MM, Costa E, Cañete A, Moreno L, Castel V. Solid ovarian tumours in childhood: a 35-year review in a single institution. Clin Transl Oncol. 2010; 12(4):287–91.
15. Papic JC, Finnell SM, Slaven JE, Billmire DF, Rescorla FJ, Leys CM. Predictors of ovarian malignancy in children: overcoming clinical barriers of ovarian preservation. J Pediatr Surg. 2014; 49(1): 144–8
16. Taskinen S, Fagerholm R, Lohi J, Taskinen M. Pediatric ovarian neoplastic tumors: incidence, age at presentation, tumor markers and outcome. Acta Obstet Gynecol Scand. 2015;94(4):425–9
17. Brookfield KF, Cheung MC, Koniaris LG, Sola JE, Fischer AC. A populationbased analysis of 1037 malignant ovarian tumors in the pediatric population. J Surg Res. 2009;156(1):45–9

18. Amatya A, Rana G, Gurung L. Ovarian tumours in childhood and adolescents - our eight years experiences. Nepal J Obstet Gynaecol (NJOG). 2008 May- June; 3(1):39-42.

19. Islam S, Yamout SZ, Gosche JR. Management and outcomes of ovarian masses in children and adolescents. Am Surg. 2008;74:1062–5

20. Graspa D, Kairi-Vassilatou E, Hsiakos D, Kondi-Pafiti A. Ovarian Mucinous cystadenoma with extended calcification in an 11-year old girl: Case report and review of literature. Clin Exp Obstet Gynecol. 2006;33:181-2.

21. Mukhopadhyay M, Shukla RM, Mukhopadhyay B, et al. Ovarian cysts and tumors in infancy and childhood. Journal of Indian Association of Pediatric Surgeons. 2013;18(1):16-19. http://dx.doi.org/ 10. 4103/ 0971-9261.107010 PMid:23599577 PMCid: PMC3628238

22. Ki EY, Byun SW, Choi YJ, Lee KH, Park JS, Lee SJ, Hur SY. Clinicopathologic review of ovarian masses in Korean premenarchal girls. International journal of medical sciences.

23. 2013;10(8):1061.http://dx.doi.org/10.7150/ijms. 6216 PMid:23801894 PMCid:PMC3691806

24. Liu H, Wang X, Lu D, Liu Z, Shi G. Ovarian masses in children and adolescents in China: analysis of 203 cases. J Ovarian Res. 2013;6:47

25. Ryoo U, Lee DY, Bae DS, Yoon BK, Choi D. Clinical characteristics of adnexal masses in Korean children and adolescents: retrospective analysis of 409 cases. J Minim Invasive Gynecol. 2010;17(2):209–13

26. Rogers EM, Casadiego Cubides G, Lacy J, Gerstle JT, Kives S, Allen L. Preoperative risk stratification of adnexal masses: can we predict the optimal surgical management? J Pediatr Adolesc Gynecol. 2014;27(3): 125–8.

27. Iyer VR, Lee SI. MRI, CT, and PET/CT for ovarian cancer detection and adnexal lesion characterization. AJR Am J Roentgenol. 2010 Feb;194(2):311–21.

28. Levine D, Brown DL, Andreotti RF, Benacerraf B, Benson CB, Brewster WR, et al. Management of asymptomatic ovarian and other adnexal cysts imaged at US: Society of Radiologists in Ultrasound Consensus Conference Statement. Radiology. 2010; 256(3):943–54.

29. Hernon M, McKenna J, Busby G, Sanders C, Garden A. The histology and management of ovarian cysts found in children and adolescents presenting to a children's hospital from 1991 to 2007: a call for more paediatric gynaecologists. BJOG. 2010;117:181–4. onsensus Conference Statement. Radiology. 2010; 256(3): 943–5

30. Loh AH, Gee KW, Chua JH. Diagnostic accuracy of preoperative alphafetoprotein as an ovarian tumor marker in children and adolescents: not as good as we thought? Pediatr Surg Int. 2013;29(7):709–13.

31. Spinelli C, Pucci V, Buti I, Liserre J, Messineo A, Bianco F, et al. The role of tumor markers in the surgical approach of ovarian masses in pediatric age: a 10-year study and a literature review. Ann Surg Oncol. 2012;19(6):1766–73.

32. Abdel-Hady el-S, Abdel-Hady Hemida R, Gamal A, ElShamey M. Fertility sparing surgery for ovarian tumors in children and young adults. Arch Gynecol Obstet. 2012;285:469–71.

33. Hermans AJ, Kluivers KB, Wijnen MH, Bulten J, Massuger LF, Coppus SF. Diagnosis and treatment of adnexal masses in children and adolescents. Obstet Gynecol. 2015;125(3):611–5.

34. Berger-Chen S, Herzog TJ, Lewin SN, Burke WM, Neugut AI, Hershman DL, Wright JD. Access to conservative surgical therapy for adolescents with benign ovarian masses. Obstet Gynecol. 2012;119(2 Pt 1):270–5.

35. Bristow RE, Nugent AC, Zahurak ML, Khouzhami V, Fox H. Impact of surgeon specialty on ovarian-conserving surgery in young females with an adnexal mass. J Adolesc Health. 2006;39(3):411–6.