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Original Research Article

Ovarian tumors in patients aged upto 20 years: a longitudinal study conducted in a tertiary care centre, West Bengal, India

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ABSTRACT

Background: International treatment guidelines dedicated to children and adolescents are not yet established, hence need for such studies like ours is required to throw light on demographic variations of ovarian tumors and developing specific guidelines for their management.
Methods: It was a descriptive longitudinal study undertaken in the Department of Obstetrics and Gynaecology from February 2018 to July 2019. According to prevalence in our setup, 50 cases of adolescent girls and children were taken for study and subjected to thorough clinical assessment and investigations. After proper diagnosis, surgery was performed in all cases and depending upon histopathology and cytology, adjuvant chemotherapy was given in selected cases. Patients were followed up till 6 months after discharge.
Results: The most common symptom was found to be abdominal pain (42%), most common sign abdominal mass (38%). Out of 50 cases, 12% were found to be malignant, all of germ cell origin. Epithelial tumors were found to be the most common ovarian tumors (52%) up to 20 years of age, out of which benign tumors had 48% epithelial origin. However, up to 10 years of age, germ cell tumors were found to be the most common (75%). Only 1 malignant case expired, belonging to mixed germ cell variety of advanced stage.
Conclusions: Ovarian neoplasm is highly challenging, especially in adolescents and children due to the need for fertility preservation. Early detection, optimal therapy and intense follow up with psychological support to patients and families are the mainstay of treatment.

Keywords: Adolescents, Neoplasms, Ovarian

INTRODUCTION

The aim of our study was to find out the proportion of adolescent and childhood ovarian tumors in a tertiary care centre, to identify different methods of their presentation and suitable management options depending upon the severity of the disease.

Adolescence is the period of transition from childhood to adulthood, during which a carefree child becomes a responsible adult. According to WHO Expert Committee, it is the period between 10-19 years of age.[1] Beginning with the onset of puberty, it ends with attaining full maturity in sexual function, somatic maturation and emotional adaptation.

Ovarian neoplasms account for top 5 gynaecological malignancies in Indian women.[2] The most common gynaecological malignancy found in girl child is of ovarian origin, constituting 1% of childhood malignancies and 8% of abdominal tumors in children.[3] It is, however, the most common genital tract malignancy in this age group.[10] Mature cystic teratomas are most common benign tumors, and chance of malignant transformation is 0.1-2%.[1] Of all ovarian tumors, 34.8% are found to be malignant. Germ cell tumors are found to

be the most common malignant ovarian neoplasm accounting for 71.1% of all malignant tumors of this age group.[3] Dysgerminoma found to be the most common malignant germ cell tumor in various studies.[11] Immature teratoma found to be the most common malignant germ cell tumor in some.[3]

Adolescent girls present most commonly with abdominal mass and pain, sometimes with pressure effects and menstrual disorders. They can also be complicated by torsion, rupture or hemorrhage. But they are often asymptomatic for long time and with non-specific signs, so almost 2/3rd cases have unfavorable staging and prognosis at the time of their presentation.[8] Apart from clinical examination, USG, MRI and CT scan are effective in diagnosing ovarian neoplasms while plain x-ray of abdomen and pelvis is quite effective in identifying calcifying areas of teratoma. Tumor-markers like CA-125, AFP, HCG, LDH are elevated in specific ovarian tumors. Hormonal assays and vaginal cytology are useful to monitor individuals with sex cord stromal cell tumors like granulosa cell tumor.

The management is multimodal and needs individualization. Ovarian tumors 5-7 cm in size of benign origin can be observed for 3 months with oral contraceptive pills, while those <5 cm in size do not need follow-up. For ovarian cysts >8 cm or undergoing torsion, rupture or hemorrhage, laparoscopic cystectomy is the treatment of choice. For ovarian malignancies, unilateral salpingo-oophorectomy is universalized for all germ cell tumors excepting postmenopausal cases where total abdominal hysterectomy with bilateral salpingo-oophorectomy is done. For epithelial ovarian malignancies, unilateral salpingo-oophorectomy is reserved for stage IA Gr_1 and Gr_2. Post-operative management includes chemotherapy while use of radiotherapy has been minimized due to fertility issues. Intense follow-up is essential for detecting recurrence. Psychological counselling and cryopreservation should always be kept in mind. International treatment guidelines dedicated to children are not yet established, causing great difficulty in making appropriate therapeutic decisions.[9] Hence, it is important to individualize treatment and offer the adolescents and children a life with possibilities of fertility and womanhood as possible.

METHODS

It was an institution based observational longitudinal study. The study has been reviewed by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards described in an appropriate version of the 1964 Declaration of Helsinki, as revised in 2013. It was undertaken in Department of Obstetrics and Gynaecology in Bankura Sammilani Medical College and Hospital from February 2018 to July 2019. One and half year duration of present study was arbitrarily divided into the following steps: a) preparatory phase: 1 month, b) phase of data collection and follow up: 12 months, c) phase of data analysis and interpretation: 3 months, d) writing up and submission of reports: 2 months.

As per hospital records, around 5 cases of ovarian tumors in patients aged up to 20 years were admitted per month. Our data collection was for 10 months. Hence, maximum 50 cases could be availed during our study period. So, 50 cases of adolescent girls and children coming to OPD and admitted to this hospital during this period had been taken for our study.

Inclusion criteria

All girls aged up to 20 years complaining of pain abdomen, abdominal mass, menstrual irregularities, delayed puberty and loss of weight were included with following criteria: i) screened with USG for adnexal mass, ii) having given informed consent.

Exclusion criteria

Patients presenting with PCOS, endometrial cysts, corpus luteal cysts, theca lutein cysts, hydrosalpinx, ectopic pregnancy, pedunculated fibroid uterus were excluded.

The study variables were age, marital status, menstrual history, obstetric history, past medical or surgical history, secondary sexual characters, family history, laparatomy finding and gross appearance of tumor.

The outcome parameters taken were percentage of benign and malignant tumors, distribution of each kind of tumor in both benign and malignant group, relevant tumor marker for each kind of malignant tumor and management protocols and requirement of chemotherapy. Pre-tested, pre-designed semi-structured questionnaire, mercury sphygmomanometer, stethoscope, relevant medical records were used for our study.

All patients were subjected to clinical assessment and routine investigations, USG and tumor markers. Following laparotomy, surgical staging was done in all malignant cases. Peritoneal biopsies and washings from resected areas were sent for histopathological examination and cytological study. Adjuvant chemotherapy was given in all malignancies except for dysgerminoma stage IA and immature teratoma stage IA Gr_1. Patients were followed up at 2 weeks and 6 months after discharge with clinical examination, tumor markers, hepatorenal profile, CXR and USG. For statistical analysis, data was collected and tabulated in Excel sheet, appropriate tables and pie diagrams were drawn for descriptive purpose with appropriate software and for analytical part, SPSS version 20 was used Chi-square test was applied.

RESULTS

Out of the patients presenting with symptoms of pain abdomen, abdominal mass, menstrual irregularities, delayed puberty and loss of weight, 26.2% were

adolescents and children. Among patients of all age groups found to have adnexal mass on USG, 10.3% patients were of adolescents and pediatric age group. Among all adnexal mass on USG, ovarian tumors constitute 44.2% out of which PCOS is most common, accounting for 51.3% in age group up to 20 years.

Table 1: Distribution of ovarian tumors according to age group in children and adolescents (n=50).

Age (in years)	No. of tumors	Percentage	Epithelial	Germ cell
5-10	4	8	1	3
11-14	14	28	7	7
15-20	32	64	18	14
Total	50	100	26	24

Table 2: Distribution of ovarian tumors according to menstrual status.

Type of tumor	Non-menstruating	Menstruating	Total
Epithelial	5 (19.2%)	21 (80.8%)	26
Germ cell	8 (33.7%)	16 (66.7%)	24
Total	13	37	50

χ^2=1.29, df=1, p value= 0.256; df= degree of freedom

It was observed that germ cell tumors had preponderance in age group of 5-10 years while epithelial tumors were higher with growing age (Table 1). Epithelial tumors were present in 80.8% cases in menstruating age group and 19.2% in non-menstruating group (Table 2). Among all tumors, benign ones comprised 86% cases out of which serous cystadenoma was 26%, mucinous cystadenoma 22%, benign cystic teratoma 38%. Malignancy comprised 12% cases out of which dysgerminoma was 6%, immature tyeratoma 4%, mixed germ cell tumor 2% (Table 3).

Table 3: Distribution of ovarian tumors according to malignancy in girls upto 20 years (n=50).

Type of tumor	Number	Percentage
1) Benign	43	86
Mucinous cystadenoma	11	22
Serous cystadenoma	13	26
Benign cystic teratoma	19	38
2) Malignant	6	12
Immature teratoma	2	4
Mixed germ cell tumor	1	2
Dysgerminoma	3	6
3) Borderline	1	2
Mucinous cystadenoma	1	2

Abdominal pain was found to be the most common symptom in 42% cases, acute pain abdomen due to torsion in 4 cases, abdominal mass in 19 cases, bleeding per vagina in 1 case and incidental finding in 3 cases (Table 4). Transabdominal sonography revealed ovarian tumors in all 50 patients, in 3 cases huge lump were present. Bilateral tumors were found in 4 cases. USG Doppler studies showed low resistance flow pattern in 6 malignant cases (Table 5). Serum AFP was found in 3 cases (2 immature teratoma, 1 mixed germ cell tumor). ß-HCG was found high in mixed germ cell tumor, LDH levels found elevated in 3 cases of dysgerminoma, CA-125 in immature teratoma and CA-19-9 in immature teratoma Gr_2. CXR detected metastasis in 1 mixed germ cell tumor, while CT scan was done in all malignant cases.

Table 4: Mode of presentation of ovarian tumor in children and adolescents, n=50.

Symptoms and signs	Number	Percentage
Abdominal mass	19	38
Abdominal pain	21	42
Acute pain abdomen (torsion)	4	8
Anorexia, loss of weight	2	4
Bleeding per vagina	1	2
Incidental	3	6
Total	50	100

Table 5: USG used as a diagnostic tool in evaluation of ovarian tumors upto 20 years aged females.

a) Size of mass	Number of patients	Percentage
5-10 cm	32	64
11-15 cm	15	30
16-20 cm	3	6
b) Laterality		
Bilateral	4	8
Unilateral	46	92
c) USG Doppler study showing low resistant flow pattern	6	12

Table 6: Details of treatment of malignant ovarian tumors in adolescent and children, n=6.

Type of tumor	Stage	Surgery	Adjuvant therapy
Dysgerminoma (3)	IA	U/L salpingo-oophorectomy	No adjuvant therapy required
Immature teratoma	IA grade 1	U/L salpingo-oophorectomy	No adjuvant therapy required
Immature teratoma	IA grade 2	U/L salpingo-oophorectomy	BEP (3 cycles)
Mixed germ cell tumor	IV	Debulking surgery with infracolic omentectomy	BEP (1 cycle) then she expired

All 3 cases of dysgerminoma were stage IA for which unilateral salpingo-oophorectomy was done with no adjuvant therapy. 1 case of immature teratoma stage IA Gr_1 underwent unilateral salpingo-oophorectomy with no adjuvant therapy. 1 case of immature teratoma stage IA Gr_2 underwent unilateral salpingo-oohorectomy with 3 cycles of BEP post-operatively. 1 case of mixed germ cell tumor stage IV was managed with debulking surgery and infracolic omentectomy with pelvic lymphadenectomy, but she expired after 1 cycle of post-operative chemotherapy with BEP (Table 6). Rest all cases of malignant tumors were followed up till 6 months with physical examination and CT scan which showed no residual disease.

DISCUSSION

Ovarian malignancy in children and adolescents are not infrequent. In our study 10.3% of ovarian tumors occur in girls aged up to 19 years, out of which 12% were malignant, which is consistent with study of Priya et al and Lawrence et al, while Nivedha et al mentioned 7.9% malignant tumors among ovarian tumors in this age group.[2,4,5] Sawai and Sirsat recorded the incidence as 11.2% in Tata Memorial Hospital, Mumbai.[12]

In our study, 52% of ovarian tumors are of epithelial cell origin which synchronises with study of Priya et al and Nivedha et al who found that 58% and 54% respectively of ovarian neoplasms in adolescents and children were of epithelial cell origin.[2,5] Bhattacharya et al found that 56% of pediatric and adolescent ovarian neoplasms are epithelial cell tumors.[11] In our series, 26 cases (52%) ovarian tumors in age group upto 20 years are of epithelial cell origin which is consistent with the above mentioned studies. However, Amatya et al found that 73.75% of all ovarian neoplasms in age upto 20 years, were of germ cell origin, which is contradictory to these studies.[8]

This is probably because of inclusion of good number of cases seen after menarche upto 19 years, where estrogen and progesterone play a role in pathogenesis of epithelial tumors. According to Tanksale et al all malignant ovarian tumors noted in pediatric and adolescent were of germ cell origin.[13] In our study, all malignant germ cell tumors are of germ cell origin-2 immature teratoma, 3 dysgerminoma, 1 mixed germ cell tumor (yolk sac component + embyronal cell component). This proportion is consistent with studies like Priya et al and Bhattacharya et al both where 66% of all malignant ovarian neoplasms in age upto 20 years were germ cell tumors.[2,11] Rajeswari et al mentioned 93% germ cell tumors among malignant ovarian tumors in this age group.[7] It is probably due to the fact that germ cell tumors are mostly silent, until they are diagnosed late after menarche and are found to be in advanced stage.

Abdominal pain is found to be the most common complaint in our study, consistent with Priya et al and Divya et al, where abdominal pain was found to be predominant in 40% and 50% cases respectively.[2,6] In our series, 8% cases have torsion whereas Lawrence et al mentioned torsion in 20% cases.[4] Mahour et al reported an incidence of torsion of 35% cases of ovarian tumors in adolescents.[14] Majhi et al reported torsion in 25% cases.[15] Abdominal position of ovarian tumor due to small pelvis and long infundibulo-pelvic ligament in younger age group explains increased rate of torsion. Possibility of other abdomino-pelvic masses including chronic ectopic, tubo-ovarian mass, appendicular abscess, mesenteric cyst and para-ovarian cyst are excluded.

USG has been found to be the most effective and non-invasive, rapid method to diagnose abdomino-pelvic mass and decrease the need for pelvic examination under general anesthesia, especially in virgin adolescent girls. Transabdominal sonography is more preferred than transvaginal sonography in adolescent virgin girls. Solid-cystic or heterogenous mass on USG and elevated specific tumor markers are generally indicative of malignancy. CXR can detect lung metastasis.

Among germ cell malignancies, dysgerminoma presents at an earlier stage, is sensitive to chemotherapy, and for stage IA, unilateral salpingo-oophorectomy results in 5-year survival rate of >95%. Tumor size >10-15 cm in diameter, age <20 years and histopathology showing numerous mitosis, anaplasia and medullary pattern are associated with higher recurrence rates.[6] Mixed germ cell tumors have multiple malignant elements and their prognosis is determined by the most aggressive element. The primary tumor size and relative size of the malignant component are the most important prognostic factors.[7] In Kurman et al series, the most common component of a mixed malignancy was dysgerminoma which occurred in 80%, followed by endodermal sinus tumor (EST) in 70%, immature teratoma in 53%, choriocarcinoma in 20% and embryonal carcinoma in 16%.[16] The most frequent combination was a dysgerminoma and a EST. In our study, mixed germ cell tumor comprised of endodermal sinus tumor and embryonal carcinoma, the latter having an aggressive course.

Epithelial tumors constitute the major proportion of ovarian neoplasms in pediatric and adolescent age group according to our study, this finding being consistent with newer studies like Priya et al, while being contradictory to the other ones.[2] This is probably because of demographic variation and many asymptomatic cases have come to light due to evolution of newer diagnostic tools over the years. In bilateral cases in our study, unilateral salpingo-oophorectomy and contralateral cystectomy have been carried out. Granulosa cell tumor and sertoli-leydig cell tumor are less common in this age group and no such case is found in our study.

The limitations of our study are due to small sample size and carrying out a hospital based study instead of population based study.

CONCLUSION

So, to conclude we can say ovarian neoplasms in pediatric and adolescent age group is highly challenging to manage, as need of conservation of future fertility, chances of malignancy and possibility of relapse are the real scenarios puzzling the gynaecologists. The treat of cancer at this crucial age leads her to darkness of despair, so a tender humanitarian attitude for psychological counselling is important. Cryopreservation should be routinely done in cases where there is need of bilateral oophorectomy in this age group.

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