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Original Article

Pathology Section

Para-Adnexal Cysts- A Clinicopathological Study

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ABSTRACT

Introduction: Para-adnexal cysts (paraovarian and paratubal) constitutes a homogenous group of cystic lesions originating from mesosalphinx or broad ligament, located in proximity of the fallopian tube and ovary. As with the lesions of the adnexa, paraovarian and paratubal cysts can be neoplastic but are often misinterpreted as true functional cysts. A correct radiological and clinical diagnosis would be useful in order to render necessary treatment.

Aim: To highlight the histomorphologic spectrum of the para-adnexal cysts and correlate with clinical findings.

Materials and Methods: The present study was a retrospective study conducted in the Department of Pathology, Rajarajeswari Medical College, Bengaluru, Karnataka, India, from January 2017 to June 2019. All specimens including salpingo-ophorectomy specimens which harboured paratubal or paraovarain cysts, or paratubal/paraovarian cysts diagnosed on radiology and resected and sent separately for histopathologic evaluation were sampled and included in the study. All surgically and radiologically proven paratubal and paraovarian cystic lesions were included and solid lesions were excluded. The results were analysed using descriptive statistics.

Results: Present study analysed 114 cases and found that 28 of the cases showed neoplastic cysts, one of them showing a serous borderline tumour, which have the potential to turn malignant. The mean age of diagnosis was 40.1 years and menstrual abnormalities was the most common presentation. Of the neoplastic cysts, paraovarian cysts (78.6%) were more common than paratubal cysts (21.4%). About 75.4 % were non neoplastic cysts and 24.6% were neoplastic.

Conclusion: Para-adnexal cysts are often misdiagnosed or not sampled as they are thought of as functional cysts. Histopathologic evaluation of these lesions would help in understanding the different histological types that would arise in para-adnexal sites which in turn helps in better management of these patients.

Keywords: Cystic lesions, Paraovarian, Paratubal

INTRODUCTION

The adnexa is a set of structures adjacent to the uterus that consist of the ovaries and fallopian tubes. The aetiology of cysts or adnexal masses ranges from physiologically normal (follicular or luteal cysts) to malignancy. The differential diagnosis of adnexal cysts range from functional cyst, endometrioma, tubo-ovarian abscess, mature teratoma, serous cystadenoma, mucinous cystadenoma, paratubal cyst, hydrosalpinx, leiomyomas to malignancies, pelvic inflammatory diseases and ectopic pregnancy [1]. Paraovarian cyst needs to be differentiated from ovarian cyst, as it is not thought to behave in the same way both clinically and biologically. Paraovarian cyst draws clinical attention in the event of complications like cyst enlargement, torsion, rupture, haemorrhage and neoplasm. There are no clear guidelines for the management of paraovarian cyst and its complications [2].

Para-adnexal cysts (paraovarian and paratubal) constitutes a homogenous group of cystic lesions, which are located in the broad ligament/mesosalphinx between the ovary and the fallopian tube [3]. If a cyst is pedunculated and located near the fimbria of the fallopian tube, it is referred to as a hydatid cyst of Morgagni, which is usually smaller than 2 cm [4]. These cysts originate from the embryologic remnants of the urogenital system (i.e, the mesonephric and paramesonephric ducts), or from the invagination of the tube's serosa (creating a mesothelial cyst). Hence, are classified into paramesonephric, mesonephric or mesothelial cysts [5].

Paratubal cysts were reported in paediatric and adolescent population (7.3%) in contrast to paraovarian cysts which have been reported in all age groups, beginning from premenarchial period up to menopause [4]. Benign tumours and cysts of mullerian (paramesonephric) or wolffian (mesonephric) duct origin are common. They are generally asymptomatic, usually diagnosed as incidental findings at operation or autopsy studies [6,7]. Although, rarely they can be identified by clinical symptoms resulting from excessive growth, haemorrhage, rupture, or torsion [4]. Paraovarian or paratubal cysts represents 5-20% of all adnexal masses in pathologically verified series [3,6]. The reported incidence of malignancy is about 2-3% in paraovarian cyst and are often misinterpreted as adnexal cysts.

Three possible sites of origin of neoplastic lesion deserve consideration. The most likely site of origin is clearly the pre-existing parovarian cyst, which is frequently seen at all ages [6]. The second site, an endosalpingiotic cyst arising within an accessory or super-numerary ovary, is not supported by the consistent absence of ovarian tissue in the cyst wall. A third possibility, i.e. origin from an endosalpingiotic focus in the parovarium [7,8].

Histopathologically, mesonephric cysts are lined by simple or stratified epithelium and have prominent muscular walls, whereas paramesonephric cysts are lined by columnar epithelium with a mixture of ciliated and non ciliated cells similar to epithelial inclusion cysts [9]. Diagnosing these cysts preoperatively is often difficult, by transabdominal and transvaginal sonography and they cannot reliably be differentiated from other cystic pelvic masses such as ovarian cysts, lymphoceles and peritoneal inclusion cysts [10].

Few features like absence of follicular structures, mobility of the mass and the dissocation of the cyst from the ovary when pushing the probe is a useful sign, called as "Split sign" [3]. Intraoperative finding with the exact location of the these cysts is essential for correct reporting by the pathologist. As pathologist depend on radiological and intraoperative findings to call a cyst as para-adnexal, cause histologically para and adnexal cysts are look alike [11].

Neoplastic lesions of these cysts have also been reported, but malignant paratubal or paraovarian lesions are rarely reported

[3]. Malignancy has been reported in 2-3% of paraovarian cystic masses, but it seems to be even less frequent in masses smaller than 5 cm [9,12]. As there are no large population studies to confirm these percentages. In few instances, paraovarian cystadenomas found to be associated with von Hippel-Lindau disease [9].

As para-adnexal cysts are mistakingly diagnosed as adnexal, there is no correct percentage of incidence of neoplastic lesions, which has led to no clear guideline for the treatment of this tumour; the treatment strategy was decided on the basis of the ovarian tumour guidelines [10].

Hence, a correlation between radiological, intraoperative and pathological diagnosis would be useful in order to understand the incidence, pathogenesis, progression and outcome of these cystic lesions, which would leads to the better planning of treatment strategies. Therefore, the aim was to study the histomorphologic features of all the para-adnexal (paratubal and paraovarian) cystic lesions and to correlate with clinical features.

A very few studies have been taken up on the histomorphologic spectrum of para-adnexal cysts in contrast to the numerous studies done on ovarian and fallopian tube lesions. At present, there are no clear guidelines prescribed for diagnosis and management of lesions/tumours of the para adnexae, hence present study tend to pave the way for further multidisciplinary studies in this field to aid in better management of the cases.

MATERIALS AND METHODS

The present study was a retrospective analysis done on 114 female patients with para-adnexal cystic lesions which were sent to the Department of Pathology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India, from January 2017 to June 2019. Collection and analysis of the cases was done between January to June 2020. Institutional Ethical Committee (IEC) approval was obtained with approval number IEC/42/2018-19. Sample size was calculated using the Yamane formula (calculated as n=106) [13].

Inclusion criteria: Cystectomy and hysterectomy specimens which were radiologically/surgically diagnosed as paratubal or paraovarian cysts and smaller cysts identified on gross examination were included in the study.

Exclusion criteria: All the ovarian cysts and solid tumours were excluded from the study.

Pathologic, clinical and radiological details of patients were reviewed from the records. Standard protocol followed in processing all samples in the institution includes all samples submitted in 10% formalin, were visually inspected for paratubal and parovarian cysts including their location, laterality, number, size, content, solid areas, foci of papillary ingrowths and locularity were recorded. Sampling done from representative areas which were paraffin-embedded, cut into sections, stained with Haematoxylin and Eosin (H&E) dye and their microscopic evaluation conducted.

STATISTICAL ANALYSIS

Statistical analysis for the study was done using Statistical Package for Social Sciences (SPSS version) 24.0 software version International Business Machines (IBM) United States of America (USA). Qualitative data was expressed in terms of percentages. For association between groups chi square test was applied and p-value <0.05 is considered as significant.

RESULTS

A total of 114 cases with para-adnexal cystic lesions were studied. Most cases were presented in the age group of 41-50 years (43.9%) [Table/Fig-1], mean age of 40.14 years with menstrual disturbance as one of the most common presenting complaint [Table/Fig-2]. On gross examination right side lesions were marginally frequent than the left side lesions [Table/Fig-3]. About 28 (24.6%) cases with cyst size more than 5 cms were identified. Statistically significant association was found between age and cyst size [Table/Fig-4]. On cut section of cystic lesions most were unilocular [Table/Fig-5,6] with two multilocular cysts [Table/Fig-7] and four cases with papillary excresences [Table/Fig-8].

Age (years)	N	Percentage (%)
20	3	2.6
20-30	20	17.5
31-40	35	30.7
41-50	50	43.9
>51	6	5.3
Total	114	100

[Table/Fig-1]: Distribution with respect to age.
Mean-40.14 years

Clinical presentation	Number	Percentage (%)
Menstrual disturbances	65	57
Incidental findings	38	33.4
Pain abdomen	7	6.1
Ectopic pregnancy	1	0.9
Others	3	2.6

[Table/Fig-2]: Distribution of clinical presentation.

Laterality	Number	Percentage (%)
Right	58	50.9
Left	56	49.1

[Table/Fig-3]: Laterality.

Age group (years)	Cyst size n (%)	
	≤5 cm	>5 cm
20	0	2 (7.1)
20-30	15 (17.4)	4 (14.3)
31-40	24 (27.9)	7 (25)
41-50	41 (47.7%)	15 (53.6)
>50	6 (7)	-
Total	86 (75.4)	28 (24.6)

[Table/Fig-4]: Relation between cyst size and age group.
p=0.00001 (chi-square test)

Unilocular		Multilocular	
Non neoplastic	Neoplastic	Non neoplastic	Neoplastic
85 (74.5%)	27 (23.7%)	1 (0.9%)	1 (0.9%)

[Table/Fig-5]: Locularity.

[Table/Fig-6]: Shows unilocular right paraovarian cyst measuring 6.5 cms.
[Table/Fig-7]: Shows multilocular left paraovarian cyst measuring 11 cm, exudes mucus material. (Images from left to right)

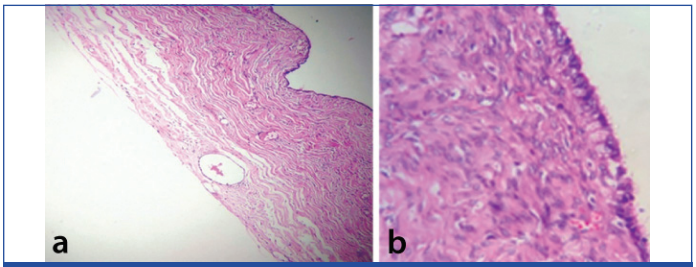
Cyst wall			
Smooth surface		Papillary excrescences	
Non neoplastic	Neoplastic	Non neoplastic	Neoplastic
86 (75.4%)	24 (21.1%)	-	4 (3.5%)

[Table/Fig-8]: Papillary excrescences.

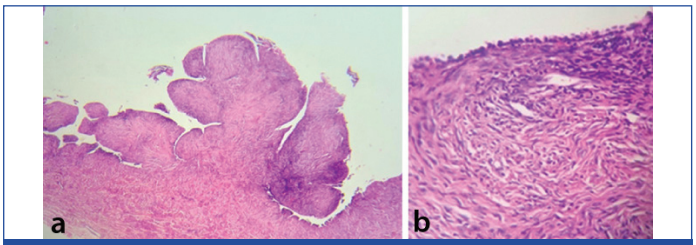
On microscopy, simple serous cyst were frequent 82 (71.9%) [Table/Fig-9] along with 28 (24.6%) neoplastic lesions which included 20 (17.5%) cases of serous cystadenoma [Table/Fig-10], 5 (4.4%) cases of serous cystadenofibroma [Table/Fig-11] and each of papillary serous cystadenoma, benign mucinous cystadenoma [Table/Fig-12] and serous borderline tumour [Table/Fig-13]. Out of 114 cases 76 (66.7%) cases were paratubal and 38 (33.3%) cases were paraovarian cysts. Among 28 neoplastic lesions six were paratubal and 22 were paraovarian cysts [Table/Fig-14]. All neoplastic lesions were more than 5 cms in size [Table/Fig-15].

Microscopic type	N (%)
Simple serous cyst	82 (71.9)
Endometriotic cyst	2 (1.7)
Torsion	1 (0.9)
Serous cystadenoma	20 (17.5)
Serous cystadenofibroma	5 (4.4)
Papillary serous cystadenoma	1 (0.9)
Serous borderline tumour	1 (0.9)
Benign mucinous cystadenoma	1 (0.9)
Broad ligament cyst	1 (0.9)

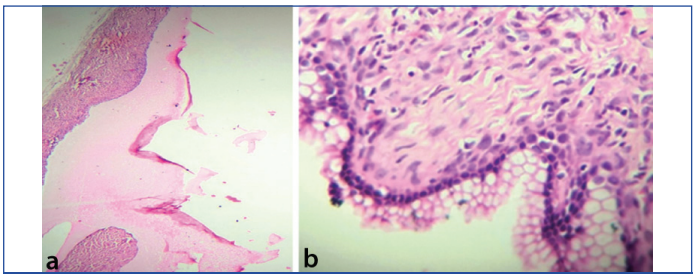
[Table/Fig-9]: Microscopic spectrum of paradanexal cysts.



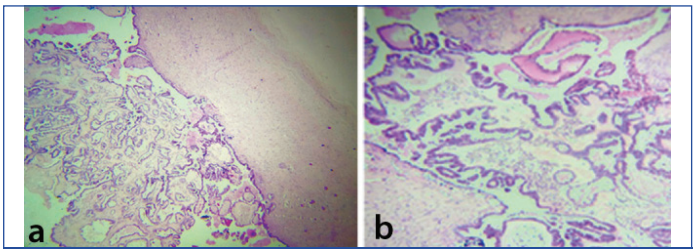
[Table/Fig-10]: Shows cyst wall lined by single uboidal epithelium with fibrous stroma (H&E, a10X, b40X).



[Table/Fig-11]: Showing papillary projections lined by cuboidal epithelium with thick fibrous stroma (H&E, a10X, b40X).



[Table/Fig-12]: Showing mucinous secretions and mucin-producing epithelial cells (H&E, a10X, b40X).



[Table/Fig-13]: Shows papillae lined by stratified cuboidal to columnar cells with minimal cytological atypia (H&E, a10X, b40X).

Locularity	
Paratubal cysts	Paraovarian cysts
6 (21.4%)	22 (78.6%)

[Table/Fig-14]: Distribution of neoplastic lesions in para-adnexal cysts (N=28).

Para-adnexal cyst		≤5 cm	>5 cm
Non neoplastic	Simple cysts	86	0
Neoplastic	Benign	0	27
	Borderline	0	1
	Malignant	0	0

[Table/Fig-15]: Distribution of para-adnexal cysts in comparison with cyst size.

DISCUSSION

Paratubal cysts and paraovarian cysts are cysts located within the mesosalpinx or the broad ligament. They can develop from the mesothelium and also from paramesonephric tissues or mesonephric remnants. As they have similarities as well as differences from the adnexal and other pelvic cysts (embryologically and pathologically), these cysts need a special reference and their lesion needs to be studied to manage them better.

In this study, para-adnexal cysts were seen in perimenopausal age group with mean age of 40.14 years which was also seen in study conducted by Gupta A et al., reported mean age as 35.7±6.9 years and Savelli L et al., reported mean age as 48 years [4,5]. Most common presentation being menstrual abnormalities (57%), whereas study conducted by Pepe F et al., showed pain abdomen (57.62%) and abnormal uterine bleeding (35.59%) as common presentation [14].

In this study laterality of para-adnexal cysts showed near equal distribution of cases on, right (50.9%) and left (49.1%) side, which was also seen in study conducted by Pepe F et al., and Smorgick N et al., [14,15]. On gross examination, 28 (24.56%) cases with >5 cm cyst size were observed which was statistically significant.

On cut section, most of unilocular cysts were non neoplastic 85 (74.56%), neoplastic unilocular cysts were 27 (23.7%) which was comparable to Smorgick N et al., [15]. There were two cases of multilocular cysts, each of non neoplastic and neoplastic, whereas Smorgick N et al., reported two cases of multilocular cyst as neoplastic [15].

Most of the cysts had smooth surface, non neoplastic 86 (75.4%) and neoplastic 28 (24.6%). Papillary excrescence were found in 4 (3.05%) cases, three of the benign and one borderline which was comparable to Savelli L et al., [5]. Whereas Smorgick N et al., found 13 cases with papillary excrescence among which 10 (66.7%) were malignant and 3 (6.8%) were benign [15]. A study conducted by Kiseli M et al., showed 15 cases with papillary projection which were all malignant [Table/Fig-16] [3,5,14].

	Papillary excrescences		
Cut surface	Benign	Borderline	Malignant
Present study	3	1	0
Smorgick N et al., [14]	3	0	10
Kiseli M et al., [3]	0	0	15
Savelli L et al., [5]	13	2	0

[Table/Fig-16]: Comparison of papillary excrescences [3,5,14].

On microscopic examination, wide spectrum of lesions, most common were simple serous cyst 82 (71.9%) along with endometriotic cyst 2 (1.7%) and torsion 1 (0.9%). Also we found 28 (24.56%) neoplastic cases, out of which, 20 (17.5%) were serous cystadenoma, 5 (4.4%) were serous cystadenofibroma, each case of papillary serous cystadenoma 1 (0.9%), benign mucinous cystadenoma 1 (0.9%) and serous borderline tumour 1 (0.9%) case.

A study by Genadry R et al., found eight neoplasms of the 140 paraovarian cysts they studied (5%) [16]. Pepe F et al., found only one case of benign cystadenoma in a series of 59 paraovarian cysts (1.7%) [14]. Stein AL et al., established that the overall incidence of malignancy in paraovarian tumours is 2% Gupta A et al., [4] showed 30% incidence of neoplastic paraovarian cyst, where has Savelli L et al., showed higher prevalence of neoplastic paraovarian cysts 30% [4,5,17]. Present study shows 28 out of 114 cases (24.6%) were neoplastic.

Present study also showed that among the para-adnexal cysts, paratubal cysts (76) had higher incidence than paraovarian cysts (38) but neoplastic lesions were more common in paraovarian 22 (78.6%) than paratubal cysts 6 (21.4%). Although, there are no large population based series, the histopathological analyses of cystic paraovarian lesions revealed 25.4% neoplastic lesions (seven cystadenomas, eight cystadenofibromas) by Savelli L et al., [5]. Few of the case reports studied by Seamon LG et al., Kumbak B et al., Terek MC et al., has shown borderline paratubal cysts [18-20].

Microscopic features of para-adnexal and adnexal cyts are at times indistinguishable, pathologists are sometimes dependent on radiology for the location of the cyst. Radiological studies have demonstrated that paraovarian cysts can be diagnosed by transvaginal sonography. With incorrect reporting of paradanexal lesions mistaken as adnexal lesions will lead to underestimation of prevalence of para-adnexal lesions. It is important to identify and report neoplastic para-adnexal lesions as benign, borderline and malignant neoplasms.

Limitation(s)

- This was a retrospective study, hence only cases where all the details and slides were available, were included in the study.
- In some cases (cystectomy), radiological evidence was taken as conclusive to call it para-adnexal cyst.
- Only cystic lesions were included as the aim was to study the cystic lesions which otherwise are not sampled extensively. Solid lesions were excluded, hence type of malignant lesions and the prevelance of malignancies in these para-adnexal lesions has not been established.
- Studies with more cases and multidisciplinary studies are needed.

CONCLUSION(S)

Paraovarian and paratubal cysts can show a wide range of morphologic changes. One should always be aware of paraovarian or paratubal masses in differential diagnosis of adnexal masses. Possible complications possess a risk for future fertility. Prevelance of neoplasms in these cystic lesions have been under reported in the past. Recent studies, including present study show a higher prevalance rate and presence of papillary projections, cyst size >5 cm has the indicators of malignancy. Hence, more reports of such cases of malignant paratubal/paraovarian pathologies are needed before a treatment modality is established.

REFERENCES

[1] Mobeen S, Apostol R. Ovarian Cyst. [Updated 2022 May 1]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022 Jan-May. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560541/.
[2] Durairaj A, Gandhiraman K. Complications and management of paraovarian cyst: A retrospective analysis. J Obstet Gynaecol India. 2019;69(2):180-84.
[3] Kiseli M, Caglar GS, Cengiz SD, Karadag D, Yılmaz MB. Clinical diagnosis and complications of paratubal cysts: review of the literature and report of uncommon presentations. Arch Gynecol Obstet. 2012;285(6):1563-69.
[4] Gupta A, Gupta P, Manaktala U, Khurana N. Clinical, radiological, and histopathological analysis of paraovarian cysts. Journal of Mid-Life Health. 2016;7(2):78.
[5] Savelli L, Ghi T, De Iaco P, Ceccaroni M, Venturoli S, Cacciatore B. Paraovarian/paratubal cysts: Comparison of transvaginal sonographic and pathological findings to establish diagnostic cr iteria. Ultrasound Obstet Gynecol. 2006;28:330-34.
[6] Janovski NA, Bozzetti LP. Serous papillary cystadenoma arising in a paramesonephric rest of the mesosalpinx. Obstet Gynecol. 1963;22:684.
[7] Janovski NA, Paramanandhan TL. Ovarian Tumors, in the series Major Problems in Obstetrics and Gynecology. Philadelphia, London, Toronto: W. B. Saunders. 1973;4:191.
[8] Honore LH, O'hara KE. Serous papillary neoplasms arising in paramesonephric parovarian cysts: A report of eight cases. Acta Obstetricia et Gynecologica Scandinavica. 1980;59(6):525-28.
[9] Humphrey PA, Dehner LP, Pfeifer JD, editors. The Washington Manual of Surgical Pathology. Lippincott Williams & Wilkins; 2008; 3rd ed;465-67.
[10] Kajiyama A, Edo H, Takeya C, Kubushiro K, Oharaseki T, Gomi T. Spontaneously ruptured paraovarian tumor of borderline malignancy with extremely elevated serum carbohydrate antigen 125 (CA125) levels: A comparison of the imaging and pathological features. The American Journal of Case Reports. 2017;18:919.
[11] Fujii T, Kozuma S, Kikuchi A, Hanada N, Sakamaki K, Yasugi T. Paraovarian cystadenoma: Sonographic features associated with magnetic resonance and histopathologic findings. J Clin Ultrasound. 2004;32:149-53.
[12] Korbin CD, Brown DL, Welch WR. Paraovarian cystadenomas and cystadenofibromas: Sonographic characteristics in 14 cases. Radiology. 1998;208(2):459-62.
[13] Nanjundeswaraswamy TS, Divakar S. Determination of sample size and sampling methods in applied research. Proceedings on Engineering Sciences. 2021;3(1):25-32. Doi: 10.24874/PES03.01.003.
[14] Pepe F, Panella M, Pepe G, Panella P. Paraovarian tumors. Eur J Gynaecol Oncol. 1986;7:159-61.
[15] Smorgick N, Herman A, Schneider D, Halperin R, Pansky M. Paraovarian cysts of neoplastic origin are underreported. J Society Lapaosco Sur. 2009;13(1):22.
[16] Genadry R, Parmley T, Woodruff JD. The origin and clinical behaviour of the paraovarian tumor. Am J Obstet Gynecol. 1977;15:873-80.
[17] Stein AL, Koonings PP, Schlaerth JB, Grimes DA, d'Ablaing G. Relative frequency of malignant paraovarian tumors: Should paraovarian tumors be aspirated? Obstet Gynecol. 1990;75:1029-31.
[18] Seamon LG, Holt CN, Suarez A, Richardson DL, Carlson MJ, O'Malley DM. Paratubal borderline serous tumors. Gynecol Oncol. 2009;113(1):83-85.
[19] Kumbak B, Celik H, Cobanoglu B, Gurates B. Paratubal borderline tumor incidentally found during cesarean section: Case report and review of literature. European Journal of Surgical Oncology (EJSO). 2010;36(8):789-91.
[20] Terek MC, Sahin C, Yeniel AO, Ergenoglu M, Zekioglu O. Paratubal borderline tumor diagnosed in the adolescent period: A case report and review of the literature. J Ped Adol Gyn. 2011; 24(5):115-16.

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