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ORIGINAL ARTICLE

Treatment Dilemma of Simple Cyst in Menopausal Women

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ABSTRACT

Objective: Can we offer conservative treatment for the menopausal women who are having simple cysts?

Study design: It is a prospective cross sectional study carried out in ZHSikder medical college & hospital, Medinova and Popular hospital. The study period was from january 2011 to January 2016.

Materials and methods: 500 menopausal women with simple cysts were enrolled after counseling and taking written consent. Inclusion criteria was cysts size should not be more than 5 cm, they should be unilocular, without having any solid component or any debris. Exclusion criteria was women with family history of cancer of ovary, breast, or colon or women with HRT therapy. Thorough history taking, clinical examination, and some investigation like CA125, TVS with Color Doppler was carried out for all the women. CT Scan.MRI, and PET Scan were reserved for selected cases. All the patients were followed up every 3 monthly for 3 to 5 years. Surgery was done if the patient developed any symptoms, or increment of sizes of cysts or there was any sonographic changes were evident. MRI1 (malignancy risk index) was calculated for each patient. Data were analyzed by SPSS where all calculation rate of less than 0.05 was considered significant.

Results: Among 500 cysts, 285 (57%) cysts resolved spontaneously which is highly significant(p = < 0.05), 165 (33%) cysts needed surgery and only 50(10%) cysts remained without significant changes. Histopathology of surgical specimen revealed all were benign except 4 cysts, i.e., < 1% became malignant or malignant potential.

Conclusion: Menopausal women with simple cysts not more than 5cm,which are unilocular, unilateral, without having any solid component and with normal Doppler study are rarely malignant. So if MRI1 is below 200 we may avoid unnecessary surgery and assure the menopausal women for the conservative treatment with regular follow up.

Keywords: Menopause with simple cyst, Solid cyst, Sonographic findings of cysts, Tumor markers.

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INTRODUCTION

Ovarian cysts in postmenopausal women are now known to be very common, and the maximum are not malignant. The exact prevalence is unknown with the given the limited amount of published data and the lack of established screening programs for ovarian cancer. However, studies have estimated the incidence to be anywhere between 5 and 17%.[1]

McDonald had reviewed an article in Clinical Obstetrics and Gynecology, where he mentioned incidence of the cysts in postmenopausal women is 18%. anIt was also mentioned from Havrilesky et al[2] study that 97% of cysts were revealed as being benign in histopathology. In Bangladesh, we do not have exact data for the incidence, but postmenopausal women with cysts are diagnosed by routine ultrasound (USG) or in a woman who complains of slight discomfort in the lower abdomen for any reason. Ovarian cancer remains the leading cause of death due to gynecological malignancy. Owing to very high mortality and severe morbidities, any postmenopausal woman is in turmoil even with the presence of a simple cyst. Before the era of USG, if pelvic examination revealed palpable ovaries, those ovaries were removed. Now USG is able to detect cysts far before it becomes palpable and most of them are benign. Many women honor the ovaries and not happy to remove it. On the contrary, once cysts are found in postmenopausal women, many of them turn panicky and request for the removal of cysts. So, the gynecologist often has to face the dilemma or challenge of whether to treat such cysts or not; however, many of them perform the surgery. But, the issue is whether surgery for these simple cysts is justified? Or is there any risk of malignancy associated with the conservative treatment?

Hence, our study aim is to see how safe these cysts are and what is the natural history of these simple cysts in menopausal women. We also aim to observe if one

can go for the conservative treatment instead of surgery without putting the women at the risk of a malignancy.

MATERIALS AND METHODS

A total of 500 menopausal women with cysts were enrolled in our study from different hospitals like ZHSWMCH, Popular hospital, and from the Medinova Consultation Center with the ethical permission from the hospital during the period of 2011 January up to 2013 January. All women gave written consent for the study. The study population included menopausal women of 50 to 60 years, who were diagnosed as having cysts; they were followed up for 5 years. Entry criteria for this study are the presence of a simple cyst not more than 5 cm, which was unilateral, unilocular with regular border, and without any solid component.

Exclusion criteria included having any previous history of malignancy or family history of ovarian cancer and using of any hormone therapy. Thorough history was taken, medical history was taken from the woman, with specific attention to risk factors and family history of bowel, breast, and ovarian cancer. Malignancy risk index was also assessed for all the cases. Clinical examination and laboratory investigation were carried out. Primarily transvaginal sonograph (TVS) with Doppler study and CA125 were done. Magnetic resonance imaging (MRI), computed tomography (CT) scan, and positron emission tomography (PET) scan were reserved for the selective cases. Women were reevaluated at 3-month intervals for 5 years. The indication for surgery was based on patients' symptoms, patient desire, and suspicious sonographic changes of the cysts. During follow-up, detailed history clinical examination was done. The TVS and CA125 were estimated. The CA125 is a well-established screening tumor marker, being raised in over 80% of epithelial ovarian cancer cases, but not in most primary mucinous ovarian cancers. If a cutoff of 30 iu/mL is used, the test has a sensitivity of 81% and specificity of 75%. Other tumor markers were not done routinely. There is currently not enough evidence to support the routine clinical use of other tumor markers, such as human epididymis protein 4 (HE4), carcinoembryonic antigen (CEA), CDX2, cancer antigen 72-4 (CA72-4), cancer antigen 19-9 (CA19-9), alfafetoprotein, and lactate dehydrogenase for the simple cysts. There are some preliminary data suggesting that HE4 is more sensitive and specific than serum CA125 for the diagnosis of ovarian cancer. A retrospective report (67 invasive and 166 benign masses) found HE4 to have a higher sensitivity (73%) compared with CA125 (43.3%) for 95% specificity in distinguishing between benign and malignant ovarian masses, and addition of HE4 to CA125 further improved sensitivity to 76%. But, all our patients had MRI bellow 200, so we did not do these markers.

Calculation of the risk management index (RMI) 1

The RMI 1 combines three features. It is a product of the serum CA125 level (iu/mL); menopausal status (M); and an ultrasound score (U) as follows:

RMI = M multiply by U and CA125.

The ultrasound result is scored 1 point for each of the following characteristics: Multilocular cysts,solid areas, metastases, ascites, and bilateral lesions. U = 0 (for an ultrasound score of 0), U = 1 (for an ultrasound score of 1), U = 3 (for an ultrasound score of 2–5).

The menopausal status is scored as 1 = premenopausal and 3 = postmenopausal. This guideline is directed at postmenopausal women and, therefore, all will be allocated the same score of 3 for menopausal status.

Serum CA125 is measured in iu/mL and can vary between 0 and hundreds or even thousands of units.

Our study was prospective and cross-sectional. The analysis was performed using Statistical Package for the Social Sciences, data were presented as frequencies, means, ranges, and in percentages. For all calculations, a p-value of < 0.05 was considered as statistically significant.

RESULTS

A total 500 postmenopausal women with cysts were analyzed. During our study period, 285 (57%) cysts resolved spontaneously, 165 (33%) cysts needed surgery and 50 (10%) cysts remained without any significant changes (Table 1 and Graph 1). The cysts size of our study were not >5 cm (range 3.8–5 cm), and SD was 5.40. The value of RMI1 were >200 (range 60–99), and SD was 9.74 (Table 2). Among 500 cysts, 185 cysts disappeared in 1st year, 85 in 2nd year and 15 in 3rd year (Table 3). The causes of the surgery includes patient's request, then due to complains of the patient and lastly due to sonographic changes of the cysts (Table 4). Most surgeries (70) were

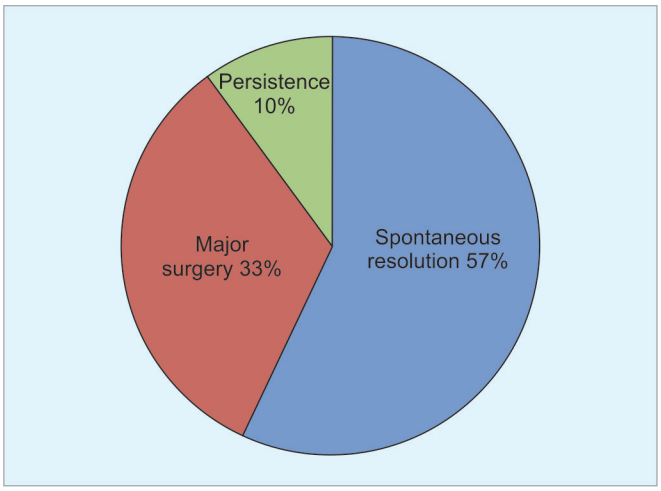
Table 1: Natural fates of cysts

Fate	*Number*	*%*	*p-value*
Spontaneous resolution	285	57	<0.05
Surgery needed for different causes	165	33	NS
Persistent, without significant changes	50	10	NS

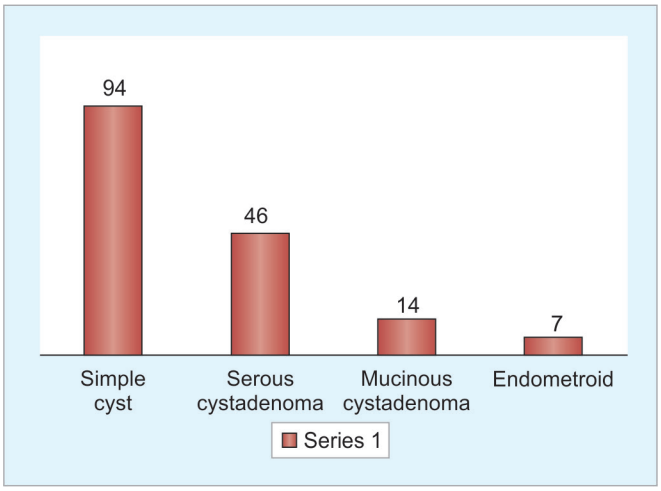
NS: Not significant

Table 2: Size of cysts and risk management index 1

		Range	*Mean*	*Standard deviation*
Cyst size	Not >5 cm	3.8–5.0 cm	4.66	5.40
RMI1	Not >200	60–99	85.66	9.74



Graph 1: Fate of cysts



Graph 2: Histopathology of benign cyst

Table 3: Natural course of cysts during the time period of the studies

	Total	*1st year*	*2nd year*	*3rd year*
Spontaneous resolution	285	185	85	15
Surgery needed	165	70	60	35
Persistent without clinical significant	50	35 reduced	size 12 slightly reduced	Same size 8 not reduced

Table 4: Causes of surgery

Surgery done	*No. of patients (n = 165)*	*For patient complaints*	*Due to USG changes*	*For patient request*
1st year	70	24	13	33
2nd year	60	15	10	35
3rd year	35	10	5	20

Table 5: Histopathology of malignant cysts

Types of malignancies	*Number of cases*
Serous cystadenocarcinoma	1
Borderline serous cystadenoma	2
Granulosa cell tumor	1

Table 6: Significant sonographic changes of cysts

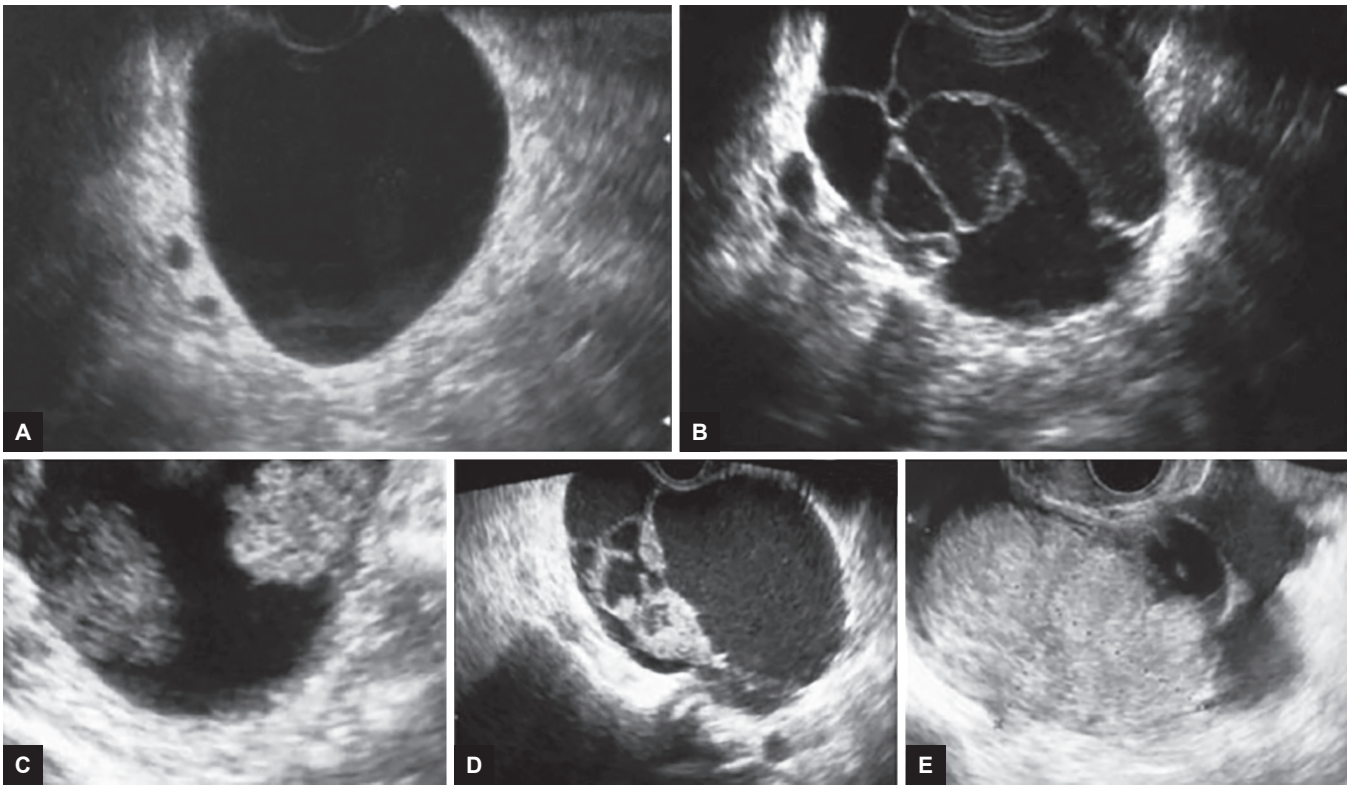
No. of cysts	*Sonographic changes*
16	Increased in sizes
9	Multilocular
3	Debris seen

done in 1st year, 50 were done in 2nd year, and 35 were done in last year (Table 4). Histopathology report of operated cysts showed that 161 were benign and 4 were malignant or malignant potential. Among malignant cysts, only one was frank cystadenocarcinoma, 2 were borderline serous cystadenoma and 1 was granulosa cell tumor (Table 5). Regarding benign tumors, 94 were simple cysts, 45 were serous cystadenoma, 14 were mucinous cystadenoma and 7 were endometrioid cystadenoma (Graph 2). During the study, 28 cysts had sonographic changes, 16 cysts increased in sizes, 9 cysts became multilocular and debris appeared in 3 cysts (Table 6).

DISCUSSION

Our study showed that almost all the cysts became benign only, while 4 out of the 500 postmenopausal cysts turned out to be malignant or malignant potential.

Numerous studies have looked at malignancy in ovarian cysts, comparing USG morphology with either histology at subsequent surgery or by close followup of those women managed conservatively. We also followed the same ways. The tool of investigations we used were TVS with Doppler study and serum C125 with cutoff point of 30 u/mL for all women. The test has a sensitivity of 81% and specificity of 75%.[3] Efficacy of USG is well established, achieving sensitivity of 89% and specificity of 73%.[4] The TVS is a very effective method of imaging (a recommendation). The CT scan, MRI, or PET should be reserved only for suspicious cases. The role of these imaging techniques in the diagnosis of ovarian cancer is yet to be established. One study indicates that MRI may be superior to CT scan and USG scan in diagnosing ovarian mass, but there is no difference in its " ability to distinguish between benign and malignant diseases".[5] Another study found that TVS has greater sensitivity than CT or MRI in this regard.[6] The CT scan is the choice of option in suspicious cases. But in our low-resource country, we should be more careful about the choice of imaging modalities, and TVS could be applied for routine cases. However, there are no currently available tests that are perfect, offering 100% specificity and sensitivity. We did Doppler study of the cysts for all the cases. The use of three-dimensional power Doppler may contribute to



Figs 1A to E: Malignancy of cysts: (A) Unilocular cyst; (B) multilocular cyst; (C) unilocular solid cyst; (D) multilocular solid tumor; and (E) solid tumor

the differentiation between benign and malignant masses because it improves detection of central blood vessels in papillary projections or solid areas.

In our study, we tried to show clearly that chance of malignancy of cysts (Fig. 1) that are not more than 5 cm, unilateral, unilocular, and without solid parts is very low, i.e., <1%. Similar studies by Roman et al,[7] Kurtz et al,[5] Tingulstad et al,[8,9] and Junor et al[10] showed that chances of malignancy in such cysts are very low, about <1%.

As the chance of malignancy is very minimal, it is reasonable to manage these cysts conservatively and it is not justified to do surgery for all postmenopausal women with simple cysts. The issue of duration of follow-up of persistent cysts has not yet been recommended. Most studies were done for 1 year; we followed the subjects of our study for about 5 years, which is the longest among all the studies. Also, we followed these cysts at intervals of 3 months, and found that 57% of them disappeared spontaneously. A large study by Levine et al[11] also had shown that more that 50% of these cysts resolved spontaneously within 3 months. Though the Royal College recommended and many studies had follow-up program at 4-month interval, we wanted to be more vigilant and did follow-up at 3-month interval. But patients of our studies were happy to attend every 3 months and, interestingly, there is no drop out of subjects from the study. Conway et al[12] meta-analyzed 76 articles and cited that no malignant condition was identified from those studies where the cysts were followed up, so simple cysts are common in postmenopausal women than previously thought and this can be managed conservatively.[13]

Our study showed 57% cysts had spontaneous resolution, 10% persisted without any significant changes, and 33% underwent surgery. Very recently, Royal College of Obstetricians and Gynaecologists (RCOG, July 2016) guidelines has almost similar study, which was a 2-year follow-up study of asymptomatic postmenopausal women with simple cysts smaller than 5 cm. These cysts were shown to disappear (53%), remain static (28%), enlarge (11%), decrease (3%), or fluctuate in size (6%). Evidence from larger screening studies found a higher rate of resolution of unilocular cysts at 70%, with only complex cysts having an increased risk of malignancy. Adnexal cysts 5 cm or smaller in postmenopausal women are rarely malignant.

In our study, we had 165 cases who needed surgery. About 28 cysts showed changes in sonography which was suspicious, 88 women did not like to be observed anymore and opted for surgery. Totally, 49 women developed pain and increased pressure in lower abdomen. Most of the women underwent hysterectomy either laparoscopically or by laparotomy. All the cysts revealed benign for which women requested surgery. We did not adopt aspiration procedure before the surgery as cytological examination of cyst fluid is poor in determining malignancy.[14,15] In addition, there is risk of cyst rupture

if the cyst is malignant. There is some evidence that cyst rupture during surgery has an unfavorable impact on disease-free survival,[16] so aspiration has no role in the management of asymptomatic ovarian cysts in postmenopausal women (RCOG 2016). Evidence level 4 recommended that laparoscopic management of ovarian cysts in postmenopausal women is suitable for conservative management, as during oophorectomy, with removal of the intact cyst in a bag may prevent cyst rupture into peritoneal cavity. But, women who are at risk of malignancy, as calculated using RMI>200 need a laparotomy and full staging procedure must be done. A suitable experienced surgeon should operate on these cases. In our study, all the women who went for surgery opted for total abdominal hysterectomy and bilateral salpingo oophorectomy after informed consent. In suspicious cases, the surgeries were done by the whole team dedicated for oncosurgery and only 4 out of 500 cysts of postmenopausal women became malignant or had malignant potential. Therefore, our study showed clearly that simple cysts of menopause women are almost benign. This finding is supported by the study of 7,700 postmenopause women with cysts where the final message was that simple small cysts may have conservative management.[17] Also, Holtz[18] reported simple cysts < 5 cm can be treated conservatively with appropriate follow-up. So, from now on, we may move forward with conservative management for cysts of menopause women and say along with Oyelese et al[19] who cited from 36 articles and commented that traditional "oophrectomy may be replaced by conservative approach" in the management of postmenopausal women with simple cysts. Recently, the RCOG established a clear protocol for the management of postmenopausal women with cysts. The RCOG Green-Top Guideline No. 34 (July 2016) emphasized TVS as routine imaging modalities and CT[20] scan was done if RMI1 was > 200. Similarly, the guideline recommended TVS for routine use.

There are many methods of malignant risk assessment. The LR2 is emerging as a risk assessment tool, but routine use is not recommended.[21,22] OVA1 is a quantitative assay measuring the protein for risk assessment, which has high sensitivity, but has lower specificity and positive predictive value than RMI1.[23] So, we used RMI1 for our all patients as a systemic review[24] showed that this method was most effective. The pooled sensitivity and specificity were 78% [95% confidence interval (CI) 71–85%] and 87% (95% CI 83–91%) respectively for RMI1 cutoff of 200 (evidence level 1++).

The findings of our study are supported by the most recent guidelines of RCOG (July 7, 2016).[25] The RCOG recommended that a symptomatic, simple, unilateral, unilocular ovarian cysts, less than 5 cm in diameter has a low risk of malignancy. In the presence of normal serum CA125 levels, these cysts can be managed conservatively, with a repeat evaluation in 4 to 6 months. It is reasonable to discharge these women from follow-up after 1 year if the cyst remains unchanged or reduces in size, with normal CA125, taking into consideration a woman's wishes and surgical fitness.

CONCLUSION

Menopausal women with simple cysts, which are unilateral, unilocular, with size of 5 cm or less, without any solid component can be managed conservatively. The natural course of these cysts was mostly benign. The RMI1 needs to be assessed in all cases. If RMI1 is below 200, we may avoid unnecessary surgery and can assure the women with optimum counseling. Also, we believe that this study might contribute to a better understanding of the management of postmenopausal women with simple cysts, and may improve the quality of care of our menopausal women.

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