# The Demographic Characteristics of Patients with Benign Ovarian Cyst and Histological Pattern in a Tertiary Center in Riyadh, Saudi Arabia

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## ABSTRACT

**Background:** Benign ovarian tumours are a very common clinically encountered condition and rarely become malignant. The outcome is generally good, varying from asymptomatic big cysts to symptomatic ones with different sizes.

**Objective:** To know the demography of patients, the types of cyst, presentation and management options. Thereafter, comparison of data with other national and international studies was done.

**Results:** This retrospective cohort study was carried out in Security Forces Hospital, Riyadh in Saudi Arabia between January 1st, 2015 to January 31st, 2018. There were 67 cases of histologically diagnosed benign ovarian neoplasms in that period. The age range of 20-49 made up 72.1% of cases and a mean of 37 years, with a BMI of 20-36.9 Kg/m². 67.2% of cases were electively admitted and 88% of cases had ovarian cyst more than 5cm in size. The affected side was almost similar being 35.8% on right side and 32.8% on the left, 28.3% were bilateral and 2.99% were paraovarian cysts. 31.3% of patients were single and 10.4% multiparous. A parity of up to 6 constituted 41.8% of cases, 58.2% were managed by laparotomy and 41.8% had laparoscopic approach. 56.7% of cases were of epithelial origin, 17.9% functional cyst and 16.4% were Germ cell tumours. Sex cord variety were seen in 5.96% of cases and a combination of epithelial and stromal components made up 2.98% of cases. During the 2-D ultrasound studies done for all patients, 10.4% did not have concomitant Doppler studies done. Of those that had doppler, 8.9% were abnormal. Blood group O positive was seen in 52.2% of cases and 23.9% were 'A' rhesus positive and 11.94% were 'B' rhesus positive. 4.48% of cases were pregnant at the time of diagnosis. 13.4% had recurrence of cyst, abdominal pain was the main presentation in 59.7% of cases, palpable mass in 4.48%, 22.4% had previous Cesarean Section.

**Conclusion:** To determine the incidence of histologically diagnosed types of benign ovarian neoplasm in a Tertiary hospital in Central part of Saudi Arabia and compare it with other regional areas, in same country, neighboring countries and international figures. Suggestions on certain aspects that were made includes improvements, and that could possibly be a future recommendation, on diagnosis and prognosis of ovarian neoplasm, such as different combinations of tumour markers (CA125 + HE4), surgical management, recurrence rate and blood groups.

**Abbreviations**
CT: Computed Tomography; MRI: Magnetic Resonance Imaging; PT/APTT: Prothrombin time/ Partial thromboplastin time; HE4: Human epididymis protein 4.

## Introduction

Benign Ovarian Tumours are very common forming 80% of all ovarian neoplasms with the commonest occurrence being in the age group of 20-40 years. The rare percentage of conversion to malignancy is more commonly encountered in the elderly age of 40-65 years.

The wide range of presentation varies from asymptomatic with accidental discovery, to slight menstrual abnormalities. Pain as a presenting symptom maybe in the form of minimal abdominal discomfort, due to peritoneal irritation, resulting from leaking in a hemorrhagic corpus luteum to the severe disabling variant due to ovarian torsion.

To achieve a diagnosis, a combination of the clinical symptoms, physical exam, Doppler ultrasound and serum tumour markers is required.

The significance of a definitive action, once an ovarian neoplasm is diagnosed, is to rule out malignancy & conserve the ovaries for fertility purposes and that would have been jeopardized by the increasing pressure of the expanding cystic neoplasm. Furthermore, the early diagnosis negates the masquerading vague symptoms that would have led to diagnosis in an advanced stage.

## Materials and Methods
### Patient population

Security Forces Hospital (SFH), is a Tertiary Center and is one of the major hospitals in Riyadh in Saudi Arabia that provides healthcare services to the Ministry of Interior personnel and their families. The hospital has a busy department of Obstetrics and Gynecology that deal with all concerned referral cases.

### Data Collection

Ethical committee approval was obtained for this study conducted in the period from January 1st, 2015 to January 31st, 2018, where only Benign Ovarian Tumours, as per histopathology findings, were included. Data collection was done from Medical Record viewer data base of the hospital. The following data were recorded:

- Demographic and clinical characteristics including maternal age, parity and marital status, Body Mass Index in Kg/m² (calculated as per height and weight of patients).
- The type of presentation, being elective or emergency, as well as clinical presentation was also scrutinized and ranged from the patients that were asymptomatic, to those with varying grades of abdominal pain and even collapse. It also included those with amenorrhea, abnormal per vaginal bleeding, gastrointestinal symptoms like nausea, vomiting and constipation.
- Also, any associated infertility was studied.
- The type of treatment, including types of surgery and route of approach whether laparoscopic or via laparotomy and percentage of conversion from one method to the other.
- Tools of diagnosis used included transabdominal/transvaginal ultrasound with Doppler studies. Other methods used like CT scan and MRI were also noted.

- The blood groups of the patient, in addition to the histopathology of Benign ovarian tumours was conformed under 5 major groups namely: Functional cysts, Germ cell, Epithelial, Sex cord stromal and Epithelial + Stromal tumours.
- Concomitant medical and surgical disorders like thyroid, renal, cardiovascular, bone, gastrointestinal as well as central nervous system diseases were studied.
- Tumour markers requested were recorded and were mainly: CA125, CA15-3, CA19-9, LDH (Lactate Dehydrogenase), CEA (Carcino Embryonic Antigen), AFP (Alphafetoprotein) and Bhcg for some patients. Other lab tests done included Complete blood count (CBC), PT/PTT, renal function tests and liver function tests.
- Pregnant cases with Benign Ovarian tumours were also studied, as well as outcome.
- The number of patients who had recurrent Benign ovarian cyst were analyzed.
- The percentage of patients who had cysts less and over 5cm in size were noted.
- The number and histopathology of patient with abnormal tumour marks were also reviewed.

## Data Analysis

Microsoft excel 2017 was used to analyze the collected data.

## Results

During the period of study from January 1st, 2015 to January 31st, 2018, there were 79 cases of diagnosed ovarian neoplasms.

The hospital data of all cases studied were available in the hospital records as per Medical Record viewer. All needed information were obtained.

After studying the histopathology reports of all patients, 12 cases were excluded because of the discovery of malignant changes in 10 cases and borderline changes in the other two.

The ages of the patients in the study ranged from 10 to 60 years and over. Table I shows the age and parity of these cases, where the highest incidence occurred in the age range of 20-49 years (making up to 73.1% of cases). The lesser frequency of occurrence was in the extremes of age of 10-19 year (11.9%) and 14.8% in 50 years and more.

The benign tumour in patients of parity of 1-3 made up to 58.2% of cases and decreasing to reach 36% in patient with 4 or more deliveries. The least occurrence is seen in nulliparous patients (6%).

Table 2 shows the histopathologic types of Benign Ovarian neoplasm, where as seen, the majority were Epithelial tumour (56.7%), followed by functional cyst and Germ cell tumour making 17.9% and 16.4% respectively. The less encountered types were Sex Cord Stromal (6%) and combined Epithelial and Stromal cells (3%).

**Table 1:** Shows the age and parity of patients with Benign Ovarian Tumour. (n=67).

| Age in years | Number | Percentage (%) |
|---|---|---|
| 10-19 | 8 | 11.9 |
| 20-29 | 24 | 35.8 |
| 30-39 | 12 | 17.9 |
| 40-49 | 13 | 19.4 |
| 50-59 | 8 | 11.9 |
| > 60 | 2 | 2.98 |
| **Parity** | | |
| P0 | 4 | 5.97 |
| 1-3 | 39 | 58.2 |
| 4-6 | 17 | 25.4 |
| 7-9 | 4 | 5.97 |
| >10 | 3 | 4.47 |

**Table 2:** Shows the histologic types of Benign Ovarian Neoplasm. (n=67).

| No | Major Histopathological Types of Ovarian tumour | Components – types under the Major category | | | Total no. | Percentage (%) |
|---|---|---|---|---|---|---|
| 1 | Functional Ovarian cyst | Corpus Luteum | | | 12 | 17.9 |
| 2 | Germ cell Tumour | Dermoid cyst | | | 11 | 16.4 |
| 3 | Epithelial Tumour | Serous Cystadenoma (n=16) | Endometriod (n=12) | Mucinous Cystadenoma (n=10) | 38 | 56.7 |
| 4 | Sex Cord Stromal | Fibroma (n=2) | Fibrothecoma (n=2) | | 4 | 5.97 |
| 5 | Both Epithelial + Stromal | Adenofibroma (n=1) | Cystadenofibroma (n=1) | | 2 | 2.98 |

**Table 3:** Shows the histopathologic types of Benign Ovarian Tumour with raised tumour level of markers (n=17).

| No. | Histopathologic type | Tumour marker raised | | |
|---|---|---|---|---|
| | | Ca125 | C19-9 | AFP |
| 1 | Endometrioma | 3 | - | - |
| 2 | Mucinous Cystadenoma | 2 | 1 | 2 |
| 3 | Teratoma | 1 | 3 | - |
| 4 | Serous Cystadenoma | 2 | - | - |
| 5 | Thecoma | - | 1 | - |
| 6 | Simple cyst | 2 | - | - |

The cornerstone of diagnosis, beside the clinical presentation was by 2D Ultrasound including transabdominal and transvaginal views, accompanied by Doppler studies. In addition, blood test for tumour markers were conducted.

For seven out of 67, Doppler studies were not available. The remaining 60 cases revealed 5 (7.4%) abnormal Doppler studies described as "Absent flow", out of these, 3 were found to have ovarian torsion. Generally, out of the total number of cases at time of surgery, 9 had torsion of an ovary (13%) and six of which had uneventful doppler studies.

Additional radiological studies done for ambiguous cases were in the form of CT scan for 15 cases (22.4%) and MRI studies for 6 patients (8.9%). A combination of both CT and MRI were ordered for one patient.

45 patients (67%) were electively admitted and the remaining were as per emergency basis. The side of occurrence of ovarian tumour was almost similar, being 35.8% on the right side and 32.8% on the left side. Bilaterality was evident in 28.3% of cases. Paraovarian cysts were seen in 2 cases (3%). The type of tumour markers ordered were negative for 40 patients and raised in 17 and not done for 10 cases. These markers were: CA125, CA15-3, CA19-9, Lactate dehydrogenase (LDH), Carcinoembryonic antigen (CEA), Alphafetoprotein (AFP), and sometimes Human chorionic gonadotrophin (HCG). However, for the 10 patients with absent tumour markers, there were 6 cases of ovarian torsion, three cases of leaking hemorrhagic cysts, and a case of recurrent ovarian cyst in a distressed patient.

Table 3 shows the histopathologic types of ovarian tumour that had abnormally raised levels mainly with 3 markers as seen. This was in 25% of cases (n=17).

The surgical approaches done for the patient were in the form of Laparotomy done for (40 patients) 60% and Laparoscopy in 40% of cases. Cystectomy was done for (31 patients) 46%, Oophorectomy for 45%, hysterectomy for 7.4% (n=5) and Deroofing for one case with endometriotic cyst (1.5%).

There were 4 cases of pregnancy with ovarian tumours and was removed via Laparotomy. Long term outcome was very good at term for 3 cases. The 4th case had poor outcome with neurological deficit and was premature delivery.

Four cases were converted from Laparoscopic approach to Laparotomy, hence, made a rate of 6% in our study.

The recurrence rate in the studied cases was (13.4%) in 9 patients, where the repeat pathology was in the form of Serous cystadenoma in 3 cases, Mucinous Cystadenoma in 2, one with granulosa cell tumour, one endometrioma, a luteal cyst and a teratoma.

The size of ovarian cysts that were less than 5cm was seen in 8 cases (12%) and the remaining were bigger or equal to 5cm making up to 88% of cases. Two cases were described as complex cysts by ultrasound (3%) but the outcome was uneventful.

Study of the blood groups of patients revealed that 52% were 'O' rhesus positive, 4.5% 'O' rhesus negative, 4.5% 'AB' positive, 12% as 'B' positive, 1.46% 'B' negative, 24% 'A' Rh positive, and 'A' negative in 1.5% cases.

### The Clinical presentation
The clinical presentation ranged widely from asymptomatic cases (11.9%) to the more frequent complaint of abdominal pain (60%) with variable sites on the abdomen. Dysmenorrhea alone was seen in 3% of cases. Associated nausea and vomiting also occurred in 7.5% of cases. Palpable abdominal masses were evident in 4.5%, and constipation in 1.5% of cases. Correlation with Infertility was seen in 7.5% of cases.

### Associated medical and surgical disorder
The existing medical and surgical condition were namely hypothyroidism (4.5%), renal disorder in 7.5% (Urinary tract infection, stone, Cystocele and urinary incontinence in 5 patients), cerebrovascular disorders made up to 6% of cases (high blood pressure and dyslipidemia), Asthma and Allergy to food and drugs was evident in 4.6% cases, Bone disorders were seen in another set of patient (4.6%), Polycystic ovary syndrome was associated with 6% of cases. Further, 18% had gastrointestinal disorders in form of hepatitis, irritable bowel, and history of gastric sleeve, cholecystectomy, and appendectomy. 4.5% has skin problems (erythema, telangiectasia and Psoriasis). There was one epileptic patient (1.5%). The most frequent surgical procedure encountered was Cesarean Section (22% of cases).

### Discussion
This retrospective study was done in a Tertiary Hospital in The Central region of Saudi Arabia. The average age in our population was 37 years which was within the wide age range of 20-51 year of Alzahrani et al. [2] in the South & Abdulla et al. [1] in the Western parts of Saudi Arabia. This average age was between the younger population of 33 years in Qatar [8] & much older females of 39 years in Bangladesh [18] & Farooq's 41 years old women in Pakistan [3].

The clinical presentation in our series was mainly in the form of abdominal pain seen in 60% of cases and palpable masses in 4.48%. This was unlike the high consecutive figures of 65.6% and 84.4% in Khanam el at study [18]. However, in that latter study, in 23% of cases there were malignant changes, while we had none in our study, as per histopathological diagnosis. Abnormal Vaginal bleeding was seen in 12% of our cases unlike Jamal et al. [11] where it was the main presentation in all the studied cases. The cornerstone of diagnosis in our study was the complementary use of combined transabdominal with transvaginal ultrasound with set guidelines for features of benign ovarian cyst. The role of transabdominal ultrasound, which should not be used alone as the exclusive study, was for the assistance in scanning of large ovarian cysts, when the field of view was beyond the dimensions of the studied pathology.

For 10% of our patients no data on spectral or pulse Doppler Ultrasound studies was available. 40% of these cases presented on emergency basis and found to have ovarian torsion at time of surgery. RCOG guidelines clearly indicated that Doppler Ultrasound of benign ovarian tumours does not seem to provide significant improvement in diagnostic accuracy [12].

There were wide variations in the incidences of histopathological types being different in the same country, region and continents. In our study the incidence of Benign ovarian neoplasm was 85% in comparison to 77% of Patrick et al. [16] in the Africa and Khanam et al. in Bangladesh [18] in Asia.

Within Saudi Arabia the incidence of Germ cell tumours in our study was 16.4%, much lesser than 37.5% in Alzahrani et al. [2] study in the Southern part of the country and the 28% of Abdullah et al. [1] in Jeddah in the Western part of Saudi Arabia. However, in that latter area another study revealed low incidence of 12.3% [17] within the region. The incidence was 17.3% in Qatar, a neighboring country [8], and almost similar to 18% in Peshawar [10] but less than 25% in Bangladesh [18] in Asia. In Africa, Patrick et al. [16] in Nigeria and Akakpo et al. [5] in Ghana, presented an outstanding respective incidence of 67.2% and 41.9% of that type of neoplasm which is much more than European and North American figures [8].

The incidence of Epithelial cell tumours in our study was 57%, almost similar to 61% in the Western part of Saudi Arabia. Both figures are more than 40.4% of neighboring country Qatar [8]. In Africa the incidence of 25.8% was observed in Nigeria [16] and 41.9% in Ghana [5]. However, the incidence was much higher in Asia being 70.8% in Bangladesh and 72% in Peshawar [10].

For Serous cystadenoma the incidence was 24% in our studied population, almost similar to Yasmin et al. [10] in Peshawar region in Asia. Within Saudi Arabia it was much less than 33% in the southern part [2] & 45% on the Western part. The incidence in Qatar [8] was 9.6%. In Bangladesh the incidence was 35.5% [10]. The highest incidence was 69% in Nigeria in Africa [16].

In our study, mucinous cystadenoma made up to 15% of the cases. This is almost comparable to 20% [1] in Southern Saudi Arabia and 21.8% of Khanam et al. [18] in Bangladesh. These figures were much more than 10% in India [13] & 8.5% [5] in Africa.

For Sex cord tumour the exceptionally high figures of 48% [13] and 43% [3] seen consecutively in India and Ghana in Africa was much more than our incidence of 6% and 4.2% in Bangladesh [18] and 7% in Nigeria [16].

The incidence of bilaterality of 28.3% for ovarian tumour was more than 13% in Qatar [8] & 20.8% in Bangladesh [18].

Several tumour markers were requested in our study, with 66% of patients being below 40 years of age & with variable ultrasound findings. However, even with normal values of tumour markers still cancer cannot be excluded. Additionally, tumour markers like CA125 could falsely be raised in non-malignant conditions, like endometriosis & accidental ovarian torsion, among other causes. In that respect the RCOG guidelines [12] pointed out that tumour markers are less sensitive, has wide variation in specificity, whether isolated or in combination & is not advised as a routine in the initial setting of diagnosis. Its usefulness is for prognostic rather that diagnostic purposes.

A tumour marker, human epididymis protein 4 (HE4), has fewer false positive results than CA125 & can possibly be used in the future instead of it for diagnostic purposes in postmenopausal women. With almost 15% of our studied patient being ≥ 50 years of age, this is an interesting aspect worth studying, with calculation of cost effectiveness in comparison to the ongoing policy. This fact was confirmed by a study [19] that revealed a sensitivity of 92.3% & specificity of 75%.

The abnormal values of raised CA125 in our study ranged from 39-280 IU/ml. Luckily, no malignant changes were seen. The probability of occurrence of malignancy is to be anticipated with higher values than those mentioned in our study. This fact is an agreement with Nazneem et al. [15] & who in addition experienced a higher incidence of epithelial rather than non-epithelial malignant changes in the tumours.

Almost 48% of our patients were non 'O' blood group. Yuzhalin et al. [13] noted that such a category of patients, regardless of the Rhesus factor, had an increased risk of up to 40-60% in developing ovarian cancer than other blood group. Further Razzagbi et al. [26] noted that there was an increased risk of developing ovarian cancer in blood group A and AB, but with limited knowledge of outcome on overall survival. This information can provide an area for research for indices of risk factors.

13% of our study population had recurrence of benign ovarian tumours. This is more than 10% rate recorded by Detho et al. [24] but with patients in childhood. The clear lesson learnt from the latter was the institution of ultrasound, follow-up for the first three year & this fact can be adopted & applied to our population. Ben-Ami et al. [25] reported 7% recurrence of benign ovarian tumours, more in postcystectomy than adnexectomy. Recurrance was more with mucinous cystadenomas rather than other types. This might have been the case with 20% of our patients with recurrences & who had mucinous cystadenoma. This provides another area of research and policy revision.

The surgical management in our setting involved a 6% conversion rate from Laparoscopic route to Laparotomy. This percentage was less than 11.5% [20] due to technical difficulties and possible diagnosis of malignancy. Mehasseb et al. [21] had an 11-36% conversion rate in obese and 5-6% in non-obese patients. Among the reasons of conversion in our study was the encountering of tenacious adhesions in some patients as well as suspicion of malignancy in others. However, 7% of cases in our study were due to presurgical suspicion of Dermoid cyst for which Laparotomy was decided, because of fear from risk of spillage & resultant granulomatous chemical peritonitis, in spite of saline wash. Menelli et al. [6] experience in that aspect, revealed that there was no justification for Laparotomy in such cases & that by the use of endoscopic bags during surgery & thorough intrapelvic lavage no long term complications have been experienced.

## Conclusion

The wide variation in the percentage occurrence of different histopathological types in the same country, different regions and continents, provides a fertile field for future Epidemiological studies directed towards possible related aetiologies. Need to evaluate via research, the cost effectiveness, sensitivity and specificity of using multiple tumour markers, and comparison & possible future replacement by the suggested combination of CA125 + HE4 (human epididymis protein 4), particularly in postmenopausal women. The same also applies for blood group studies and correlation to malignancy. Surveillance of recurrent cases of benign ovarian neoplasms with correlation to histopathological types with a view of adoption of a revised approach in management.

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