

# Evaluation of Ovarian Tumours using International Ovarian Tumour Analysis (IOTA) Simple Ultrasound Rules and its Correlation with Histopathological Examination

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**Abstract:** *The study aimed to evaluate the diagnostic accuracy of IOTA simple ultrasound rules for the differentiation of ovarian tumors. A total of 100 patients suspected of ovarian pathology either by pelvic examination or by the previous ultrasonographic report were included in the study. The patients were assessed using IOTA simple rules at the time of the first visit by a resident physician in the department of OBGY followed by an expert sonologist in the radiology department by transabdominal sonography. Patients were assessed by histopathological investigations. The mean age of the patients was 35.55±13.9 years. According to IOTA simple rules 20 were malignant, 58 were benign and 22 ovarian masses were inconclusive. A total of n=67 patients had surgery of which 19 were malignant, 26 were benign and 22 were indeterminate. Kappa statistics showed a high level of agreement between expert (Sonologist) and non - expert (Resident of Obstetrics and Gynaecology) in diagnosing benign tumour (k = 1, 100%) and malignant tumour (k = 0.968, 96.8%) with P value less than 0.05. The sensitivity and specificity of the IOTA simple rules in predicting malignant ovarian mass were 93.33% and 83.33% respectively. Positive predicting value (PPV) and Negative predictive value (NPV) were 73.68% & 96.15 % respectively. After considering indeterminate mass as malignant mass and all followed - up cases as benign as those all were benign at a follow - up visit, sensitivity, specificity, PPV and NPV were 94.4%, 69.51%, 40.47%, and 98.27% respectively. IOTA simple ultrasound rules are effective in classifying ovarian masses as benign and malignant masses and can be used by both experts and non - experts with good accuracy.*

**Keywords:** Benign ovarian cancer, IOTA simple rules, Malignant ovarian cancer, Ovarian cancer.

## 1. Introduction

Ovarian cancer presents late and responds poorly to treatment, making it the most fatal gynecological malignancy. [1] The seventh leading cause of mortality and morbidity for women worldwide is ovarian cancer. [2] Worldwide, ovarian cancer (OC) is thought to cause 152,000 fatalities and 239,000 new cases each year. [3] A complicated neoplastic assemblage, ovarian cancer often affects women over the age of 65. The age range of 50 to 79 years was described as the norm for diagnosis in earlier research. [2] Numerous studies suggested that the majority of ovarian carcinomas are derived from ovarian germinal epithelium or postovulatory epidermoid cysts developed during follicular rupture and healing. [4 - 6]

One of the more frequent diseases in women is ovarian cancer, which is typically discovered at a more advanced stage. The inability of gynecological sonography to use standardized terms and processes is what prevents early diagnosis. [7] Before surgery, ovarian diseases must be distinguished as benign or malignant because each type requires a completely distinct treatment strategy for care.

IOTA (International Ovarian tumor analysis) is one such method for differentiation. One of the greatest studies on ultrasound diagnosis completed to date is the one on IOTA. It started in 1999 and involved nine European nations. It is a standardized method for ovarian pathology preoperative classification that was developed by the IOTA group. [1] The IOTA simple guidelines, which distinguish between benign (B - features) and malignant (M - features) ovarian tumors, are two sets of ultrasonic criteria. There are five benign and five malignant characteristics that can identify an adnexal tumor. The five B - features are B1, unilocular cyst, B2, solid components (biggest diameter less than 7 mm), B3, the presence of acoustic shadowing, B4, smooth multilocular tumor with maximum diameter less than 100 mm, and B5 (color score 1). The five M - features are M1, an irregular solid tumor; M2, ascites; M3, the presence of four or more papillary structures; M4, an irregular, multilocular solid tumor with a maximum diameter equal to or greater than 100 mm; and M5—very high blood flow (color score 4). The tumor is unclassified or ambiguous if no characteristics are present or if both malignant and benign features are present. [7, 8] Even though various studies are available confirming the efficacy of these rules, still a prospective study directly

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applying these diagnostic rules to the patient are lacking. The present study was undertaken to evaluate the diagnostic accuracy of IOTA simple ultrasound rules for the differentiation of ovarian tumors.

## 2. Materials and method

The present prospective observational study was conducted at a tertiary referral center, Indira Gandhi Institute of Medical Sciences, Patna from December 2020 to June 2022 after institutional ethical committee approval. A total of 100 patients suspected of ovarian pathology either by pelvic examination or by the previous ultrasonographic report were included in the study. Whereas, patients with non - adnexal mass in the pelvis and not willing to surgery, those who refused to give consent, and known cases of adnexal mass who were under treatment for the same were excluded from the study.

Written informed consent was obtained before the initiation of the study. A routine history was obtained and a physical examination of each participant was done. Each patient was evaluated by IOTA simple rules at the time of the first visit by a resident of obstetrics and gynecology in the department of obstetrics and gynecology followed by an expert sonologist in the radiology department by transabdominal sonography (2.5 - 5 MHz) and the diagnosis was made as benign and malignant ovarian mass. Whereas, the mass which was not classified with B features or M features or with both B and M features was termed inconclusive or indeterminate.

Routine investigations, CA - 125, other tumor markers, and any other investigation were also advised as per the decision of the treating consultant.

Patients with benign ovarian masses were kept for follow - up when the size of ovarian masses was  $\leq 8$ cm with normal tumor markers. Any type of mass on IOTA which seemed to be inflammatory per vaginal examination was also kept for follow - up under an antibiotic course and the rest were operated on within 30 days of diagnosis.

Ovarian masses classified as indeterminate on IOTA were taken up for surgery as indeterminate masses were of size more than 10 cm.

Some patients underwent surgery due to other reasons (ex - abdominal uterine bleeding/fibroid) and she had a small ovarian mass removed during the operation that was also taken into account for the evaluation as the IOTA diagnosis was done before surgery.

Plan for surgery was kept in mind for the cases of follow - up, for any of the following indications:

- 1) Increase in size of the mass at a follow - up visit
- 2) Transformation of mass into malignancy at follow - up visits

All followed - up patients were re - evaluated by both expert sonologist and residents of obstetrics and gynecology  $\geq 3$  months after the first visit.

Diagnosis made by IOTA simple rules was confirmed by:

- 1) Histopathology report after laparotomy in operated cases after considering the histopathological report as the gold standard test.
- 2) Patients with benign ovarian mass with no indication of surgery have been re - evaluated at  $\geq 3$  months to see regression of mass or transformation of mass into malignant pathology.

### Statistical analysis

Collected data were recorded in an Excel sheet. Analysis was done by using SPSS Version 21 and analyzed by the Kappa statistical method. The sensitivity, specificity, positive predictive value, and negative predictive value of the IOTA were calculated. In the case of bilateral masses, larger malignant or benign masses were considered for analysis.

## 3. Results

The maximum number of patients was of age in the range of 21 to 40 years followed by 10 - 20 years with a mean age of  $35.55 \pm 13.9$  years.

In this study a maximum number of patients present with pain abdomen (n=75) followed by lump abdomen (n=26), dysmenorrhoea (n=23), pelvic discomfort (n=14), bowel complaint (n=11), bladder complaint (n=2), abdominal discomfort (n=2) and weight loss (n=3).

Out of 100 cases of ovarian masses classified by IOTA simple rules, 20 were malignant, 58 were benign and 22 ovarian masses were inconclusive or indeterminate. However, among 100 patients, 67 patients underwent surgery of which 19 were malignant, 26 were benign and 22 were indeterminate. Whereas, 33 patients were re - evaluated at  $\geq 3$  months of the interval to see regression of mass or transformation of mass into malignant pathology. Only one benign lesion (B1) was found to be malignant which was serous carcinoma of high grade.

Including all the cases (operated and followed - up cases), B1 was the most prevalent benign factor (table 1). One malignant ovarian mass on IOTA simple ultrasound rule was kept under follow - up because it seemed to be an inflammatory lesion on per - vaginal examination and an antibiotics course was given, size regressed after 6 weeks and disappeared after 6 months.

**Table 1:** IOTA classification of ovarian masses in followed - up patients

Followed - up cases on IOTA (33)		
BENIGN - 32	B1	20
	B2	1
	B3	3
	B4	8
	B5	0
MALIGNANT - 1 (Seemed Inflammatory on per - vaginal examination)	M4	1

B1 was the most commonly occurring factor in all benign lesions followed by B4. But, B2, B3, and B4 predicted the result more correctly followed by B1. Whereas in malignant

cases, M2 was the most commonly occurring factor followed by M3 & M4. But M1, M4 & M5 predicted the result more correctly (100%). (Table 2)

**Table 2:** Prevalence and Predictive Power of Benign and Malignant Classification of IOTA

Benign	Predicted	Result	Percentage (%)
B1	16	15	93.75
B2	1	1	100
B3	3	3	100
B4	6	6	100
B5	No cases	-	-
Malignant	Predicted	Result	Percentage (%)
M1	3	3	100
M2	8	5	62.5
M3	4	2	50
M4	3	3	100
M5	1	1	100

In benign findings, the most prevalent lesion was the Serous cyst adenoma (26.53%) followed by Mature teratoma (24.48%). In malignant findings, the most prevalent lesion was Serous carcinoma (29.41%) followed by Dysgerminoma (23.52%). One lesion was borderline that was Borderline mucinous tumour. (table 3)

**Table 3:** Histopathological Report of All the Operated Case

HPE REPORT	NO
<b>BENIGN (TOTAL)</b>	<b>49</b>
Mucinous cyst adenoma	8
Chocolate cyst	1
Benign cystic adenoma	1
Endometriotic cyst	1
Serous cyst adenoma	13
Benign cystic lesion	2
Mature teratoma	12
Acutely inflamed cyst	1
Haemorrhagic cyst	3
Sero - mucinous adenoma	2
Corpus luteal cyst	1
Benign para - ovarian cyst	1
Benign serous cyst	1
Follicular cyst	1
Chronic inflammatory lesion	1
<b>MALIGNANT (TOTAL)</b>	<b>17</b>
Dysgerminoma	4
Sex cord - stromal tumour	2
Serous carcinoma	5
Endometrioid adenocarcinoma	2
Granulosa cell tumour	1
Malignant surface epithelial compatible with adenocarcinoma	1
Malignant mixed germ cell tumour	1
Mucinous adenocarcinoma	1
<b>BORDERLINE (TOTAL)</b>	<b>1</b>
Borderline mucinous tumour	1

Out of 26 benign cases, 25 were found to be benign (96.15%) and 1 was malignant (3.84%) on HPE. Whereas, out of 19 malignant cases, 14 were found to be malignant (73.68%) and 5 were benign (26.31%) on HPE. Out of 22 indeterminate cases, 19 were benign (86.36%), 2 malignant, and 1 borderline lesion. (table4)

**Table 4:** Correlation of IOTA Classification and HPE

	HPE		
	Benign	Malignant	Borderline
Total Operated Cases (67)			
Benign on IOTA (26)	25 (96.15%)	1 (3.84%)	0
Malignant on IOTA (19)	5 (26.31%)	14 (73.68%)	0
Indeterminate on IOTA (22)	19 (86.36%)	2 (9.09%)	1 (4.54%)

Among 67 operated subjects, an equal number (n=26) of benign cases were diagnosed by residents of Obstetrics and Gynaecology and sonologist whereas 18 malignant cases were diagnosed by residents of Obstetrics and Gynaecology and 19 were detected by sonologist. In the case of indeterminate masses, 23 cases were diagnosed by residents of Obstetrics and Gynaecology and 2 were diagnosed by a sonologist. (table5)

**Table 5:** Agreement between USG findings of expert and non - expert

IOTA findings (operated cases - 67)	By: obgy - resident	By: expert sonologist
Benign	26	26
Malignant	18	19
Indeterminate	23	22

Kappa statistics showed a high level of agreement between expert (Sonologist) and non - expert (Resident of Obstetrics and Gynaecology) in diagnosing benign tumour (k = 1, 100%) and malignant tumour (k = 0.968, 96.8%) with P value less than 0.05. (Table 4)

The sensitivity and specificity of the IOTA simple rules in predicting malignant ovarian mass were 93.33% and 83.33% respectively. Positive predicting value (PPV) and Negative predictive value (NPV) were 73.68% & 96.15 % respectively.

After considering indeterminate mass as malignant mass and all followed - up cases as benign as those all were benign at a follow - up visit, sensitivity, specificity, PPV, and NPV were 94.4%, 69.51%, 40.47%, and 98.27% respectively.

#### 4. Discussion

The present prospective observational study was carried out in the Department of Obstetrics and Gynaecology of Indira Gandhi Institute of Medical Sciences, Patna for over a period of 18 months. A total of 100 patients satisfying inclusion and exclusion criteria were included in the study.

In this study, the maximum number of patients was in the 21 - 40 years of age group (49%), and the minimum was 10 - 20years of age (15%) with a mean age of 35.55±13.9 years), which is similar to the findings of the study conducted by Jyothi et al. [9] Clinical features of the study showed that patients with ovarian mass mainly present with pain abdomen (48%) followed by a lump abdomen (17%) which is similar to the study of R Nigam et al. [10]

In the present study, out of 100 patients, IOTA Simple Rules classified 78 (78%) ovarian masses as benign or malignant, and 22 were (22%) inconclusive. In this the percentage of inconclusive mass was 22% which is almost similar to the outcomes of a study conducted by D. Timmerman et al [11]

in which IOTA Simple Rules were applied to 76% and could not be applied to 24%, TheeraTongsong et al [12] in which inconclusive results were in 20.7%, Alcazar JL et al [13] in which 20.58% were inconclusive and Nunes N et al [8] in which 21.78% were inconclusive.

Among IOTA Simple Rules applied ovarian masses, 58 were benign, and 20 were malignant. Out of 58 benign, 32 benign ovarian masses and 1 malignant mass on IOTA (Inflammatory mass) were followed - up.

HPE of all the operated cases showed that, in benign findings, the most prevalent lesion was the Serous cyst adenoma (26.53%) followed by Mature teratoma (24.48%) which is similar to the result of the study done by Solanki v. et al [14], Nigam R. et al. [10] but, it is in contrast to the result of the study done by Alcazar JL. et al. [13], Testa A. et al. [15]Tantipalakorn C. et al. [16], and Tongsong T. et al. [12] in which percentage of endometriotic cyst is more in benign mass. In malignant findings, the most prevalent lesion was Serous carcinoma (29.41%) followed by Dysgerminoma (23.52%) similar to the findings of Solanki V. et al. [14] One lesion was borderline that was borderline mucinous tumour similar to the result of the Tantipalakorn C. et al. study. [16]

96.15% of benign ovarian masses on IOTA came to be benign and 3.84% of benign ovarian masses came to be malignant which is almost similar to the study conducted by Tinnangwattana D. et al. [17] in which 94.82% of benign ovarian masses were benign. Around 73.68% of malignant ovarian masses on IOTA were malignant and 26.31% of malignant ovarian masses were found to be benign which is compared to a few studies in which 68 - 70% of malignant lesions were found to be malignant [17, 18] and in some studies, even 80 - 90% of the malignant tumour were malignant. [9, 13, 14]

Here, 86.36% of indeterminate ovarian mass on IOTA were found to be benign, while 9.09% of indeterminate masses were found to be malignant and 4.54% were borderline which is almost similar to the findings study conducted by D. Timmerman et al. [11]

For the prediction of malignancy, the study yielded a sensitivity of 93.33%, specificity of 83.3%, PPV of 73.68%, and NPV of 96.15% respectively after excluding the inconclusive masses, when ovarian masses were classified by an expert Sonologist using IOTA Simple Rules. This high Sensitivity, Specificity, PPV, and NPV are showing that IOTA Simple rules can be an effective tool for differentiating the ovarian masses as benign and malignant ovarian masses for proper management.

After considering indeterminate mass as malignant mass and all followed - up cases as benign as those all remained benign at the follow - up visit, the Sensitivity, Specificity, PPV and NPV were 94.4%, 69.51%, 40.47%, and 98.27% respectively.

Though the inclusion of inconclusive ovarian masses decreases the specificity but all the indeterminate/inconclusive ovarian masses should undergo

surgery as their size was generally more than 10cm and there was also a chance of malignancy around 10% in this study which is almost similar to the Tinnangwattana D. et al. [17] in which 16% of the indeterminate mass was malignant.

Kappa statistics showed a high level of agreement between expert (Sonologist) & non - expert (Resident of Obstetrics & Gynaecology) in diagnosing benign tumour ( $k = 1$ , 100%) and malignant tumour ( $k = 0.968$ , 96.8%) with P value less than 0.05 (Table 10, 11, 12, 13). This is compared with the study B. Ruiz De Gauna et al [19] in which the percentage of agreement was also good with a kappa value of 0.76.

Thus, this study indicates that IOTA Simple Rules are simple, easy, and can be effectively performed by expert and non - expert examiners with high sensitivity and specificity.

## 5. Conclusion

IOTA Simple ultrasound rules are effective in classifying ovarian masses as benign and malignant masses and it can be used by both experts and non - experts with good accuracy. The main disadvantage is that it gives a high percentage of inconclusive results and all have been operated in this study as the size was more than 10cm.

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