



cancer, but sometimes they have nonspecific symptoms. Two-thirds of women have advanced disease at the time of diagnosis; this is because of the paucity of specific early symptoms [9]. The most common symptoms reported by women with ovarian cancer are pelvic or abdominal pain; increased abdominal size; bloating; urinary urgency, frequency, or incontinence; difficulty eating; and weight loss. Abdominal fullness and pressure; back pain; and lack of energy may also be prominent symptoms [11]. Grayscale transvaginal ultrasonography remains the standard for the evaluation of adnexal masses [12]. The combination of ultrasonography and Doppler flow studies is superior to either alone [13]. MRI can increase the specificity of imaging evaluation in cases where the ultrasound appearance of the lesion is indeterminate [14].

Current guidelines of the Royal College of Obstetricians and Gynaecologists (RCOG) [15] and the National Institute for Health and Care Excellence (NICE) stipulate that the Risk of Malignancy Index (RMI) should be used to evaluate ovarian masses in secondary or tertiary care in both premenopausal and postmenopausal women. A Scottish Intercollegiate Guidelines Network (SIGN) clinical practice guideline on the management of epithelial ovarian cancer in 2013 also supported the use of RMI as the 'benchmark' test in secondary care [16]. The RMI classifies women as being at high or low risk of having ovarian cancer based on a total score derived from a combination of ultrasound findings (multi-locularity, solid components, bi-laterality, ascites, and the presence or absence of intra-abdominal metastases), menopausal status and the serum CA125 concentration [17]. A score above 200 is generally used to define a positive test result for cancer, leading to the woman being referred for specialist oncological treatment. Some triaging protocols in UK hospitals advise second-line imaging with MRI to obtain a confident diagnosis for tumours with an intermediate RMI score (25-200) [18]. The RMI is calculated as:

$RMI = \text{ultrasound score} \times \text{menopausal score} \times \text{CA-125 level in U/ml}$  [19]

The International Ovarian Tumour Analysis (IOTA) group was founded in 1999 by Dirk Timmerman, Lil Valentin, and Tom Bourne. Its first aim was to develop standardized terminology. In 2000, IOTA published a consensus statement on terms, definitions, and measurements to describe the sonographic features of adnexal masses, which is now widely used. IOTA now covers a multitude of studies examining many aspects of gynaecological ultrasonography within a network of contributing centres throughout the world [20].

The IOTA Simple Rules is a preoperative classification system for ovarian tumours which is based on five ultrasound features of malignancy (M-features) and five ultrasound features suggestive of a benign lesion (B-features) [21]. An adnexal mass is classified as malignant if at least one M-feature and no B-features are present and vice versa. When no B-features or M-features are present or if both B-features and M-features are present, then simple rules are considered inconclusive (uncertain), and in the approximately 20% of masses where this is the case, a secondary diagnostic test should be used to classify these masses [22]. The model was developed by clinicians and statisticians from the International Ovarian Tumour Analysis (IOTA) group and is based on clinical and ultrasound data from almost 6000 women recruited at 24

centres in 10 countries (Italy, Belgium, Sweden, Czech Republic, Poland, France, UK, China, Spain, and Canada) [23]. ADNEX estimates the probability that an adnexal tumour is benign, borderline, stage I cancer, stage II- stage IV cancer, or secondary metastatic cancer (i.e. metastasis of non-adnexal cancer to the ovary) [24]. The ADNEX model uses nine predictors. There are three clinical variables, age, serum CA-125 level, and type of centre (oncology referral centre vs. other), and six ultrasound variables, (maximal diameter of lesion, proportion of solid tissue, more than 10 cyst locules, number of papillary projections, acoustic shadows, and ascites). As with all current diagnostic models for adnexal tumours (e.g. IOTA models, RMI, it implies that patients selected for expectant management were excluded when creating the model. As a consequence, ADNEX cannot be applied to conservatively treat adnexal tumours. The ADNEX model has been externally validated in the original paper and six subsequent studies [23-25]. The parameters used in ADNEX are based on the terms and definitions as published by the IOTA group [26].

The study aims to compare the sensitivity, specificity, predictive value, and accuracy of the risk malignancy index, simple rules, and the ADNEX model, in the diagnosis of adnexal mass.

## METHODS

### Study design and setting

This prospective observational cohort study was carried out in the Department of Obstetrics and Gynaecology/ Baghdad Teaching Hospital, Baghdad Medical City, Baghdad, Iraq. This study was conducted for eighteen months starting from the first of January 2016 to the end of June. 2017. The study protocol was approved by Arab Board for Medical Specialization and by the Department of Obstetrics and Gynaecology of Baghdad Teaching Hospital. A total number of 100 patients with the adnexal mass of different age groups were enrolled in this study.

### Ethical consideration

The purpose and procedures were explained to all participants and were given the right to participate or not, verbal consent was taken with reassurance that interpretations gained will be kept confidential and not to be used for another research object.

### Inclusion criteria

All patients presented with unilateral adnexal mass  $\geq 50$  mm. For bilateral adnexal masses, the mass with the most complex ultrasound features was included. If both masses had similar ultrasound morphology, the largest mass was included. If both had similar size and morphology, the most easily accessible mass by ultrasound was included. All those patients had decided to have surgery. The decision for surgery depends on clinical assessment and RMI and is not affected by the results of ADNEX or simple rules. Those patients completed their workup which includes: CA-125, TVS, and Doppler ultrasound of the abdomen and pelvis.

### Exclusion criteria

1. Pregnant patients at the time of the study.
2. Patients who received neoadjuvant chemotherapy.
3. If patients didn't do CA-125, TVS examination or lost during

follow-up.

- If the adnexal mass proved to be not ovarian in origin.

### Data collection

Data were collected entirely by the researcher herself from patients who visited the Gyne-oncology clinic in Baghdad Teaching Hospital. All patients with adnexal mass were sent for serum CA125 to the same laboratory. Doppler transvaginal pelvic and abdominal ultrasound was done by the same radiologist for all patients. For each patient, we record:

- Risk Malignancy Index (RMI).
- Simple rules; whether benign, malignant, or inconclusive.
- ADNEX model.

For ADNEX we calculate the results using the application developed by IOTA, and the results are:

- Chance of benign or malignant tumour.
- Stage of malignancy:
  - Percentage of a borderline tumour.
  - Percentage of stage I ovarian cancer.
  - Percentage of stage II-IV ovarian cancer.
  - Percentage of metastasis.

These data are collected preoperatively All patients had surgery in our hospital and histopathological examination was done in the Teaching Labs of Medical City by a consultant pathologist.

### Ultrasound examination and apparatus

The patients were examined by a consultant radiologist using hospital-type ultrasound equipment (Philips HD11 XE Netherland). Transabdominal evaluation using a curved array (5 MHz transducer) and pelvic evaluation transvaginal high frequency (10 MHz transducer).

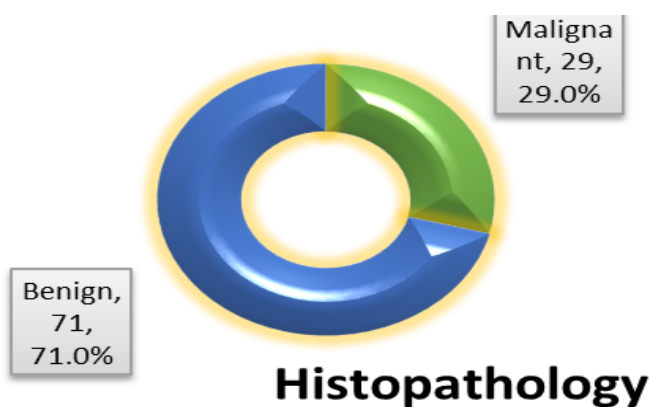


Fig. 1. Distribution of histopathological results of adnexal masses

### CA-125 samples collection

All tests were done in Oncology Teaching Hospital laboratory. 5 ml of the patient's blood was collected by routine veni-puncture, and the blood is collected into a purple-top tube with Ethylene Diamine Tetra Acid (EDTA). Centrifugation was done to the sample in the collecting tube and then the result of the test was obtained using a Cobas e 411 analyser machine.

### Statistical analysis

Analysis of data was carried out using the available statistical package of SPSS-24 (Statistical Packages for Social Sciences-version 24). Data were presented in simple measures of frequency. The significance of the difference of different percentages (qualitative data) was tested using the Pearson Chi-square test ( $\chi^2$ -test) with the application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal to or less than 0.05. The sensitivity, specificity, false negative%, false positive%, predictive value of the positive test, the predictive value of the negative test, and accuracy rate were calculated according to the following equations.

### RESULTS

A total of 100 women with an adnexal mass of different age groups who underwent surgery were included in this study and assessed preoperatively. Histo-pathologically, 71 (71%) women were confirmed with a benign tumor, and 29 (29%) women were confirmed with malignancy, as shown in Figure 1.

The largest distribution of benign cases was in the premenopausal age groups, while the largest distribution of malignant cases was in the postmenopausal age groups, as shown in (Table 1).

Regarding the distribution of the histopathological results of the adnexal masses, our cases were of ovarian origin. Table 6 shows that the majority of benign histopathology was serous cystadenoma (35.2%), then mature teratoma (25.4%) and the last was mucinous cystadenoma (7.0%). While for the malignant histopathology, the main group was serous cystadenocarcinoma (58.6%), then mucinous cystadenocarcinoma, and endometrioid adenocarcinoma (17.2%) for both. 5 of 29 (17.2%) malignant cases were borderline, 10/29 (34.4%) of those with malignancy were in stage I, 2/29 (6.8%) patients were in stage II, 9/29 (31.0%) in stage III, 2/29 (6.8%) in stage IV, and 1/29 (3.4%) metastasis.

Table 3 shows that for RMI, the low & intermediate risk agreed with histopathology was more common in benign (91.5%), and the high risk was agreed more common in malignant (58.6%). For the simple rules, it was found that it is 85.9% agree with the histopathology for diagnosis of benign mass. While the ADNEX diagnose 94.4% of those with benign who were diagnosed by

Tab 1. Distribution of women's age according to histopathology findings

Variable (Age)	Benign histopathology		Malignant histopathology	
	No.	%	No.	%
<20 years	8	11.3	2	6.9
20 years-29 years	14	19.7	2	6.9
30 years-39 years	21	29.6	2	6.9
40 years-49 years	14	19.7	6	20.7
50 years-59 years	6	8.4	8	27.6
≥ 60 years	8	11.3	9	31.0
Total	71	100.0	29	100.0

Tab. 2. Types of adnexal masses according to histopathological findings	Benign Histopathology			Malignant Histopathology and operative staging		
	No.	%		No.	%	
Serous cystadenoma	25	35.2		Serous cystadenocarcinoma	17	
				Stage I	9	
				Stage II	1	58.6
				Stage III	4	
				Stage IV	2	
				Metastasis	1	
Mucinous cystadenoma	5	7		Mucinous cystadenocarcinoma (Borderline)	5	17.2
Mature teratoma (Dermoid)	18	25.4		Immature teratoma (stage I)	1	3.4
Fibroma	6	8.5		Endometrioid adenocarcinoma	5	
				Stage II	0	17.2
				Stage III	1	
				Stage IV	4	
Endometrioma	10	14.1		Malignant Mixed Mullerian tumor (stage III)	1	3.4
Hemorrhagic corpus luteal cyst	7	9.8		-	-	-
Total	71	100		-	29	100

Tab. 3. Distribution of RMI, simple rules, and ADNEX model according to histopathological findings	Variable		Benign Histopathology		Malignant Histopathology		Total No.
			No.	%	No.	%	
RMI	Low risk (<200)		65	91.5	12	41.4	77
	High risk (≥ 200)		6	8.5	17	58.6	23
	Total		71	100	29	100	100
Simple rules	Benign		61	85.9	2	6.9	63
	Inconclusive		10	14.1	5	17.2	15
	Malignant		0	-	22	75.9	22
	Total		71	100	29	100	100
ADNEX	Benign		67	94.4	4	13.8	71
	Malignancy		4	5.6	25	86.2	29
	Total		71	100	29	100	100

Tab. 4. Validity test results of RMI in comparison to histopathology		Malignant Histopathology (Total=29)		Benign Histopathology (Total=71)		P value
		No.	%	No.	%	
RMI	High risk (≥ 200)	17	58.6	6	8.5	0.0001*
	Low risk (< 200)	12	41.4	65	91.5	

\*Significant difference between proportions using Pearson Chi-square test at 0.05 level  
 Sensitivity=58.6%, False Positive Percentage=41.4%, Specificity=91.5%, False Negative Percentage=8.5%, Positive Predictive Value=73.9%, Negative Predictive Value =84.4%, Accuracy rate = (17+65)/100=82.0%

Tab. 5. Validity test results of simple rules in comparison to histopathology		Malignant Histopathology (Total=29)		Benign Histopathology (Total=71)		P value
		No.	%	No.	%	
	Malignant	22	75.9	-	-	0.0001*
Simple rules	Inconclusive	5	17.2	10	14.1	
	Benign	2	6.9	61	85.9	

\*Significant difference between proportions using Pearson Chi-square test at 0.05 level  
 Sensitivity=75.9%, False Positive Percentage=6.9%, Specificity=85.9%, False Negative Percentage=0%, Positive Predictive Value=100% , Negative Predictive Value =96.8%, Accuracy rate = (22+61)/100=83.0%, Inconclusive rate=15.0% (33.3% after surgery were found to be malignant & 66.7% were found to be benign by histopathology)

histopathology.

The validity results of RMI findings regarding histopathology were sensitivity (58.6%), specificity (91.5%), positive predictive value (73.9%), negative predictive value (84.4%), and accuracy (82.0%). All these findings were shown in Table 4.

The validity results of simple rules regarding histopathology were sensitivity (75.9%), specificity (85.9%), positive predictive value (100%), negative predictive value (96.8%), and accuracy (83%). All these findings were shown in Table 5.

The validity results of ADNEX model findings regarding histopathology were sensitivity (86.2%), specificity (94.4%), positive predictive value (86.2%), negative predictive value (94.4%), and accuracy (92%). All these findings were shown in Table 6.

Table 7 shows the comparison between the validity results of RMI, simple rules, and ADNEX findings to their corresponding histopathology. For RMI results were sensitivity (58.6%), specificity (91.5%), positive predictive value (73.9%), negative

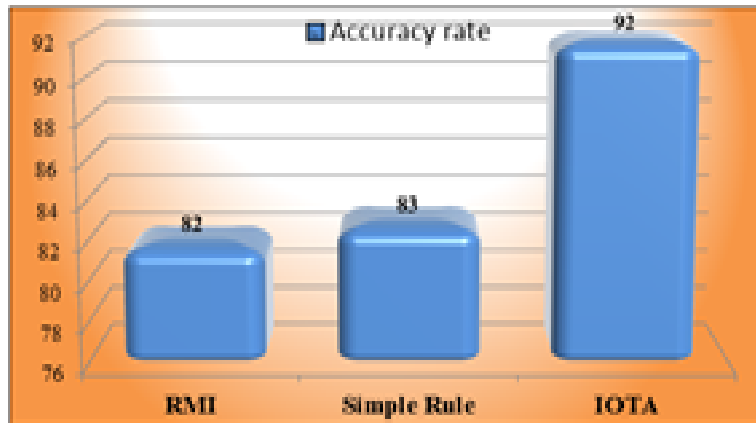
**Tab. 6.** Validity test results of ADNEX model findings in comparison to histopathology

ADNEX	Malignant Histopathology (Total=29)		Benign Histopathology (Total=71)		P value
	No.	%	No.	%	
Malignant	25	86.2	4	5.6	0.0001*
Benign	4	13.8	67	94.4	

\*Significant difference between proportions using Pearson Chi-square test at 0.05 levels  
 Sensitivity=86.2%, False Positive Percentage=13.8%, Specificity=94.4%, False Negative Percentage=5.6%, Positive Predictive Value=86.2%, Negative Predictive Value =94.4%, Accuracy rate = (25+67)/100=92.0%

**Tab. 7.** The validity results of RMI, simple rules, and ADNEX to their corresponding histopathology

Test	Sensitivity	Specificity	Positive PV	Negative PV	Accuracy
RMI	0.586	0.915	0.739	0.844	0.82
Simple Rules	0.759	0.859	1	0.968	0.83
ADNEX	0.862	0.944	0.862	0.944	0.92



**Fig. 2.** Comparison between accuracy rates of RMI, Simple rules, and ADNEX model

predictive value (84.4%), and accuracy (82.0%). For simple rules, the results were sensitivity (75.9%), specificity (85.9%), positive predictive value (100%), negative predictive value (96.8%), and accuracy (83.0%). For ADNEX results were sensitivity (86.2%), specificity (94.4%), positive predictive value (86.2%), negative predictive value (94.4%), and accuracy (92%).

We see that the highest results were achieved by the ADNEX model with the highest accuracy in diagnosing ovarian masses, as shown in (Figure 2).

## DISCUSSION

The etiology of adnexal masses ranges from physiologically normal luteal cysts to ovarian cancer. The clinician needs to interpret symptoms and findings from multiple organ systems and use appropriate imaging to differentiate expeditiously between a benign and a malignant cause of an adnexal mass [27].

Adnexal masses present a diagnostic dilemma; the differential diagnosis is extensive, with most masses representing benign processes. However, without histopathologic tissue diagnosis, a definitive diagnosis is generally precluded. Physicians must evaluate the likelihood of concerning pathologic process using clinical and radiologic information and balance the risk of surgical intervention for a benign versus malignant process [28, 29].

The validity results of RMI findings regarding histopathology in our study were: sensitivity (58.6%), specificity (91.5%), positive predictive value (73.9%), negative predictive value (84.4%), and accuracy (82.0%) in the current study. While in Javdekar R et al. RMI had a sensitivity of 70.5 %, a specificity of 87.8 %, a positive predictive value of 70.5 %, and a negative predictive value of 87.8 % [30]. This may be attributed to the differences in sample size collection when the current study has a larger sample size than the

sample in that study.

The validity results of simple rules in the present study regarding histopathology were sensitivity (75.9%), and specificity (85.9%), compared with 92% and 96%, respectively, in the original IOTA study [30]. Moreover, it agrees with Fathallah et al., who conducted a single-centre external validation study on 122 ovarian tumours over 4 years. They found a simple rule with a sensitivity of 73% and specificity of 97% [31].

The current study revealed that the validity results of ADNEX findings regarding histopathology were sensitivity (86.2%), specificity (94.4%), positive predictive value (86.2%), negative predictive value (94.4%), and accuracy (92%). Szubert S et al., in 2016, reported that when the study was done in two centers-1<sup>st</sup> in Poland and 2<sup>nd</sup> in Spain-and two sets of data were used for the diagnosis of benign and malignant ovarian tumors, the accuracy of the ADNEX model was 79.9%, and 81.3%, in Centre I and Centre II, respectively) [23]. Multiclass accuracy was substantially lower than in binary classification (malignant vs. benign): 64.2% and 74.0% in Centres I and Centres II, respectively. Sensitivity and specificity for the diagnosis of specific tumour types in Centre I were as follows: benign tumors-72.4% and 94.3%; borderline tumors-33.3% and 87.0%, stage I ovarian cancers-00.0% and 91.8%; stage II- stage IV ovarian cancers-68.2% and 83.1%; and metastatic tumors-00.0% and 99.5%. Sensitivity and specificity in Centre II were as follows: benign tumors-75.3% and 97.1%; borderline tumors-50.0% and 88.2%, stage I ovarian cancers-40.0% and 97.5%; stage II- stage IV ovarian cancers-95.0% and 88.3%; and metastatic tumors-20.0% and 98.3%. In another study, Hu J et al found that the accuracy, sensitivity, and specificity of the ADNEX model were 78.70%, 93%, and 72%, respectively with a positive predictive value of 60.6% and negative predictive value of 95.7% [32].

The differences between our study and these studies may be due to the larger samples being included and more than one centre included in the study.

In general, for any test to diagnose ovarian malignancy, a high sensitivity (preferably over 90%) is essential because correctly identifying women with cancer is key to appropriate triage to specialists in high-volume oncology centres [33]. In Testa A study, using a score of 200 to indicate malignant disease, RMI misses one in three patients with ovarian cancer. This is not an appropriate cut-off to triage women. Likewise, as shown in IOTA phase 3, a negative test result for RMI is associated with a disproportionately high risk of cancer (of around 50%) [34].

The disadvantage of the simple rules is that they yield an inconclusive result in about 25% of all tumours [35]. Our study found that the inconclusive simple rule represents only 15% of all tumour masses. After comparing the validity results of RMI, simple rules, and ADNEX to their corresponding results of

histopathology in our study, we found that the most accurate test was the ADNEX model with an accuracy of 92% and so it can be used as a first-line preoperative test in the diagnosis of adnexal masses.

## CONCLUSION

ADNEX model can be used as a first-line test for the diagnosis of adnexal mass preoperatively. For more accurate findings we required a larger sample size and multicentre study.

## CONFLICT OF INTEREST

None.

## FUNDING

None.

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