DIAGNOSTIC ACCURACY AND APPROPRIATE CUT OFF VALUE OF RISK OF MALIGNANCY INDEX IN PREOPERATIVE DESCRIMINATION BETWEEN MALIGNANT AND BENIGN OVARIAN TUMORS IN JIMMA MEDICAL CENTER, JIMMA TOWN, OROMIA REGION, SOUTH WEST ETHIOPIA, 2020

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JIMMA, ETHIOPIA

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ABSTRACT

Background: Risk of malignancy index is scoring system which was introduced to differentiate between benign and malignant ovarian tumor. It incorporates CA-125, ultrasound score and menopausal status for prediction of ovarian malignancies in preoperative period. There is no universal screening method to discriminate between benign and malignant adnexal masses yet. So, this study was conducted to determine the diagnostic accuracy of RMI and determine best cut off value for RMI.

Methods: Prospective cross-sectional study was carried out among women with ovarian mass admitted to Gynecology ward and operated from September 1, 2019 to June 30, 2020.Data analysis was carried out using SPSS version 26. CA-125 level, menopausal status and ultrasound score were used to calculate RMI. Finally, RMI score was compared to histopathology result used as gold standard.

Results: 99 patients were enrolled in this study. Prevalence of benign ovarian tumors were 61.6% (61/99) and that of malignant ovarian tumors were 38.4% (38/99). The mean age for benign tumors was 30±9yrs and the mean age for malignant tumors was 50.6±10.8yrs. Among benign tumors, serous cystadenoma was the most common (36%), followed by dermoid cyst (32.9%), mucinous cyst adenoma (14.8%). The most common malignant ovarian tumor was serous cyst adenocarcinoma (63.2%), followed by mucinous cystadenocarcinoma (23.8%) and dysgerminoma (5.3%). Overall, using RMI score cut off value 220 has good sensitivity (84.2%), specificity (77%), PPV (69.5%), NPV (88.7%) and diagnostic accuracy (79.8%) for discriminating between benign and malignant ovarian tumors.

Conclusion: From this study there were high proportion of women with RMI>=220 in malignant ovarian tumor group. The study shows that there is significant role of RMI in prediction of ovarian malignancy thus helping in deciding which patients need referral to a center where gynecologic oncologists are available. It is good practice to use it in developing countries including our country because of its simplicity, safety and applicability in initial evaluations of patients with adnexal mass.

Keywords: Risk of malignancy index; CA 125; ovarian mass, diagnostic accuracy, cut off, Ethiopia

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ABBREVIATIONS

ASIR-Age standardized incidence rate

AUC-Area under the curve

BSO-Bilateral salpingo-opherectomy

BTL-Bilateral tubal ligation

CIR-Crude incidence rate

CRC-Colorectal cancer

CT-Computer tomography

GYN/OBS-Gynecology and obstetrics

HRT-Hormone replacement therapy

JMC-Jimma medical center

JUTH-Jimma university teaching hospital

MRI-Magnetic resonance imaging

NPV-Negative predictive value

PPV-Positive predictive value

RMI-Risk of malignancy index

ROC-Receiver operating characteristic curve

SEP-September

SNNP-Southern nation nationalities and population

TAS-Trans abdominal ultrasound

TVS-Trans vaginal ultrasound

USG-Ultrasonography

USPSTF-United states preventive service task force

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CHAPTER ONE: INTRODUCTION

1.1 Background

Ovarian cancer is the second most common type of female reproductive cancer, and more women die from ovarian cancer than cervical cancer and uterine cancer combined(1). Woman's risk at birth of ovarian cancer at some time in her life is 1 % to 1.5% and that of dying from cancer is almost 0.5%(1).In 2018 4.4% of all cancer related mortality is attributed to ovarian cancer(2). It is the seventh most common cancer in women, and incidence rates are highest in developed countries(2,3). The incidence of ovarian cancer increases with age. Interest in early detection as a method of reducing mortality developed with the discovery of serum tumor markers associated with ovarian malignancies (particularly CA 125) and with the improved diagnostic accuracy of pelvic ultrasonography(3).

Survival from ovarian cancer is related to the stage at diagnosis; five-year survival is over 90 percent for the minority of women with stage I disease. This number drops to about 75 to 80 percent for regional disease and 25 percent for those with distant metastases(3). The high mortality rate in ovarian malignancy is mainly due to late detection of disease(4). If it can be detected at an early stage then disease can be treated with optimal primary cytoreduction and achievement of optimal cytoreduction (single most important prognostic criteria) becomes possible(5).Pelvic examination is not specific and sensitive in detecting ovarian malignancy. Cancers detected by pelvic examination are often far advanced, so pelvic examination for screening is not recommended(5). Tumor markers when used alone are not specific to be used as screening test. They are raised in a number of benign conditions and are not raised in poorly differentiated cancer, borderline tumors and mucinous tumors(6). In a prospective study conducted to evaluate sensitivity and specificity of CA-125 as a marker for ovarian malignancy and concluded that measurement of serum CA-125 levels, particularly at a reference value of 35 IU/mL, is not sufficiently sensitive to be used alone as a screening test for the detection of ovarian cancer(6). Ultrasound can differentiate between solid, cystic and multilocular masses, although malignancy cannot be diagnosed, unequivocally(6).Risk of malignancy index is a scoring system which can be introduced to differentiate between malignant and benign ovarian tumor(5). RMI in ovarian malignancy incorporates CA-125, USG and

Menopausal status for the accurate prediction of likely ovarian cancer in preoperative period(5). RMI is useful for Predicting if an ovarian mass is malignant or benign, screening for suspected pelvic mass, deciding appropriate management protocol and triage of patients(5).Jacobs RMI Score (RMI I) -Total Score = USG Score X Menopausal Score X CA -125(U/ml)

USG score: 0 - No risk factor ,1 - One risk factor, 3 - Two - Five risk factors. High risk factors in USG: Multiloculated cysts, solid areas, bilateral lesions, ascites and evidence of metastasis. Menopausal status: 1- Pre- menopausal, 3 - Post-menopausal

CA125- Absolute value (IU/mI).

RMI Score <200 - Low risk (risk of ovarian malignancy is 0.15 times) ,RMI Score >200 - High risk (risk of ovarian malignancy is 42 times(5).

When 200 is taken as cut -off for RMI, Sensitivity is 85%, Specificity is 97%(5).

1.2 Statement of the problem

Worldwide, the number of new cases of ovarian cancer each year is approaching 250,000(2). Ovarian cancer has been defined as an occult disease of insidious onset (silent killer) with non-specific clinical symptoms-hence possesses the greatest clinical challenge of all gynecologic malignancies(3). The anatomic site of ovaries makes it inaccessible to simple diagnostic procedure like smear and biopsy like cancers of uterus and cervix(4). Absence of effective screening method for ovarian cancer yet is another contemporary challenge. Patients with malignant tumors should be evaluated by gynecologic oncologist as the quality of cytoreduction surgery and surgical staging/ lymph node dissection are critical prognostic parameters in ovarian malignancy(5,7). The finding of an ovarian mass raises questions about the most suitable management and the place where this management is to be implemented(7). The risk of malignancy index (RMI) is a simple scoring system depends on menopausal status, ultrasound findings, and the serum CA125 level(7). This score has given significantly superior results than the use of a single parameter(7).After obtaining the histopathology result of specific tumor types the following were calculated for RMI: sensitivity [(true positive/true positive+ false negative)x100],Specificity [(true negative/true negative+false positive)x100],PPV [(true positive/true positive+false positive)x100],NPV [(true negative/true negative+false negative)x100],Diagnostic accuracy [(true positive+true negative/true positive+true negative+false positive+false negative)x100] .The aim of the current study is to assess the diagnostic accuracy, specificity, sensitivity, PPV and NPV of RMI, as there is no similar studies conducted in our country.

1.3 Significance of the Study

The finding of the study will rebound to benefit the society considering that ovarian tumor is one of the major health problems of women in all age groups, as there is no effective screening strategy yet in the world. It will also put the basis for health policy makers and resource allocators to reconsider strengthen further study to decrease mortality associated with ovarian tumor. The finding of the study will also help us to triage patients preoperatively whether to be operated by Gynecologic oncologist or General Gynecologist thus decreasing health costs. It will also provide the basis for further research as there are no similar studies in our county yet.

CHAPTER TWO- LITERATURE REVIEW

The presence of an adnexal mass is a frequent reason for a woman to be referred to a gynecologist. Ovarian cancer is the leading cause of death from gynecologic malignancy in the United States[2]. Local data on cancer epidemiology in Ethiopia are lacking(8). Studies from the Global Burden of Disease Cancer Collaboration and the Cancer Incidence in Five Continents Collaboration have estimated cancer incidence by cause for countries globally, and both studies used evidence from neighboring African countries to estimate cancer incidence in Ethiopia(8). In Ethiopia In females 15 years and older, the most common cancer was breast cancer, followed by cervical cancer , ovarian cancer, colorectal cancer, and leukemia(8).Ovarian cancer is 3rd most common cancer next to breast and cervical cancer among female older than 15yrs old with crude incidence rate(CIR) of 4.9 per 100,000 population and age standardized incidence rate(ASIR) of 8.1 per100,000 population(8). Based on 2013 data from the Addis Ababa Cancer Registry, breast cancer accounted for 31.4%, cervical cancer for 14.3% and ovarian cancer for 6.3% of all cancer cases(9)

As the symptoms of the ovarian cancer are very vague like bloating, pelvic or abdominal pain, poor appetite, feeling full quickly, and urinary urgency it is also known as “silent killer”. Thus, silent occurrence and slow progression, added to the fact that few effective methods for early diagnosis and no universal screening method for diagnosis of malignant ovarian tumor exists, made its mortality rate highest among gynecologic malignancies(10–12). Of all gynecologic malignancies ovarian cancer has the worst prognosis since is detected at advanced stage(13)

The main challenge is to identify patients with high-risk adnexal masses preoperatively and this is compounded by the lack of definitive noninvasive diagnostic test(14). The discrimination between benign and malignant adnexal mass is central to decision regarding clinical management and surgical planning in such patients(15).Jacob et.al originally developed a risk of malignancy index based on ultrasound findings, menopausal status and CA-125(15).the main advantage of this method compared to other

approaches such as color Doppler ultrasound(15) or use of different tumor markers(16,17) is that RMI can be used easily in less specialized unit (18).

United states preventive service task force found adequate evidence that screening for ovarian cancer doesn't reduce ovarian cancer mortality and thus recommend against screening for ovarian cancer in asymptomatic women who are not known to have high risk hereditary cancer syndrome(19,20). Prompt identification of ovarian malignancies and referral to Gynecologic oncologist can enhance patient survival, but a single method which can accurately predict ovarian malignancies are unavailable(21).RMI is widely studied for prediction of ovarian malignancies in western populations. However, little is known about its implication in developing countries(21–23). Subsequent studies have shown RMI is reliable tool in differentiating benign and malignant adnexal mass(24,25). Because of this Authors wish to see if RMI score, can be applied in present low resource setting of our population for setting up a better diagnosis, referral and management system

2.1 Conceptual frame work

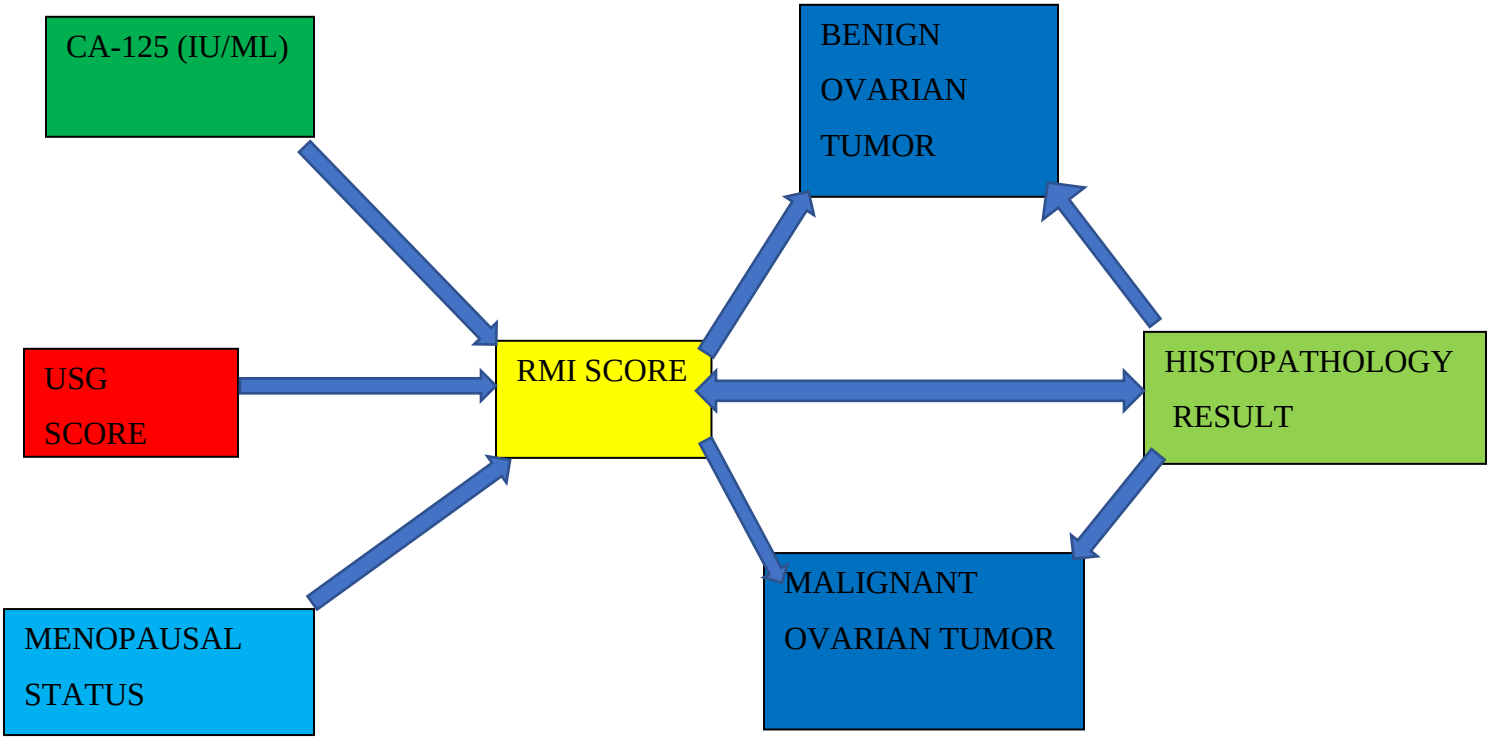


Figure 1:Conceptual frame work

CHAPTER THREE- OBJECTIVES

3.1 General objective

Determine diagnostic accuracy and appropriate cut off value of RMI score in preoperative discrimination between malignant and benign ovarian tumor in Jimma Medical Center,2020

3.2 Specific objectives

3.2.1 To determine specificity and sensitivity of RMI in JMC

3.2.2 Calculate negative predictive value and positive predictive value of RMI

3.2.3 To determine best cut off value of RMI score to differentiate between benign and malignant ovarian tumor

CHAPTER FOUR- METHODS AND MATERIALS

4.1 Study area and period

Jimma University teaching Hospital (JUTH) is one of the oldest public hospitals in the country. It was established in 1922 G.C. Geographically, it is located in Jimma city 352 km to southwest of the capital Addis Ababa, Ethiopia. It has been governed under the Ethiopian government by the name of “Ras Desta Damtew Hospital” and later “Jimma Hospital" during Dergue regime and currently Jimma University Specialized Teaching Hospital and recently Jimma Medical center. Currently it is the only teaching and referral hospital in the south western part of the country providing service for approximately 115,000 in patient ,16000 outpaient,11000 emergency case and 4500 deliveries per year.it gives services to about 15 million populations coming from Oromia, Gambella and SNNP(26) . study was conducted from September 1, 2019 to June 30, 2020G.C

4.2 Study design

Prospective cross-sectional study was employed.

4.3 Population

4.4.1 Source population

All patients with adnexal mass who visited Gynecologic OPD of Jimma Medical Center during study period

4.4.2 Study population

All patients with ovarian mass admitted to gynecology ward and operated during study period.

4.4 Sample size determination and sampling technique

All patients who fulfilled the eligibility criteria and came during study period was enrolled in the study.

4.5 Eligibility criteria

All patients with suspected ovarian mass was included and patients with previous history of ovarian cancer, abdominal mass other than ovarian mass was excluded. For patients who had undergone hysterectomy age cut off point greater than or equals to 51.3yrs was considered as post-menopausal.

4.6 Study variables

Dependent variable

Benign ovarian tumor

Malignant Ovarian tumor

RMI score

Independent variable

Age

Sex

Marital status

Religion

Ethnicity

Gravidity

Parity

Menopause

CA-125

Ultrasound score

4.7 Data collection process and techniques

Structured questionnaire which was prepared in English by reviewing literature and translated to local language (Afaan Oromoo) by principal investigator was used to collect data. Data was collected by interviewing the patients and reviewing their charts. USG done by radiologist or Gynecologist were used for USG score.

Two BSc Nurses were selected to collect data after getting proper training and orientation by principal investigator in how to record and fill data on written questionnaire

4.8 Data quality control

At the end of each data collection day the questionnaire was checked for consistency and completeness and close supervision was carried out during data collection by principal investigator

4.9 Data processing and analysis

The collected data were entered into epidata version 4.6.0.2 and then exported to SPSS (statistical packages for social sciences) version 26 computer software for analysis. Descriptive statistics and analytic statistics methods were used for analysis. To determine the best cut off value of RMI, Receiver operating characteristic curve (ROC) was plotted and odds ratio with 95% CI was calculated. Best cut off value was chosen according to highest sensitivity and lowest false positive rate. Histopathology result was used as gold standard to differentiate malignant from benign adnexal mass. P-value less than 0.05 considered statistically significant. Finally obtained results were presented using tables and figures.

4.10 Ethical consideration

Before proceeding with actual data collection process, ethical clearance letter was obtained from Jimma University institutional review board (IRB). Patients' records were kept confidential and verbal consent was taken from each study participants.

4.11 Dissemination of result

After the completion of the study, formal report was prepared and copy of the research paper was given to Jimma university department of Gynecology and Obstetrics, Jimma University institute of Health, research and post graduate study coordinator office.

4.12 Operational definition

RMI-Is scoring system that uses CA-125 level, USG score and menopausal status to predict presence or absence of ovarian malignancies

Sensitivity-How accurate is the test in correctly diagnosing presence of a condition

Specificity-How accurate is the test in correctly diagnosing absence of a condition

PPV-The probability that subjects with positive test result actually has a condition/disease

NPV-The probability that subjects with negative test result has no a condition/disease

Diagnostic accuracy-How accurate is the test in diagnosing presence and absence of a condition/disease

Likelihood ratio -How much does the test improve the likelihood of making correct diagnosis.

ROC curve-Is used to evaluate the sensitivity and specificity of diagnostic test

CHAPTER FIVE- RESULTS

A total of 99 patients were enrolled in this study. The incidence of benign ovarian tumor in all patients presented with adnexal mass and operated for suspected ovarian malignancy at JMC is 61.6% and that of malignant ovarian tumor is 38.4%. From this study the youngest patient was 15 years old and the oldest patient is 73 years old. All benign tumors were in age group 15-54. Malignant tumors were found in age group 25-65 and older than sixty-five years. Total of 63 patients were premenopausal and 36 were postmenopausal. Among premenopausal patients 28.6% were in age group 15-24, and 72.4% were in age group 25-54. Among post-menopausal patients 21(58.3%) were in age group 25-54;12(33.3%) patients were in age group 55-64 and 3(8.3%) were >=65 years. The mean age of women with benign tumors were 30±9years and the mean age for malignant tumor were 50.6±10. 8years.The difference in age between the two groups was statistically significant 95% CI [16.4-24.5, P=.000, t=9.99]. Majority of patients were from rural 62(62.6%) and the rest were from urban 37(37.4%). Fifty (50.5%) patients were Muslims in religion 30(30.3%) were Orthodox,17(17.2%) were protestants and 2(2%) were Catholic. Majority of patients were Oromo in ethnicity (58.6%), followed by Amhara (12.1%), Kaffa (12.1%), Waliyita (4%) and others (1%). Seventy-six (76.8%) patients were married,12(12.1%) were single,4(4%) were divorced and 7(7%) were widowed. Majority of patients can't read and write (58.6%),11.1% learned up to grade 8 and 12.1% were in grade 9-10. The mean income of patients was 2809±1928 birr. There was moderate association between income level and histopathology result(eta=0.541)

Table 1: Distribution of cases according to age, menstrual status, USG score, serum CA-125 level, RMI

Parameters	Benign(n=61)	Malignant(n=38)	P-value
Age (in yrs.)			
mean	30±9	50.6±10.8	
15-24	18(18.2%)		
25-54	43(43.4%)	23(23.3%)	
55-64		12(12.1%)	
>=65		3(3%)	
USG characteristics			
Multilocular cyst	11(34.4%)	21(65.6%)	.000
septation	31(49.2%)	32(50.8%)	.062
bilaterality	1(33.3%)	2(66.7%)	.308
solid component	37(44.0%)	47(56.0%)	.006
ascites	2(6.3%)	30(93.7%)	.000
Serum CA-125(U/ml) ±Sd	71.9±90.5	798±918	.000
RMI (mean ±Sd)	164.9±277.8	4386.4±5153.6	.000
USG score 3	20(31.3%)	44(68.7%)	.000
USG score 1	31(88.6%)	4(11.4%)	
RMI<220	47(88.7%)	6(11.3%)	.000
RMI>=220	14(30.4%)	32(69.6%)	
Menstrual status			
Premenopausal	54(85.7%)	9(14.3%)	.000
Postmenopausal	7(19.4%)	29(80.6%)	.000

Age group between 25-54 account for majority of both benign (43.4%) and malignant (23.3%) ovarian tumor cases. In this study multilocular cysts were found in 32.3% (32/99) of cases. Out of which 34.4% (11/32) cases were benign and 65.6% (21/32) were

malignant by histopathology. Multilocular cyst is higher in malignant group compared to benign and it was also statistically significant(P=000). thick septation was found in 63.6% (63/99) of cases and out of which 49.2% (31/63) were benign and 50.8% (32/63) were malignant but the P-value .062 is not statistically significant in our study. Bilaterality in adnexal mass was found 3% (3/99) of cases and out of which 33.3% (1/3) were benign and 66.7% (1/3) were malignant but it fails to be statistically significant in our study(P=.308). Solid component was found in 44% (37/84) of benign cases and 56% (47/84) cases of malignant cases. More solid component was found in malignant ovarian tumor than benign ovarian tumor and it was found to be statistically significant with P-value of .006.Ascites was found in only 6.3%(2/32) of benign cases and 93.8%(30/32) of malignant cases .The study showed larger cases of malignant adnexal mass has ascites compared to benign adnexal mass which was statistically significant with p-value of .000.we assigned ultrasound score of 3 based on presence of two or more finding or score of 1 based on absence specific finding or presence of one finding to study subjects based on USG findings.35.4%(35/99) had score of 1 and 64.6%(64/99) had score of 3.with USG score of 1 benign tumor was found in 88.6%(31/35) and malignant tumor was found in 11.4%(4/35).With USG score of 3 malignant tumor was found in 68.7%(44/64) cases and benign tumor was found in 31.3%(20/64) cases. USG score of 3 with malignant tumor was higher than USG of 3 with benign tumor(P=.000).The mean value of RMI for malignant adnexal mass was(4386.4±5153.6) compared to the mean value of (164±277.8) for benign adnexal mass (P=.000).The mean value of CA-125 for malignant adnexal mass was (798±918)U/ml compared to the mean value of benign adnexal mass (71.9±90.5)U/ml (P value=.000).

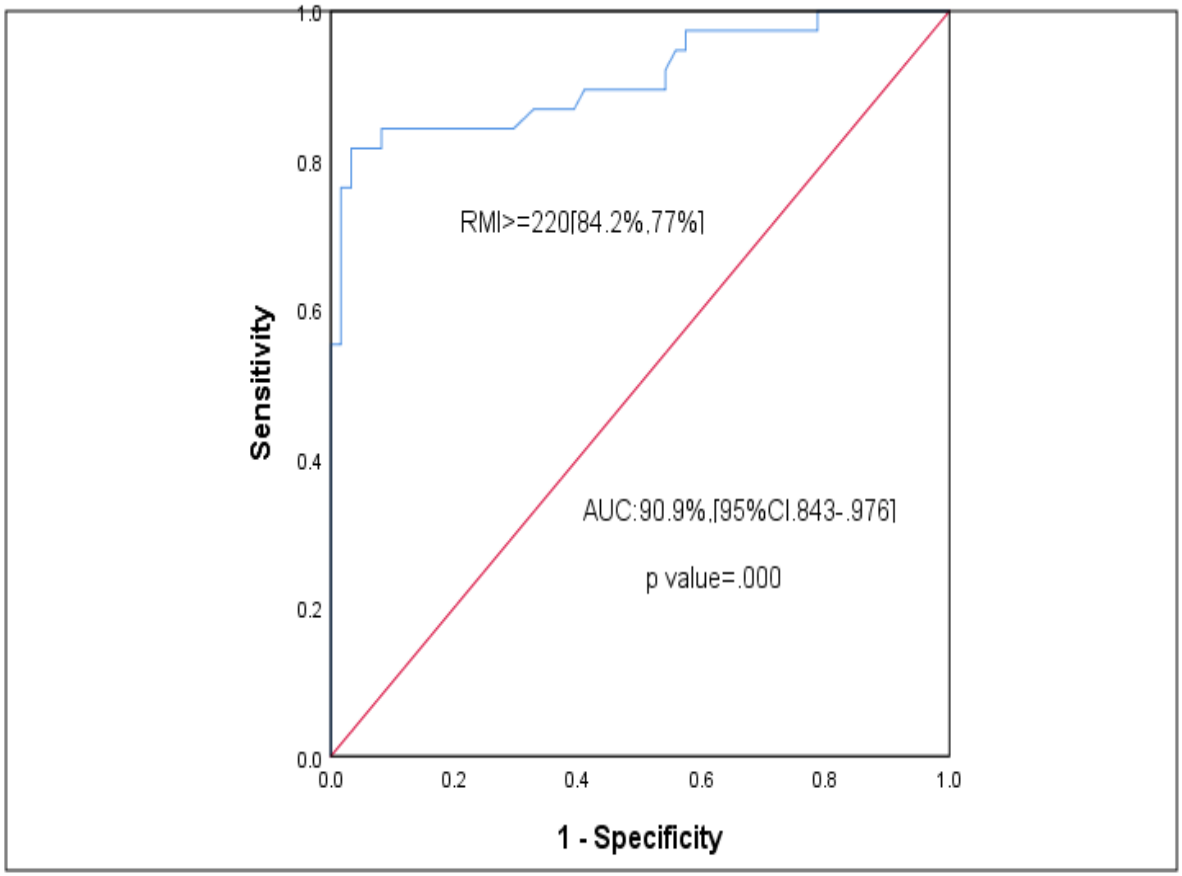
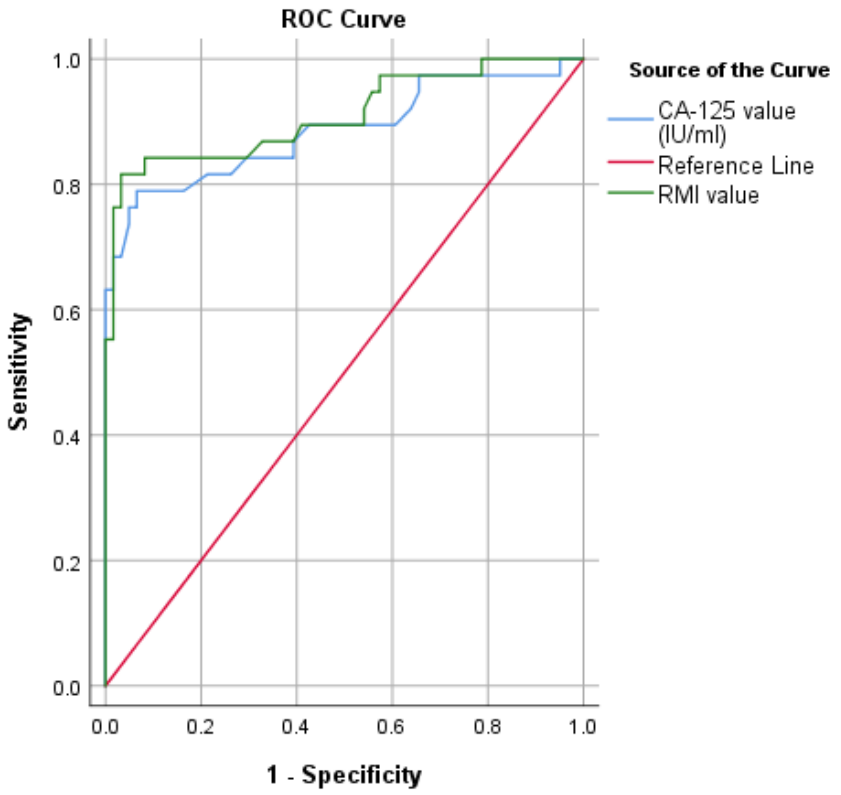


Figure2:ROC curve of RMI for discriminating between benign and malignant adnexal mass

Table 2: Diagnostic efficacy of RMI score as a marker of malignancy

		histopathology		
		benign	malignant	Total
RMI score	<220	47	6	53
	>=220	14	32	46
Total		61	38	99

Sensitivity	specificity	PPV	NPV	diagnostic accuracy
84.2%	**77%**	**69.5%**	**88.7%**	**79.8%**



AUC of RMI=.909 CI 95% [.806-.963]

AUC of CA-125=.885 CI 95% [.842-.977]

Figure 3:Comparison of ROC curves of RMI and CA-125 for discriminating between benign and malignant adnexal mass

As shown on table 2 above, RMI score >=220 has good sensitivity of 84.2%; specificity of 77%; positive predictive value of 69.5%; negative predictive value of 88.7% and diagnostic accuracy of 79.8%.The binary logistic regression analysis show that RMI score >=220 has 17.9 times more likely to have malignant ovarian tumor 95% CI [5.7-47.6],P<0.05.For every 1 unit increment in RMI value there is 0.3% increment in the risk of ovarian ca.

The ROC curve for cut of point of 220 for RMI has excellent area under the curve [AUC:90.9%, (95%CI .843-.976] as depicted by figure 2. As shown by table 2, 69.5% (32/46) of patients with malignant adnexal mass shows positive test result with RMI. 88.7% (46/52) patients with benign adnexal mass showed negative test result with RMI

As shown by figure 3 RMI has larger area under the curve when compared to CA-125.This means RMI has better sensitivity and specificity when compared to CA-125 alone to discriminate between benign and malignant adnexal mass. At cut off point of 96IU/ml CA-125 has sensitivity, specificity, PPV, NPV and diagnostic accuracy of 84.2%,70.5%,64%,87.8%,75.8% respectively.

Table 3: Evaluations of RMI, USG score, CA-125, menopausal status

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic accuracy (%)
RMI>=220	84.2	77	69.5	88.7	79.8
USG score 3	83.5	50.8	53.1	88.6	65.7
CA-125>=96	84.2	70.5	64	87.8	75.8
Menopausal score3	73.7	75.5	64.6	84.4	77.2

As shown by table 3 above when we comparing diagnostic efficacy of individual parameters for CA-125>=96, USG score of 3, menopausal score of 3 to RMI>=220 it has better sensitivity, specificity, PPV, NPV and diagnostic accuracy.

Table 4:Comparison of sensitivity, specificity, PPV, NPV and diagnostic accuracy of RMI at different cut off points

Cut off point RMI	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic accuracy (%)	Odds ratio CI 95%
175	84	75.4	68	87.5	78	16.4 5.73-46.68
200	84.2	75.4	68.8	88.5	78.8	16.4 5.73-46.68
220	84.2	77	69.5	88.7	79.8	17.9 6.22-51.50

As depicted by table 4 above, at cut off point 175 RMI has sensitivity 84%, specificity 75.4%, PPV 68%, NPV 88.5% and diagnostic accuracy of 78%.RMI at cut of point of 220 has better specificity, PPV, NPV and diagnostic accuracy compared to RMI of 200.RMI>=220 will increase probability of diagnosing malignant adnexal mass from 38.4% to 56.7%.RMI<220 will decrease the probability of diagnosing malignant ovarian tumor from 38.4% to 7.1%

Table 5:Distribution of patient symptoms and signs by histopathology result

Symptoms and signs	Histopathology result	
	Benign(n=61)	Malignant(n=38)
Bloating	31(50.8%)	37 (97.4%)
Abdominal pain	57 (93.4%)	38 (100.0%)
Constipation	12 (19.7%)	32 (84.2%)
Urinary compliant	16 (26.2%)	28 (73.7%)
menstrual Irregularity	26 (42.6%)	18 (47.4%)
Early satiety	5 (8.2%)	5 (13.2%)
Appetite loss	6 (9.8%)	27 (71.1%)
Family history	1 (1.6%)	1 (2.6%)
Mass	53 (86.9%)	37 (97.4%)
Ascites	1 (1.6%)	30 (78.9%)

According to table 5, bloating is present in 50.8% of benign cases and 97.4% of malignant cases. Abdominal pain is present in 93.4% of benign cases and all cases of malignant tumors. Constipation present in 19.7% of benign and 84.2% of malignant cases. Urinary compliant is associated with 26.2% of benign cases and 73.7% of malignant cases. Menstrual irregularity is present in 42.6% of benign cases and 47.4% of malignant cases. Early satiety in 8.2% of benign cases and 13.2% of malignant cases. Abdominal mass is present in 86.9% of benign cases and 97.4% of malignant cases. Proportions of patients in malignant group compared to benign group is higher for symptoms and signs described in above table.

Table 6:Result of histopathology

Benign(n=61)	Frequency	Percent
serous cyst adenoma	22	36
fibroma of ovary	1	1.6
mucinous cyst adenoma	9	14.8
dermoid cyst	20	32.9
follicular cyst	3	4.9
corpus luteal cyst	2	3.3
endometrioma	1	1.6
para ovarian cyst	2	3.3
Borderline serous tumor	1	1.6
Malignant(n=38)	**Frequency**	**Percent**
serous cyst adenocarcinoma	24	63.2
mucinous cyst adenocarcinoma	9	23.8
dysgerminoma	2	5.3
clear cell carcinoma	1	2.6
adult granulosa cell tumor	1	2.6
Serous papillary carcinoma	1	2.6

Table 6 above shows that benign ovarian tumor accounts for 61.6% and malignant ovarian tumor accounts for 38.4%. among benign tumors, serous cystadenoma is the most common (27.9%), followed by dermoid cyst (32.9%), mucinous cyst adenoma (14.8%) and follicular cyst (6.6%). Other benign tumors are, corpus luteal cyst (1.6%), endometrioma (3.3%), para ovarian cyst (1.6%) and fibroma of ovary (1.6%). from this study most common malignant ovarian tumor is serous cyst adenocarcinoma (60.5%), followed by mucinous cystadenocarcinoma (23.7%) and dysgerminoma (5.3%). other less common types include clear cell carcinoma (2.6%), adult granulosa cell tumor (2.6%), serous papillary carcinoma (2.6%) and borderline serous tumor (2.6%).

CHAPTER SIX DISCUSSION

Among all gynecologic malignancies ovarian cancer has the worst prognosis since it is diagnosed at advance stage(10–13).Definitive diagnosis of ovarian cancer can be made only after laparotomy(13).About 10% women undergo exploratory laparotomy for ovarian tumor during their life time(27).To detect ovarian cancer at early stage several approaches have been tried including, single cut off CA-125,USG score, Doppler USG parameters but none of them found to be effective (11,20,22).Clinical impression and USG examinations are still major preoperative diagnostic tools for adnexal mass. However due to their limitation, Gynecologists are often faced with unexpected finding intraoperatively and has to perform unplanned procedure. RMI is the most widely used method for preoperative discrimination between benign and malignant adnexal mass(12,13).

In this study the incidence of benign ovarian tumor in all patients presented with adnexal mass and operated for suspected ovarian malignancy is 61.6% and that of malignant ovarian tumor is 38.4%. among malignant cases 23.7% occurs in premenopausal patients and 76.3% cases occur in postmenopausal patients and it is comparable to previous study report(28,29). The mean age for benign tumor is 30±9yrs and the mean age for malignant tumor is 50.6±10.8yrs. The mean age is comparable to previous studies(30)

Most studies reported an increased diagnostic accuracy and performance of RMI with cut off 200(4,5,7,13,17,19,28).In this study, at cut of point 220 RMI had high sensitivity(84.2%),specificity (77%),PPV(69.5%) and NPV(88.7%) and ROC curve showed excellent AUC 90.9% ,CI 95%[.843-.976].Most expert feel that screening protocol for ovarian cancer should have PPV of at least 10% ,that is no more than nine healthy women with false positive screening would undergo unnecessary procedure for each case of ovarian cancer detected(3,20,31). Our study showed RMI at cut off point 220 had larger PPV (69.5%) thus it could be used as screening tool. In this study, binary logistic regression analysis showed that at RMI cut of point >=220 has 17.9 times more likely to have malignant adnexal mass compared to RMI value of<220 95% CI[6.2-51.5].Systematic review of study in 2009 on 116 diagnostic studies on adnexal mass

malignancy was reviewed and showed that RMI cut of 200 had sensitivity 78% and specificity 87% which is similar to our study(32). (5) at cut of point of 200 RMI had sensitivity ,specificity ,PPV,NPV of 80.5%,85.9%,76.3%,88.7% respectively.(13) on 126 found that at cut off point of 200,RMI had sensitivity, specificity ,PPV and NPV of 73.9%,96.5%,96.2%,75.3% respectively slightly better specificity and NPV than this study which can be explained by larger sample size in that study. ROC curve shows that when comparing CA-125 at cut off point 96(IU/ml) to RMI, CA-125 has lower area under the curve (.885 vs .909) which means RMI has better sensitivity and specificity than CA-125 alone to differentiate between malignant and benign ovarian tumor. This finding is similar to previous studies(5,7,13,15,18,23,25). In any scoring system to exclude malignancy ,the false negative rate should ideally be zero or close to zero(13).In our study there is five false positive patients(6/99)(6%).two cases were dysgerminoma, one adult granulosa cell tumor, and two serous cyst adenocarcinoma.

In this study abdominal pain was the most common compliant of the patients presenting in 93.4% of benign cases and all patients with malignant disease; followed abdominal mass present in 89.6% of benign cases and 97.4% of malignant cases. According to study published in AJOG states that, Patients with early ovarian cancer were significantly more likely to have symptoms of mass effect (urinary frequency, constipation, palpable mass, pelvic pressure) compared with patients with benign ovarian neoplasms and borderline cancer(24).study done in Pakistan also state similar finding; 66%of patients with benign tumor and 70% patients with ovarian malignancy had abdominal symptoms of which abdominal pain was the commonest complaint (76%). Abdominal enlargement and abdominal mass were significantly more pronounced in malignant tumors as compared to their benign counterpart(25).

From this study serous cystadenoma is the commonest benign ovarian tumor(36%) followed by dermoid cyst which accounts for (32.9%) followed by mucinous cystadenoma, accounts for(14.8%).In this study, serous cyst adenocarcinoma is the commonest malignant ovarian cancer which accounts for (63.2%) followed by mucinous cyst adenocarcinoma accounts for(23.8%) followed by dysgerminoma which accounts

for(5.3%).Our finding is similar to study conducted in Addis Ababa(26). Unfortunately, serous tumors are mostly high-grade serous carcinomas and characterized by aggressive behavior, late-stage diagnosis, and low survival, contributing to the poor survival for ovarian cancer overall(27)

6.1 Limitation of the study

COVID-19 outbreak worldwide contributed to low cases of adnexal mass operated during study period

Short study period

Borderline tumor was included under benign adnexal mass

CHAPTER SEVEN: CONCULSIONS AND RECOMMENDATIONS

From this study there is high proportion of women with RMI>=220 in malignant ovarian tumor group. Overall, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of RMI are**,84.2%,77%,69.5%,88.7%,79.8%** respectively. The study shows significant role RMI in prediction of ovarian malignancy thus helping in deciding which patients needs laparotomy and which patients need referral to a center where gynecologic oncologists are available. RMI can be used as screening tool short of reliable diagnostic method for ovarian cancer especially in developing countries.

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