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A PROSPECTIVE OBSERVATIONAL STUDY ON ASSESSMENT OF VALUE OF MODIFIED RMI IN PRE-OPERATIVE DISCRIMINATIONBETWEEN BENIGN AND MALIGNANT ADNEXAL MASSES

Original Research

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ABSTRACT

Background: Adnexal masses present a diagnostic challenge, requiring accurate differentiation between benign and malignant lesions for optimal management. Ovarian cancer remains a leading cause of gynecologic cancer mortality, often diagnosed in advanced stages due to the absence of early symptoms. The Risk of Malignancy Index (RMI) combines ultrasound findings, menopausal status, and CA-125 levels to aid clinical decision-making. However, its predictive accuracy remains suboptimal. Incorporating Doppler blood flow analysis into the scoring system (RMI-5) has been proposed to enhance diagnostic performance.

Objective: This study aimed to evaluate the diagnostic accuracy of RMI models, particularly RMI-5, in differentiating benign and malignant adnexal masses.

Methods: A prospective observational study was conducted at a tertiary care hospital over 12 months, enrolling 102 patients with adnexal masses. Patients underwent preoperative assessment, including transabdominal and transvaginal ultrasound with Doppler imaging and serum CA-125 measurement. RMI-1, RMI-2, RMI-3, RMI-4, and RMI-5 scores were calculated and compared with histopathological findings. Diagnostic accuracy was assessed using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and receiver operating characteristic (ROC) curve analysis.

Results: Histopathological analysis confirmed malignancy in 32.4% of cases. RMI-1 demonstrated the highest sensitivity (90.9%) but low specificity (15.9%), while RMI-3 had the highest specificity (69.6%) but lower sensitivity (39.4%). The addition of Doppler blood flow parameters in RMI-5 did not significantly improve diagnostic accuracy. ROC analysis showed no substantial advantage of RMI-5 over existing models.

Conclusion: Although RMI remains a useful tool for risk stratification, the integration of Doppler blood flow analysis did not significantly enhance diagnostic accuracy. Further research is needed to refine predictive models and improve non-invasive preoperative assessments.

Keywords: Adnexal mass, Doppler ultrasound, Malignancy risk, Ovarian cancer, Preoperative diagnosis, Risk of Malignancy Index, Ultrasound.

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INTRODUCTION

Adnexal masses are frequently encountered in gynecological practice, presenting a diagnostic challenge due to their diverse etiologies, ranging from functional cysts to benign and malignant tumors of abdominal and pelvic organs (1). Among gynecologic malignancies, ovarian cancer poses the greatest clinical challenge, with high mortality rates attributed to delayed diagnosis and the absence of early symptoms (2). Epithelial ovarian cancer is the most common histological subtype, accounting for approximately 65% of cases, with most patients presenting in advanced stages due to the asymptomatic nature of early disease progression (3,4). Early detection is critical, as timely intervention significantly improves prognosis (5). However, definitive diagnosis often necessitates surgical exploration, as percutaneous biopsy is not recommended due to the risk of malignant cell spillage into the peritoneal cavity (6). Diagnostic accuracy in distinguishing benign from malignant adnexal masses remains suboptimal when relying solely on demographics, ultrasound (US), or biochemical markers. To enhance diagnostic precision, composite scoring systems such as the Risk of Malignancy Index (RMI) have been developed. The RMI integrates ultrasound findings, menopausal status, and serum CA 125 levels to stratify patients based on malignancy risk, thereby aiding in clinical decision-making (7). The original RMI (RMI-1) has undergone modifications, leading to RMI-2 (1996), RMI-3 (1999), and RMI-4 (adjusted by Yamamoto et al.), each refining the scoring criteria for improved diagnostic performance (8,9). Despite these advancements, no single test has been universally accepted to definitively rule out ovarian malignancy (10-12). Consequently, many patients undergo surgical intervention solely to exclude malignancy, which carries its own risks (13). Screening for ovarian cancer is not routinely recommended for average-to-high-risk women, as the lack of mortality reduction and the high rate of false positives often lead to unnecessary surgeries (13).

To further enhance the predictive accuracy of RMI, a modified RMI (RMI-5) has been introduced by incorporating Doppler blood flow analysis into the scoring system. Doppler ultrasound has demonstrated high diagnostic accuracy, with studies reporting its efficacy in differentiating malignant tumors, which typically exhibit irregular vascular patterns and a resistive index (RI) below 0.6 in contrast to benign masses (10,11). Although prior research has shown promising sensitivity and specificity for modified RMI models (14,15), additional validation is required to establish their clinical utility. The current study aims to determine the incidence of ovarian malignancy in the study population and assess the diagnostic accuracy of different RMI scores. Specifically, it seeks to evaluate whether the inclusion of Doppler parameters in RMI-5 improves preoperative differentiation between benign and malignant adnexal masses, facilitating early referral to gynecologic oncologists for timely intervention.

METHODS

This prospective observational study was conducted in the Obstetrics and Gynecology Department, JPMC Ward 8, Karachi, over a duration of 12 months following the approval of the study protocol by CPSP Review Board and the Ethical Review Committee (ERC). The primary objective was to assess the diagnostic accuracy of various Risk of Malignancy Index (RMI) models, with a particular focus on evaluating the effectiveness of a modified RMI (RMI-5) incorporating Doppler blood flow analysis in differentiating benign from malignant adnexal masses (16). A total of 102 patients with adnexal masses were enrolled in the study, determined using a sample size calculation based on an 80% study power, a 5% level of significance, and a 95% confidence interval. A non-probability consecutive sampling technique was employed for participant selection. Inclusion criteria encompassed all women, regardless of age or parity, who presented with an adnexal mass identified on a prior pelvic ultrasound but without a confirmed histopathological diagnosis. Women scheduled for laparotomy or laparoscopy for suspected ovarian masses were eligible for participation. Written informed consent was obtained from all patients after a thorough explanation of the study objectives and procedures. Exclusion criteria included patients with uncontrolled infections, those unable to provide consent or cooperate, pregnant and lactating women, individuals who had not undergone preoperative CA 125 testing, and those with a prior histopathological diagnosis through previous surgical interventions (17-19).

Each participant underwent a comprehensive clinical assessment, including a detailed history, general physical examination, and focused abdominal and pelvic examinations. Transabdominal and transvaginal ultrasound assessments with Doppler imaging were conducted using a 5 MHz transabdominal probe and a 7.5 MHz transvaginal probe (Medison, Sonoace X6, Korea). To maintain consistency, all ultrasound scans were performed by a single experienced sonographer blinded to the clinical history. Serum CA 125 levels were

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measured preoperatively, and RMI-1, RMI-2, RMI-3, RMI-4, and RMI-5 scores were calculated and later compared with histopathological findings, which served as the gold standard for diagnosing malignancy (20). RMI-1 was computed as U × M × CA 125, where ultrasound scores (U) were assigned based on the presence of malignancy-associated features: U=0 for no suspicious findings, U=1 for one suspicious feature, and U=3 for two or more suspicious features. Menopausal status (M) was assigned a value of 1 for premenopausal women and 3 for postmenopausal women. RMI-2 was similarly calculated but assigned a higher ultrasound weighting (U=4) for masses with ≥2 suspicious features, and menopausal status was scored as M=1 for premenopausal and M=4 for postmenopausal women. RMI-3 retained the scoring system of RMI-1. RMI-4 incorporated tumor size (S) into the calculation, where S=1 for tumors <7 cm and S=2 for tumors ≥7 cm (21).

In this study, a modified RMI (RMI-5) was introduced by incorporating Doppler blood flow (D) into the scoring formula: RMI-5 = CA 125 × U × M × D. Serum CA 125 levels above 30 U/ml were considered abnormal. Ultrasound scoring (U) followed the same parameters as previous RMIs, while menopausal status (M) was graded as 1 for premenopausal and 3 for postmenopausal women (defined as ≥1 year of amenorrhea or age >50 in hysterectomized patients). Doppler blood flow was assessed based on vascularity patterns within the mass, with high blood flow assigned D=2 and low blood flow assigned D=1 (22). All patients underwent surgical intervention, and histopathological findings were documented as the definitive diagnostic outcome. Data analysis was performed using Microsoft Excel 2010 and the Statistical Package for Social Sciences (SPSS) version 26.0. Continuous variables were presented as mean ± standard deviation for normally distributed data, while categorical variables were expressed as frequencies and percentages. Comparative analysis between benign and malignant cases was conducted using the independent Student's t-test for normally distributed continuous variables, the Mann-Whitney U test for non-parametric variables, and the chi-square test for categorical variables. The predictive performance of RMI scores was evaluated using receiver operating characteristic (ROC) curve analysis, with sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) calculated to determine diagnostic accuracy. A p-value of <0.05 was considered statistically significant (23).

RESULTS

A total of 102 patients were included in the study, with a mean tumor size of 7.2 ± 2.6 cm. The majority of the participants (58.8%) resided in urban areas, while 41.2% were from rural regions. Regarding body mass index (BMI), 39.2% of patients had a normal BMI, 27.5% were overweight, 22.5% were obese, and 10.8% were underweight. Previous abdominal or pelvic surgery was reported in 39.2% of cases, whereas 60.8% had no prior surgical history. Multiparous women comprised 74.5% of the cohort, while 25.5% were nulliparous. Menopausal status was nearly evenly distributed, with 49% of patients being postmenopausal and 51% premenopausal. The risk stratification of patients using the Risk of Malignancy Index (RMI) categorized 25.5% as high risk (>200), 42.2% as intermediate risk (25-200), and 32.4% as low risk (<25). Ultrasound findings revealed that 47.1% of patients had multilocular cysts, while 52.9% did not. Solid areas within adnexal masses were present in 58.8% of cases. Bilateral ovarian masses were identified in 32.4% of patients, and ascites was detected in 42.2%. Metastases were observed in 19.6% of cases based on sonographic evaluation.

Doppler blood flow assessment demonstrated high vascularity (D2) in 58.8% of cases, whereas 41.2% exhibited low blood flow (D1). Among the study population, 25.5% had diabetes mellitus, 41.2% had hypertension, 26.5% were obese, and 11.8% had coronary heart disease. A family history of ovarian cancer was noted in 19.6% of cases. Regarding clinical symptoms, abdominal pain was the most commonly reported symptom, present in 58.8% of patients, followed by pelvic pain (46.1%), dysmenorrhea (46.1%), menorrhagia (36.3%), and metrorrhagia (25.5%). Ascites was present in 31.4% of cases, while weight loss was reported in 37.3%. Histopathological findings confirmed malignancy in 32.4% of cases, while 67.6% were classified as benign. Preoperative serum CA-125 levels had a mean value of 149.4 ± 77.2 U/mL. Doppler indices revealed a mean resistive index (RI) of 0.7 ± 0.1 and a mean pulsatility index (PI) of 1.2 ± 0.3. Comparison of benign and malignant cases using independent t-tests showed no statistically significant difference in tumor size (7.1 ± 2.6 cm vs. 7.5 ± 2.6 cm, p=0.442) or CA-125 levels (151.3 ± 77.2 U/mL vs. 145.4 ± 77.2 U/mL, p=0.698). Similarly, no significant differences were observed in RI (0.7 ± 0.1 vs. 0.6 ± 0.1, p=0.222) or PI (1.3 ± 0.3 vs. 1.2 ± 0.3, p=0.529).

Diagnostic accuracy analysis using receiver operating characteristic (ROC) curves showed area under the curve (AUC) values of 0.510, 0.518, 0.462, 0.428, and 0.476 for RMI-1, RMI-2, RMI-3, RMI-4, and RMI-5, respectively. Sensitivity was highest for RMI-1 (90.9%) and lowest for RMI-3 (39.4%), whereas specificity was highest for RMI-3 (69.6%) and lowest for RMI-4 (14.5%). Positive predictive value (PPV) ranged from 33% (RMI-4) to 38.2% (RMI-3), while negative predictive value (NPV) varied from 70.6% (RMI-3) to 78.6% (RMI-1). The highest Youden's Index was observed for RMI-2 (0.109), while RMI-4 had the lowest value (0.024). Paired ROC analysis comparing RMI-5 with other RMI models using the Wilcoxon test revealed statistically significant differences between RMI-5 and RMI-

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1 (p=0.000) and RMI-5 and RMI-3 (p=0.033), while comparisons with RMI-2 (p=0.107) and RMI-4 (p=0.129) were not statistically significant. McNemar's test assessing sensitivity and specificity differences between RMI-5 and other models showed no statistically significant differences, with p-values of 1.000 for all comparisons.

Table 1: Frequency and Percentage of Demographic and Clinical Variables

Variable	Category	Frequency	Percentage (%)
Residential Status	Rural	42	41.2
	Urban	60	58.8
BMI	Normal (18.5-24.5 kg/mÂ²)	40	39.2
	Obese (>30 kg/mÂ²)	23	22.5
	Overweight (25-29.5 kg/mÂ²)	28	27.5
	Underweight (<18.5 kg/mÂ²)	11	10.8
Previous Surgery	No	62	60.8
	Yes	40	39.2
Parity	Multipara	76	74.5
	Nullipara	26	25.5
Menopausal Status	Postmenopausal	50	49
	Premenopausal	52	51
RMI Risk	High risk (>200)	26	25.5
	Intermediate risk (25-200)	43	42.2
	Low risk (<25)	33	32.4

Table 2: Frequency and Percentage of Ultrasound Findings for RMI Calculation

Variable	Category	Frequency	Percentage (%)
Multilocular Cyst	No	54	52.9
	Yes	48	47.1
Solid Areas	No	42	41.2
	Yes	60	58.8
Bilateral Masses	No	69	67.6
	Yes	33	32.4
Ascites	No	59	57.8
	Yes	43	42.2
Metastases	No	82	80.4
	Yes	20	19.6

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Table 3: Frequency and Percentage of Clinical Data and Risk Factors

Variable	Category	Frequency	Percentage (%)
Doppler Blood Flow	High blood flow (D2)	60	58.8
	Low blood flow (D1)	42	41.2
Diabetes Mellitus	No	76	74.5
	Yes	26	25.5
Hypertension	No	60	58.8
	Yes	42	41.2
Obesity	No	75	73.5
	Yes	27	26.5
Coronary Heart Disease (CHD)	No	90	88.2
	Yes	12	11.8
Family History	No	82	80.4
	Yes	20	19.6
Abdominal Pain	No	42	41.2
	Yes	60	58.8
Pelvic Pain	No	55	53.9
	Yes	47	46.1
Dysmenorrhea	No	55	53.9
	Yes	47	46.1
Menorrhagia	No	65	63.7
	Yes	37	36.3
Metrorrhagia	No	76	74.5
	Yes	26	25.5
Ascites	No	70	68.6
	Yes	32	31.4
Weight Loss	No	64	62.7
	Yes	38	37.3
Histopathology Outcome	Benign	69	67.6
	Malignant	33	32.4

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Table 4: Mean and Standard Deviation (SD) of Key Diagnostic Variables

	Variable	Mean	Standard Deviation (SD)
Tumor Size (cm)	Tumor Size (cm)	7.2	2.6
Preoperative CA-125 (U/mL)	Preoperative CA-125 (U/mL)	149.4	77.2
Resistive Index (RI)	Resistive Index (RI)	0.7	0.1
Pulsatility Index (PI)	Pulsatility Index (PI)	1.2	0.3

Table 5: Comparison of Benign vs. Malignant Groups (Statistical Analysis Results)

Variable	Test Applied	Benign Mean	Malignant Mean	P-value
Tumor Size (cm)	Independent t-test	7.1	7.5	0.442
Preoperative CA-125 (U/mL)	Independent t-test	151.3	145.4	0.698
Resistive Index (RI)	Independent t-test	0.7	0.6	0.222
Pulsatility Index (PI)	Independent t-test	1.3	1.2	0.529

Table 6: Diagnostic Accuracy of RMI Models (ROC Analysis, Sensitivity, Specificity, PPV, NPV, and Youden's Index)

RMI Model	Test Applied	Value
RMI-1	ROC Analysis	0.51
RMI-2		0.518
RMI-3		0.462
RMI-4		0.428
RMI-5		0.476
RMI-1	Sensitivity	0.909
RMI-2		0.848
RMI-3		0.394
RMI-4		0.879
RMI-5		0.788
RMI-1	Specificity	0.159
RMI-2		0.261
RMI-3		0.696
RMI-4		0.145
RMI-5		0.29
RMI-1	PPV	0.341

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RMI-2		0.354
RMI Model	**Test Applied**	**Value**
RMI-3		0.382
RMI-4		0.33
RMI-5		0.347
RMI-1	NPV	0.786
RMI-2		0.783
RMI-3		0.706
RMI-4		0.714
RMI-5		0.741
RMI-1	Youden's Index	0.069
RMI-2		0.109
RMI-3		0.09
RMI-4		0.024
RMI-5		0.078

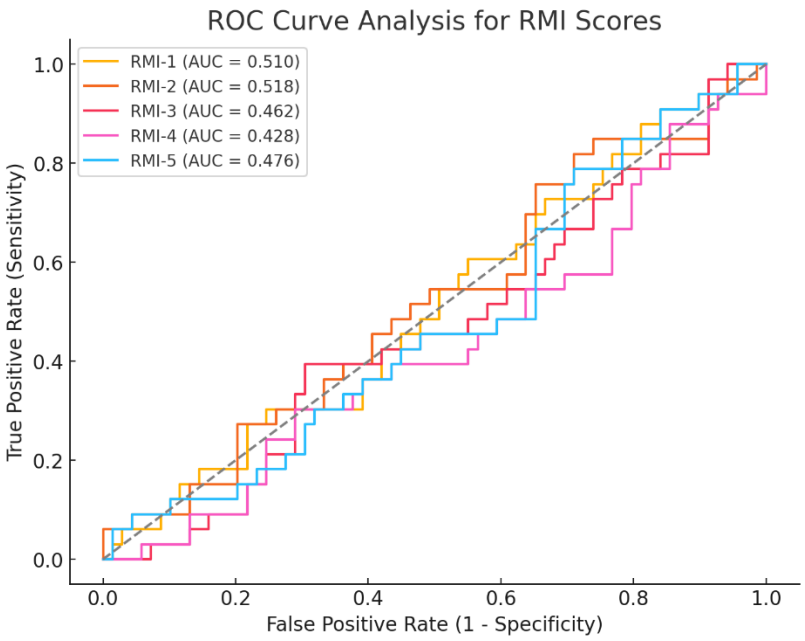


Figure 1 ROC Curve Analysis for RMI Scores

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Table 7: Paired ROC Analysis and McNemar's Test for RMI-5 vs. Other RMI Models

Comparison	Test Applied	P-value
RMI-5 vs. RMI-1	Paired ROC Analysis (Wilcoxon Test)	0.0
RMI-5 vs. RMI-2		0.107
RMI-5 vs. RMI-3		0.033
RMI-5 vs. RMI-4		0.129
RMI-5 vs. RMI-1	McNemar's Test	1.0
RMI-5 vs. RMI-2		1.0
RMI-5 vs. RMI-3		1.0
RMI-5 vs. RMI-4		1.0

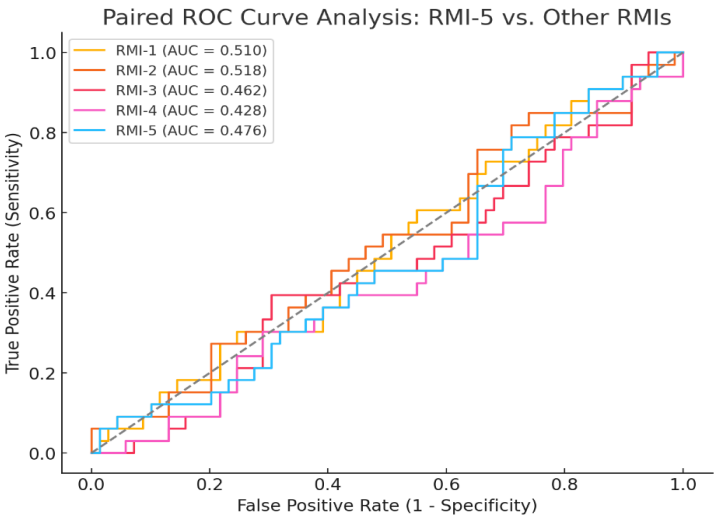


Figure 2 Paired ROC Curve Analysis

DISCUSSION

The study evaluated the diagnostic performance of the modified Risk of Malignancy Index (RMI-5) in preoperative differentiation between benign and malignant adnexal masses. Findings indicated that none of the RMI models, including RMI-5, exhibited an optimal balance of sensitivity and specificity. Although RMI-1 demonstrated the highest sensitivity, its specificity was considerably low. Conversely, RMI-3 showed higher specificity but at the cost of reduced sensitivity. The incorporation of Doppler blood flow parameters in RMI-5 did not result in significant improvement compared to the conventional RMI models. This suggests that while Doppler ultrasound is a valuable adjunct in gynecologic oncology, its role within a composite scoring system like RMI-5 may not be as impactful as previously anticipated (24). Comparative analysis with prior literature reveals varying results regarding the utility of Doppler parameters in malignancy risk assessment. Several studies have reported improved diagnostic accuracy when incorporating Doppler flow characteristics, particularly resistive index and pulsatility index, into RMI calculations. However, findings from this study did not substantiate a statistically significant advantage of Doppler integration. These discrepancies may be attributed to variations in Doppler assessment protocols, operator expertise, and differences in patient populations. The mean resistive index and pulsatility index values

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between benign and malignant groups did not show significant variation, further supporting the notion that Doppler parameters alone may not be definitive indicators of malignancy (25).

Despite these findings, the study provided valuable insights into the limitations of existing RMI models. The reliance on CA-125 as a key component within these indices has long been debated, given its limited specificity in premenopausal women and conditions such as endometriosis or pelvic inflammatory disease. The present study reaffirmed that while CA-125 remains a useful biomarker, its elevated levels were not consistently predictive of malignancy. Similarly, ultrasound-based morphological scoring, though instrumental in risk stratification, yielded considerable overlap between benign and malignant masses, contributing to diagnostic uncertainty (26). The strengths of this study included a prospective design, standardized ultrasound and Doppler evaluation protocols, and histopathological confirmation as the gold standard. The use of multiple RMI models for comparative analysis provided a comprehensive assessment of their diagnostic utility. However, certain limitations warrant consideration. The study was conducted at a single center, potentially limiting the generalizability of the findings. Sample size constraints may have influenced the statistical power, particularly in subgroup analyses. Additionally, interobserver variability in Doppler assessment, despite the use of a single sonographer, remains a potential confounder (18). Future research should focus on refining composite risk assessment tools by integrating novel biomarkers and advanced imaging modalities. The emergence of artificial intelligence-driven ultrasound interpretation, machine learning algorithms, and biomarker panels holds promise for enhancing diagnostic precision. Prospective multicenter studies with larger cohorts would provide more robust validation of modified RMI models. Given the persistent challenge of ovarian cancer diagnosis, continued efforts are essential to develop non-invasive, high-accuracy predictive models that minimize unnecessary surgical interventions while ensuring timely detection of malignancy.

CONCLUSION

The study assessed the diagnostic accuracy of various Risk of Malignancy Index models, including a modified version incorporating Doppler blood flow analysis, to enhance preoperative differentiation between benign and malignant adnexal masses. While traditional RMI models remain valuable in clinical decision-making, the addition of Doppler parameters did not significantly improve predictive performance. The findings highlight the persistent challenge of optimizing non-invasive diagnostic tools for ovarian malignancy, emphasizing the need for more refined risk stratification methods. Integrating novel biomarkers and advanced imaging techniques may offer a more precise approach, reducing unnecessary surgical interventions while ensuring timely detection and management of malignant cases.

AUTHOR CONTRIBUTIONS

Author	Contribution
Bisma Shaikh	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Haleema Yasmin*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Nighat	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Hira Jam	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Farzana	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published

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