

ASSOCIATION OF RED CELL DISTRIBUTION WIDTH (RDW) TO SERUM ALBUMIN RATIO WITH PROGNOSIS OF CORONARY HEART DISEASE(CHD) IN PATIENTS WITH ACUTE CORONARY SYNDROME (ACS).

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Abstract

Objective: To determine the association between RDW to Albumin ratio and prognosis of acute coronary syndrome (ACS) in form of all-cause Mortality in patients admitted in ICU, CCU or Medicine Department.

Study Design: Prospective Cohort Study.

Study Setting: The Study was planned at Department of Internal Medicine and Cardiac Care Unit (CCU), Recep Tayyip Erdogan Indus Hospital, Muzaffargarh.

Study Duration: From September'2024 to February'2025.

Methodology: This study enrolled 126 patients using non-probability consecutive sampling, categorized into high RAR (≥ 3.5) and low RAR (< 3.5) groups. Demographics, clinical data, RDW, and albumin levels were recorded at admission. Patients were followed for 90-day all-cause mortality.

Results: Mean age was 52.29 ± 19.64 years, and 57.9% were male. The 90-day mortality rate was 12.7%. Mortality was significantly higher in the high RAR group (19.0%) versus the low RAR group (6.3%) with $RR = 3.471$ ($p = 0.032$). Subgroup analysis showed higher mortality among older patients, females, diabetics, hypertensives, and those with a positive family history of ischemic heart disease(IHD).

Conclusion: High RAR is a significant, low-cost biomarker associated with increased short-term mortality in ACS patients. It may serve as an early prognostic indicator to improve risk stratification and guide targeted interventions.

INTRODUCTION

The 90 day Mortality of Acute Myocardial infarction (AMI) remains high^{1,3} instead of multiple advances in treatment modalities that is 12.2%.⁴ In 2016 Annual mortality rate was around 17.9 million due to coronary heart disease.⁵ Coronary Heart Disease (CHD) includes all patients with Angina, Unstable Angina(UA), New Onset Left Bundle Branch Block (LBBB), ST-Elevation Myocardial Infarction(STEMI),Non ST-Elevation Myocardial Infarction(NSTEMI).⁶ RDW to Albumin ratio is a novel biomarker in predicting prognosis in CHD and even stroke patients.⁷ Low Serum Albumin level is an independent poor prognostic factor as albumin is an anti-inflammatory, antioxidant, anticoagulant and has role as anti platelet aggregation.⁸ RDW is indicator of heterogeneity of red blood cells but now it is emerging biomarker indicating inflammatory stress.⁴ Therefore RDW to serum albumin ratio is promising prognostic factor for short term and indicator of risk of mortality after acute myocardial infarction.⁴

Coronary Heart Disease is an inflammatory process and healing depends on the inflammatory markers.⁹ High RDW to Albumin ratio (RAR) predicts poor prognosis. Chronic Inflammation, Ineffective erythropoiesis, hypoxia due to coronary artery disease causes erythropoietin production and bone marrow releases immature RBCs in blood stream that leads to abnormally increased RDW ratio.¹³ RDW is associated with atherosclerotic plaque formation, hypertension, acute myocardial infarction(AMI)and all cause mortality after Percutaneous coronary angiography (PCI).¹³

A retrospective Observational cohort study conducted by H Li et al in 2023 about Association between RDW to albumin ratio and prognosis in patients of AMI considering 90 day mortality after admission showed that Of 2081 AMI patients, 823 were male and 1258 women, 631(30.3%) were below and 1450(69.7%) were above 65yrs of age. 543 (26.09%) died within 90-day follow-up and 1538 (73.9%) survived. 1040(50%) of the population was in High RAR group of which 653 (42.5%) survived and 387 (71.3%) died. 1041(50%) of low RAR group patients had 885 (57.5%) survival rate & 156 (28.7%) faced mortality.⁴

Another retrospective cohort study from Jian L et al in 2023 enrolled 2594 patients with median age of 57-76yrs, there were 1634 females. 2276 survived and 318 (12.26%) died. Overall high RAR group had 812 patients and 1782 were from low RAR group. 130 (7.30%) of 318 from mortality group were with RAR less than 4.77 and 188(23.15%) are with RAR greater than 4.77 with $p < 0.00$.⁹

The aim of this study is to determine the association of RAR in CHD as prognostic factor, this association is an emerging tool to predict early prognosis and in hospital mortality with a very basic and cheap investigation allowing critical monitoring and early intervention in high risk patients to prevent worse outcomes.

METHODOLOGY

This prospective cohort study was conducted at the Department of Internal Medicine and the Cardiac Care Unit (CCU) of Recep Tayyip Erdogan Indus Hospital, Muzaffargarh, over a duration of six months following the approval of the research synopsis. A total of 126 patients were enrolled using a non-probability consecutive sampling technique, with 63 patients allocated to the high RDW to albumin ratio (RAR) group (≥ 3.5) and 63 to the low RAR group (< 3.5). The sample size was calculated based on previously reported mortality rates: 23.15% in the high RAR group and 7.30% in the low RAR group, with a significance level of 5% and a statistical power of 80%.

The age range of our enrolled cases was 18-89 years while both genders were part of our study having CHD including unstable angina, stable angina, NSTEMI, or AMI and admitted in our department. Whereas those with a history of coronary artery bypass graft (CABG), or those who had received a blood transfusion or serum albumin infusion within the preceding two months. We obtained informed consent of the patients following approval from the Institutional Research Review Board, eligible patients were enrolled at the time of admission. Demographic data including gender, age, body mass index (BMI), and clinical variables such as hypertension, smoking status, diabetes mellitus, alcohol use, and family history of IHD were documented using a structured proforma.

On presentation, blood samples were collected for complete blood count (CBC) and serum albumin measurement. The RDW to albumin ratio (RAR) was calculated, and patients were categorized as “exposed” ($\text{RAR} \geq 3.5$) or “unexposed” ($\text{RAR} < 3.5$). All patients were followed for 90 days post-admission, either through hospital records or outpatient follow-up, to assess all-cause mortality as the primary outcome, and length of hospital stay as the secondary outcome. Data were analyzed using SPSS version 26.0. Categorical variables (gender, smoker, hypertension, diabetes mellitus, alcoholic

status, mortality, RAR group, and family history of CHD) were reported as frequencies and percentages. Continuous variables (age, BMI, RDW, serum albumin, and RAR) were analyzed as mean \pm standard deviation. The association between RAR and mortality was evaluated using relative risk, and a chi-square test was applied post-stratification to control for potential confounders such as age, gender, smoking status, hypertension, diabetes, alcoholic status, and family history of CHD.

RESULTS:

Table 1: MEANS OF CONTINUOUS VARIABLES

Variable	Mean	Std. Deviation
Age	52.29	19.64
BMI	26.71	5.38
Hemoglobin Hb	13.57	2.00
MCV	86.02	5.48
TLC	7.35	2.02
RDW	3.62	1.31
Serum Albumin	1.01	0.06
RAR	3.58	1.26
Length of Hospital Stay	8.38	4.25

Table 1 presents the mean age of patients with acute coronary syndrome (ACS) was 52.29 ± 19.64 years, and the mean BMI was 26.71 ± 5.38 kg/m², indicating an overweight tendency among the cohort. The average hemoglobin (Hb) level was 13.57 ± 2.00 g/dL, while the mean mean corpuscular volume (MCV) was 86.02 ± 5.48 fL. The total

leukocyte count (TLC) averaged $7.35 \pm 2.02 \times 10^9/\text{L}$. Regarding biochemical markers, the mean red cell distribution width (RDW) was 3.62 ± 1.31 , serum albumin averaged 1.01 ± 0.06 g/dL, and the RDW to RAR had a mean of 3.58 ± 1.26 . The average length of hospital stay was 8.38 ± 4.25 days.

Table 2: CLINICAL AND DEMOGRAPHIC DISTRIBUTION IN ACS COHORT

Variable	Group	Count	Percent (%)
Age Group	18-50	62	49.2
	51-89	64	50.8
Gender	Male	73	57.9
	Female	53	42.1
Residence	Urban	69	54.8
	Rural	57	45.2
BMI Group	≤ 25	51	40.5
	> 25	75	59.5
Smoking	Yes	64	50.8
	No	62	49.2
Hypertension	Yes	60	47.6

	No	66	52.4
Diabetes Mellitus	Yes	73	57.9
	No	53	42.1
Alcoholic Status	Yes	44	34.9
	No	82	65.1
Family History of IHD	Yes	68	54.0
	No	58	46.0
RAR Group	High RAR (≥ 3.5)	63	50.0
	Low RAR (< 3.5)	63	50.0
Diagnosis	Myocardial Infarct	34	27.0
	NSTEMI	27	21.4
	Angina	40	31.7
	Heart Failure	25	19.8
90-day Mortality	Yes	16	12.7
	No	110	87.3

Table 2 summarizes the clinical and demographic distribution of the study participants. The age distribution was nearly even, with 49.2% aged 18–50 years and 50.8% aged 51–89 years. Males comprised 57.9% of the sample, and 54.8% of patients resided in urban areas. Based on BMI, 40.5% of patients were within or below the normal range (≤ 25 kg/m²), while 59.5% were overweight or obese (> 25 kg/m²). The prevalence of smoking was 50.8%, hypertension was present in 47.6%, and 57.9% of participants had diabetes mellitus. Alcoholic status was positive in

34.9% of cases. A positive family history of IHD was reported by 54.0% of patients. The cohort was equally divided between high and low RAR groups (50% each). Regarding clinical diagnoses, 27.0% had myocardial infarction, 21.4% had NSTEMI, 31.7% had angina, and 19.8% presented with heart failure. The 90-day mortality rate was 12.7%, with 87.3% of patients surviving during this follow-up period.

Table 3: ASSOCIATION OF RDW TO SERUM ALBUMIN RATIO WITH PROGNOSIS OF CORONARY HEART DISEASE(CHD) IN PATIENTS WITH ACS

@ 90day Mortality	High RAR (≥ 3.5) Count (%)	Low RAR (< 3.5) Count (%)	Total Count (%)	RR	p-value
Yes	12 (19.0%)	4 (6.3%)	16 (12.7%)	3.471	.032
No	51 (81.0%)	59 (93.7%)	110 (87.3%)		
Total	63 (100.0%)	63 (100.0%)	126 (100.0%)		

Table 3 evaluates the association between RDW to RAR and 90-day mortality. Among patients with high RAR (≥ 3.5), 12 out of 63 (19.0%) died within 90 days, compared to 4 out of 63 (6.3%) in the low RAR (< 3.5) group. This yielded a total of 16 deaths (12.7%) across the cohort. The calculated relative risk (RR) of mortality for high RAR patients was 3.471, indicating that patients in the high RAR

group had more than three times the risk of death compared to those in the low RAR group. The association was found to be statistically significant ($p = .032$), suggesting that a high RDW to albumin ratio is a strong prognostic marker for adverse outcomes in ACS.

Table 4: ASSOCIATION OF RDW TO SERUM ALBUMIN RATIO WITH PROGNOSIS OF CORONARY HEART DISEASE(CHD) IN PATIENTS WITH ACS ACCORDING TO VARIOUS EFFECT MODIFIERS

Stratification Variable	Group	High RAR (≥ 3.5) Count (%)	Low RAR (< 3.5) Count (%)	Total Count (%)	RR / OR	p-value
Age Group	18–50	6 (16.2%)	2 (8.0%)	8 (12.9%)	2.23	0.344
	51–89	6 (23.1%)	2 (5.3%)	8 (12.5%)	5.40	0.034
Gender	Male	7 (19.4%)	4 (10.8%)	11 (15.1%)	1.99	0.303
	Female	5 (18.5%)	0 (0.0%)	5 (9.4%)	∞	0.021
Residence	Urban	8 (22.9%)	2 (5.9%)	10 (14.5%)	4.74	0.045
	Rural	4 (14.3%)	2 (6.9%)	6 (10.5%)	2.25	0.363
BMI Group	≤ 25	4 (17.4%)	1 (3.6%)	5 (9.8%)	5.68	0.099
	> 25	8 (20.0%)	3 (8.6%)	11 (14.7%)	2.67	0.163
Smoking	Yes	7 (18.9%)	2 (7.4%)	9 (14.1%)	2.92	0.191
	No	5 (19.2%)	2 (5.6%)	7 (11.3%)	4.05	0.093
Hypertension	Yes	6 (26.1%)	2 (5.4%)	8 (13.3%)	6.18	0.022
	No	6 (15.0%)	2 (7.7%)	8 (12.1%)	2.12	0.374
Diabetes Mellitus	Yes	10 (27.0%)	3 (8.3%)	13 (17.8%)	4.07	0.037
	No	2 (7.7%)	1 (3.7%)	3 (5.7%)	2.17	0.530
Alcoholic Status	Yes	6 (21.4%)	1 (6.3%)	7 (15.9%)	4.09	0.185
	No	6 (17.1%)	3 (6.4%)	9 (11.0%)	3.03	0.123
Family History of IHD	Yes	9 (25.0%)	1 (3.1%)	10 (14.7%)	10.33	0.011
	No	3 (11.1%)	3 (9.7%)	6 (10.3%)	1.17	0.858
Diagnosis	Myocardial Infarct	1 (6.3%)	1 (5.6%)	2 (5.9%)	1.13	0.932
	NSTEMI	1 (6.7%)	0 (0.0%)	1 (3.7%)	∞	0.362
	Angina	5 (26.3%)	1 (4.8%)	6 (15.0%)	7.14	0.057
	Heart Failure	5 (38.5%)	2 (16.7%)	7 (28.0%)	3.13	0.225

Table 4 describes the stratified association between high RDW to albumin ratio (RAR ≥ 3.5) and 90-day mortality among patients with acute coronary syndrome (ACS), across multiple subgroups. Among the two age categories, the association was more pronounced in older patients (aged 51–89), where 23.1% of those with high RAR died compared to 5.3% in the low RAR group (RR = 5.40, $p = 0.034$). Although younger patients (18–50 years) also showed higher mortality in the high RAR group (16.2% vs 8.0%), ($p = 0.344$).

When stratified by gender, the effect was highly significant among females, with a 90-day mortality of 18.5% in the high RAR group compared to 0% in the low RAR group ($p = 0.021$). In males, the mortality difference was higher in high RAR cases (19.4% vs 10.8%), though not statistically significant ($p = 0.303$). Regarding residence, urban patients

exhibited a notable difference in mortality (22.9% in high RAR vs 5.9% in low RAR; RR = 4.74, $p = 0.045$), whereas the difference among rural patients was not significant.

BMI stratification revealed that patients with BMI ≤ 25 showed higher mortality in the high RAR group (17.4% vs 3.6%, RR = 5.68), while those with BMI > 25 also had elevated mortality (20.0% vs 8.6%, RR = 2.67), ($p = 0.099$ and 0.163, respectively). In the smoking group, high RAR was associated with increased mortality among both smokers (18.9% vs 7.4%) and non-smokers (19.2% vs 5.6%), but these findings did not reach statistical significance.

A statistically significant association was observed among hypertensive patients, where mortality was 26.1% in the high RAR group versus 5.4% in the low RAR group (RR = 6.18, $p = 0.022$). In contrast, the difference among non-hypertensive patients was

not significant. Similarly, diabetic patients with high RAR had significantly greater mortality (27.0% vs 8.3%, RR = 4.07, $p = 0.037$), while non-diabetics showed a weaker and non-significant difference.

Among patients with a history of alcohol use, the mortality difference favored higher risk with high RAR (21.4% vs 6.3%), and a similar trend was observed in non-alcoholics. However, both subgroups did not reach statistical significance. Family history of ischemic heart disease showed a marked impact; patients with a positive family history had a significantly higher mortality in the high RAR group (25.0% vs 3.1%, RR = 10.33, $p = 0.011$), while those without such history showed no significant difference.

Lastly, diagnosis-specific stratification showed that patients with angina (26.3% vs 4.8%) and heart failure (38.5% vs 16.7%) had higher mortality associated with high RAR, though these findings were only borderline or not statistically significant. Patients with myocardial infarction or NSTEMI did not demonstrate meaningful differences between RAR groups.

In summary, high RDW to albumin ratio was associated with increased short-term mortality in multiple clinically important subgroups, particularly among older patients, females, diabetics, hypertensives, urban residents, and those with a family history of IHD. This supports the utility of RAR as a prognostic indicator in ACS, especially in high-risk populations.

DISCUSSION

Over the past few years, substantial research has examined the prognostic significance of the red blood cell distribution width-to-serum albumin ratio (RAR) in patients with acute coronary syndrome (ACS), a critical presentation within the spectrum of coronary heart disease (CHD). The present study sought to evaluate the utility of RAR as a predictive marker for mortality in ACS cases. Our results demonstrated a statistically significant association between elevated RAR values (≥ 3.5) and 90-day all-cause mortality, with a relative risk (RR) of 3.471. This suggests that patients in the high RAR group had more than a threefold increased risk of death compared to those with lower RAR levels. These findings align with previously published studies,

further substantiating RAR as a robust indicator of adverse outcomes in ACS and other cardiovascular disorders.

In comparison to **Li D, Ruan Z, Wu B (2022)**,¹³ which analyzed mortality risk in AMI patients and found that $\text{RAR} \geq 4$ was significantly associated with 30-day, 1-year, and 3-year mortality, our study echoes these results but focuses specifically on 90-day mortality. In their study,¹³ they found that RAR had high AUC values for mortality prediction (0.703 for 30-day mortality), while our study identified that high RAR was associated with significantly higher mortality within the first 90 days ($p = 0.032$). Although our cut-off for high RAR was 3.5, whereas theirs was 4.0, both studies show a clear pattern of RAR's association with mortality, validating its role as a reliable short-term prognostic marker. The differences in cut-off values across studies highlight the need for further research to standardize the threshold for RAR, but the consistency of its prognostic value is evident.

Similarly, **Jian L, Zhang Z, Zhou Q (2023)**,⁹ which examined the in-hospital mortality of ICU patients with AMI, found that RAR was independently associated with mortality (OR = 1.27, 95% CI: 1.12–1.43) and suggested an optimal RAR cut-off value of 4.776.⁹ Our study complements this finding, particularly in the ICU and high-risk patients, as we also found that patients with high RAR experienced significantly higher mortality compared to those with low RAR (RR = 3.471, $p = 0.032$). Both studies highlight that RAR is a stronger predictor of mortality compared to its individual components, RDW or albumin, reinforcing the value of RAR as a composite marker. However, while focused on in-hospital mortality, our study provides further evidence by extending the follow-up to 90 days, offering insights into the predictive value of RAR beyond hospitalization.

The findings of **Li H, Xu Y (2023)**,⁴ who analyzed 2081 AMI patients and found a significant association between high RAR (≥ 4.32) and 90-day mortality (HR = 1.65), are also aligned with our results. Both studies confirm that RAR is a strong predictor of mortality in AMI patients, with our study showing a slightly lower cut-off of 3.5. Despite the difference in thresholds, the similarity in findings across studies is noteworthy, suggesting that RAR

may be a universally applicable marker for mortality prediction in ACS patients. However, the authors also emphasized the protective role of high albumin, which we also found to be an important factor in our cohort, though we did not examine albumin in isolation.

In contrast, **Liu Z et al. (2023)**,¹⁶ in their cross-sectional study, demonstrated that RAR was a strong predictor of carotid plaque in CHD patients (OR = 6.738), which is a different outcome compared to our study's focus on mortality. However, their findings reinforce the notion that RAR is not only a mortality marker but also a valuable predictor of atherosclerotic disease progression. This suggests that RAR could be a versatile biomarker for cardiovascular risk assessment, indicating both acute and chronic disease progression. While our study focused on short-term mortality, and showed that RAR could also serve as a marker for vascular damage, which may have long-term implications for patient management in CHD.

Additionally, the study by **Pan Y et al. (2023)**¹⁷ on heart failure patients highlighted that RAR was an independent predictor of in-hospital mortality (HR = 1.62), and combining it with the SOFA score improved predictive accuracy. This mirrors the findings in our study, where we observed that high RAR was significantly associated with mortality in ACS patients. Although they focused on heart failure patients, their findings corroborate our results by emphasizing the predictive value of RAR in critically ill cardiovascular patients. The combination of RAR with other clinical scores, like SOFA, could further enhance its utility in risk stratification, and this is an avenue we plan to explore in future studies.

Our study also highlighted the clinical importance of RAR across different patient subgroups. Stratification by age, gender, and comorbid conditions revealed that RAR was particularly predictive of mortality in older patients, females, and those with diabetes or hypertension. This is consistent with the findings of **Liu M et al. (2023)**,¹⁸ who demonstrated that RAR was an independent predictor of all-cause mortality in patients undergoing coronary angiography. It was also reported a significant association between RAR and long-term mortality, further emphasizing the potential of RAR as a universal risk marker across

different stages of CHD. The high mortality observed in our study among older patients and those with comorbidities supports the growing recognition that RAR can help identify high-risk individuals who may benefit from more intensive monitoring and therapeutic strategies.

One of the key strengths of our study is the robust association between RAR and mortality observed across a well-defined ACS cohort. By examining 90-day mortality, our study provides a clearer understanding of RAR's short-term prognostic value, extending its applicability to routine clinical practice for early risk stratification. Additionally, our use of a non-probability consecutive sampling method helps ensure that the findings are representative of real-world clinical scenarios.

Nonetheless, this study has certain limitations that should be acknowledged. Firstly, it was conducted at a single healthcare facility, which may restrict the broader applicability of the findings. To enhance external validity, future research should involve multi-center trials with diverse patient populations. Secondly, although efforts were made to adjust for potential confounding variables such as age, gender, and common comorbid conditions, the possibility of residual confounding from unmeasured variables cannot be excluded. Additionally, the study excluded patients with a history of coronary artery bypass graft (CABG) surgery, as well as those who had received blood transfusions or albumin infusions within the previous two months. This may limit the generalizability of the results to these specific subgroups.

The findings from our study, in conjunction with the supportive studies, suggest that RAR could be integrated into clinical decision-making for ACS patients. Given its strong association with mortality and its ease of measurement, RAR could serve as a low-cost, widely accessible biomarker for identifying high-risk patients in both hospital and outpatient settings. Incorporating RAR into routine clinical practice could enhance risk stratification, allowing for more targeted and timely interventions, particularly in high-risk populations such as older adults, diabetics, and hypertensives.

CONCLUSION

The association of RDW to serum albumin ratio (RAR) with mortality in ACS patients is well-supported by the literature. Our study, along with the supportive studies, consistently demonstrates that high RAR is a significant predictor of short-term mortality in ACS patients. However, considering its low cost, simplicity, and strong predictive value, RAR has the potential to be a key biomarker and can be commonly use in clinical practice for early identification of high-risk patients. However, further multicenter researches are needed to standardize the cut-off values for RAR and validate its predictive accuracy in diverse populations.

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