Original Research Article

RED CELL DISTRIBUTION WIDTH AS A MARKER OF OUTCOME IN ORGANOPHOSPHATE POISONING

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Background: Organophosphate (OP) poisoning is a major public health issue, particularly in developing nations, due to its widespread agricultural use. It induces a cholinergic crisis, often requiring intensive care and mechanical ventilation. Identifying reliable prognostic markers is vital for early risk assessment. Red Cell Distribution Width (RDW), a measure of erythrocyte size variation, is a potential marker of inflammation and oxidative stress. **Objectives:** To determine an association between Red Cell Distribution Width and mortality in Organophosphate poisoning. To determine a correlation between Red Cell Distribution Width and duration of hospital stay. To determine a correlation between Red Cell Distribution Width and pseudo cholinesterase levels.

Materials and Methods: This observational cross-sectional study was conducted in the casualty, ICU and wards of the General Medicine department, Government Medical College, Kottayam, over 12 months (24/6/2023–23/6/2024). With approvals from the department, SRC, and IRB, the study commenced. Data from 106 eligible patients were collected using a semi-structured proforma, after obtaining informed consent. RDW-CV at admission was analysed in relation to need for mechanical ventilation, duration of hospital stay, pseudocholinesterase levels, and mortality. Patients were categorized into two groups based on RDW-CV ($\leq$14 and >14). Data were analyzed using SPSS version 20. The Mann-Whitney U test assessed RDW's association with ventilation, mortality, and pseudocholinesterase levels, while Spearman correlation evaluated its relationship with hospital stay. An ROC curve determined the optimal RDW cutoff for predicting mechanical ventilation and mortality.

Results: Among 106 patients (median age: 51 years, IQR: 22), 75% were male and 25% female. RDW was >14 in 5 patients (4.7%). Mechanical ventilation was required in 43 patients (40.3%), and 10 (9.4%) died. The median respiratory rate was significantly lower in patients with RDW >14 (16/min, IQR: 3/min) than in those with RDW $\leq$14 (18/min, IQR: 5/min) ($p < 0.05$). Median SpO2 was 92% (IQR: 15%) in RDW >14 and 96% (IQR: 3%) in RDW $\leq$14 ($p < 0.05$). Median RDW was higher in ventilated (13.6, IQR: 0.7) compared to non-ventilated patients (12.6, IQR: 0.9) and in deceased (13.7, IQR: 1.27) compared to survived patients (12.8, IQR: 1.15). RDW had moderate positive correlation with duration of hospital stay (r = 0.62, p = 0.001) and strong negative correlation with pseudocholinesterase level (r = -0.66, p = 0.001).

Conclusion: Elevated RDW was significantly associated with need for mechanical ventilation, prolonged hospital stay, lower pseudocholinesterase levels, and higher mortality.

Keywords: RDW-CV: Red Cell Distribution Width - Coefficient of variation, Organophosphate (OP) poisoning, Mechanical ventilation, Mortality, Hospital stay, Pseudocholine esterase.

INTRODUCTION

Organophosphate (OP) poisoning constitutes a formidable global health crisis, disproportionately affecting agricultural workers and communities in developing nations.1,2

The global burden of OP poisoning is staggering, with an estimated several hundred thousand deaths annually, primarily concentrated in low- and middle-income countries 3 The World Health Organization (WHO) recognizes pesticide poisoning, including OP compounds, as a major public health concern, particularly in regions where agricultural practices involve widespread use of these chemicals and where safety regulations and access to appropriate medical care may be limited.4 The economic impact of OP poisoning is also substantial, encompassing direct medical costs, lost productivity due to illness and disability, and long-term health consequences for survivors. 5

The clinical management of OP poisoning presents a significant challenge to healthcare providers. The wide spectrum of clinical presentations, influenced by factors such as the specific OP compound involved, the route and magnitude of exposure, the time elapsed before medical intervention, and individual patient susceptibility, makes it difficult to accurately assess the severity of poisoning and predict patient outcomes.6 Rapid and accurate risk stratification is crucial for guiding appropriate treatment strategies, including the administration of antidotes like atropine and pralidoxime (2-PAM), supportive care, and the timely initiation of critical interventions such as mechanical ventilation in cases of respiratory compromise.7

Red cell distribution width (RDW), a routine parameter obtained from a complete blood count (CBC), has emerged as a potential marker of systemic inflammation and oxidative stress.8 RDW reflects the variation in the size of red blood cells within a given sample. While traditionally used in anemia, RDW has gained recognition for its association with various non-hematological conditions.

In the context of OP poisoning, several pathophysiological mechanisms may influence RDW. OP poisoning is known to induce oxidative stress, a state of imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defences.9 Oxidative stress can damage various cellular components, including red blood cells, potentially leading to increased variability in their size and consequently, elevated RDW.

This study aims to investigate the association between RDW and clinical outcomes in patients with acute organophosphate poisoning. The primary objective is to determine whether RDW levels are associated with the need for mechanical ventilation, a critical intervention required in patients with severe respiratory compromise.

MATERIALS AND METHODS

It was an Observational cross sectional study conducted for a period of 12 months after obtaining clearance from Institutional Review Board from 24/6/2023 to 23/6/2024 Casualty, ICU and wards of General Medicine Department, Government medical college Kottayam.

Semi structured proforma, which collected details such as demographic details such as baseline characteristics,medical history, physical examination and blood investigations Patients with age $\geq$13 yrs admitted with Organophosphate poisoning in Government Medical College, Kottayam

Sample size:

Sample size is calculated by the formula,

$$n = \frac{2(Z\alpha + Z\beta)^2 pq}{d^2}$$

Where α error taken 0.1%, $Z\alpha$ = 3.29 β error taken as 1%, $Z\beta$ = 2.33

$$n = \frac{p1 + p2}{2}$$

In the study conducted by Arun Pranaav in 2019, proportion of patients intubated with low RDW was 13/102, and proportion of patients intubated with RDW high was 65/98.

$$N = \frac{2(3.29 + 2.33)^2 0.39 \times 0.61}{0.53^2}$$

Inclusion Criteria

Patients in the age $\geq$13 yrs admitted with Organophosphate poisoning.

Exclusion Criteria

- Patient with poisoning other than Organophosphate
- CLD
- CKD
- Haemoglobin <11
- Hematologic malignancies
- Patient on immunomodulators

Sampling Method: Convenient sampling till sample size was reached

Study Procedure

This was a observational cross-sectional study done in the casualty, wards and ICU of Department of General Medicine, Government Medical College Kottayam for a period of 12 months after receiving IRB clearance from 24/6/2023 to 23/6/2024. With approvals from the department, SRC, and IRB, the study commenced. From the patients admitted with Organophosphate poisoning, those who meeting the inclusion criteria and exclusion criteria was recruited for this study after obtaining consent.

Data collection was done using a semi structured proforma that included demographic details like age and gender, clinical history, and detailed examination findings. Red Cell Distribution Width – Coefficient of Variation (RDW- CV) values at the time of

admission was studied. RDW-CV was assessed using a Coulter Hematology Analyzer. The need for mechanical ventilation was recorded, and mortality was analyzed. Serum pseudocholinesterase levels were monitored in all patients, while the duration of hospital stay was documented for survivors

DATA MANAGEMENT AND STATISTICAL ANALYSIS

Data collected were entered into Microsoft excel 2019 and the master chart was loaded into Statistical Package for Social Sciences (SPSS) version 20 for further analysis. The analysis employed both descriptive and inferential statistics.

For quantitative variables, the data were expressed using the median and IQR, whereas for qualitative factors, the data were expressed using percentages. When displaying the data as a diagram, bar charts and pie charts were employed. Since RDW displayed a non-normal distribution, the Mann-Whitney U test was employed to determine the relationship between RDW and different factors.

Spearman correlation was utilized to determine the relationship between RDW, hospital stay duration, and pseudocholinesterase levels. There was a positive correlation if the "r" value was greater than zero, and a negative correlation if it was less than zero. When the "r" value was less than 0.25, it was considered weak; when

it was greater than 0.68, it was considered strong. Statistical significance was defined as a P value of less than 0.05. The ideal cutoff threshold for RDW for predicting mortality and the necessity for mechanical ventilation was established using the Receiver Operating Curve (ROC) curve.

RESULTS

Table 1: Distribution of study participants based on age group

Age	Frequency	Percentage
< 30	11	10.4
31-40	23	21.7
41-50	18	17.0
51-60	30	28.3
61-70	22	20.8
>70	2	1.9
Total	106	100.0

Of the study participants, 30 (28.3%) are in the 51–60 age group, 23 (21.7%) are in the 31–40 age group, and 22 (20.8%) are in the 61–70 age group. The study population's median age is 51 years, with an interquartile range of 22 years. Lower age was 22 years and highest was 77 years.

Table 2: Distribution of study participants based on hospital stay

Duration of hospital stay	Frequency	Percentage
<7 days	16	16.7
7-14 days	69	71.9
>14 days	11	11.5
Total	96	100.0

Median duration of hospital stay in survived group is 8days with an IQR of 5days.

Table 3: Distribution of study participants based on pseudocholinesterase levels

Pseudocholinesterase levels	Frequency	Percentage
Low	60	56.6
High	46	43.4
Total	106	100.0

Of all study subjects, 46 (43.4%) had normal pseudocholine esterase levels and 60 (56.6%) had low level.

Table 4: Distribution of study participants based on association between RDW and various quantitative variables

Quantitative variables	High RDW		Low RDW		P value	Mann whitney U statistic
	Median	IQR	Median	IQR		
Age (years)	53	20	51	22	0.85	240.5
SBP (mmHg)	120	15	126	22	0.80	236
DBP (mmHg)	80	13	80	16	0.66	223.5
Respiratory rate (breaths/min)	16	3	18	5	0.04	119.5
SpO$_2$ (%)	92	15	96	3	0.01	86.5
Duration of hospital stay (days)	14	12	8	5	0.11	146.5
Pseudocholine esterase (U/L)	678	359	4598	5720	0.014	-87.5

Participants with high RDW had a median respiratory rate (RR) of 16 breaths/min with an IQR of 3, whereas those with low RDW had a median RR of 18 breaths/min with an IQR of 5. A p-value of less than 0.05 indicated that this difference was statistically significant. Participants with high RDW had a median SpO2 value of 92% with an IQR of 15, whereas those with low RDW had a median SpO2 value of 96 % with an IQR of 3. A p-value of less than 0.05 indicated that this difference was statistically significant. Participants with high RDW had a median PChE value of 678 (IQR 359) whereas those with low RDW had a median of 4598 (IQR 5720) with a test statistic of -87.5 and a p-value of 0.014, this difference was statistically significant. The duration of hospital stay, age, SBP, DBP, and other factors did not exhibit any statistically significant association with RDW.

Table 5: Distribution of study participants based on association between RDW and need for mechanical ventilation in Organophosphate poisoning

Need for mechanical ventilation	Median RDW	IQR	P value, test statistic
Present	13.6	0.7	P value- 0.001 Mann whitney U - 349
Absent	12.6	0.9	

Participants who needed mechanical ventilation had a median RDW value of 13.6 with an IQR of 0.7, while those who did not had a median RDW value of 12.6 with an IQR of 0.9. With a p-value of 0.001 and a Mann-Whitney U test statistic of 349, this RDW difference was significant.

Table 6: Distribution of study participants based on association between RDW and mortality in Organophosphate poisoning

Mortality	Median RDW	IQR	P value, test statistic
Expired	13.7	1.27	P value- 0.043 Mann Whitney U -293.50
Survived	12.8	1.15	

Participants who died had a median RDW value of 13.7 with an IQR of 1.27, whereas those who lived had a median RDW value of 12.8 with an IQR of 1.15. With a test statistic of 293.50 and a p-value of 0.043, this difference was statistically significant.

Table 7: Correlation between RDW and duration of hospital stay

	Spearman correlation	
RDW and duration of hospital stay	Correlation coefficient	P value
	0.62	0.001

The length of hospital stay and RDW have a moderate positive correlation, as indicated by the correlation coefficient of 0.62. The length of hospital stay tends to rise in tandem with RDW. With a p-value of 0.001, this link is statistically significant, indicating a positive correlation between longer hospital stays and higher RDW levels.

Table 8 Distribution of study participants based on correlation between RDW and Pseudo choline esterase levels

	Spearman correlation	
RDW and Pseudo choline esterase levels	Correlation coefficient	P value
	-0.66	0.001

With a p-value of 0.001, the Spearman correlation coefficient between RDW and pseudocholinesterase levels is -0.66. This strong negative association implies that there is a negative correlation between higher RDW levels and lower pseudocholinesterase levels, with pseudocholinesterase levels tending to drop as RDW increases.
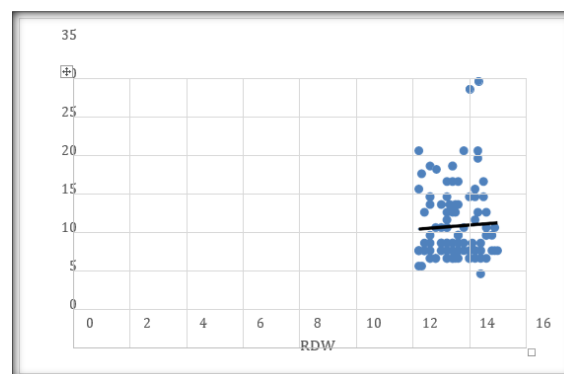

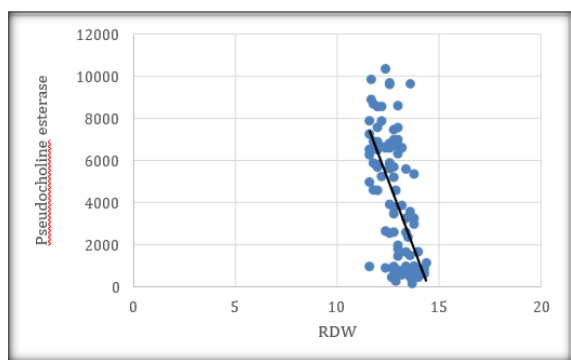**Figure 1: Scatter plot between RDW and duration of hospital stay**

Figure 2: Scatter plot between RDW and Pseudo choline esterase levels
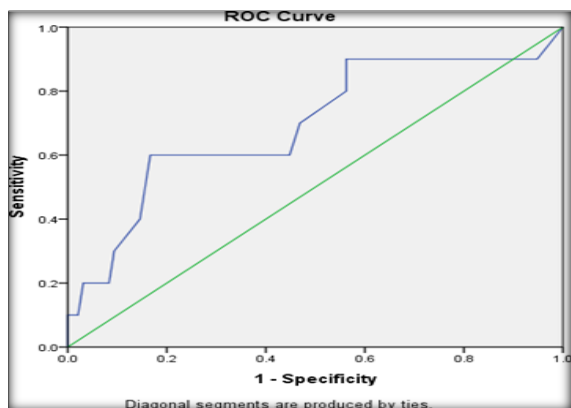

Figure 3: ROC curve of RDW and mortality

When predicting death in patients with OPI poisoning, RDW had a cut-off value of 13.65, a sensitivity of 60%, and a specificity of 84%. Area Under the Curve is 0.69 indicating that the test can moderately differentiate between test positive and negative groups.

DISCUSSION

In the present study, included 106 patients diagnosed with organophosphate (OP) poisoning were studied, with data analysed using SPSS Version 20.0.

In the current study, age distribution ranged from 22 to 77 years, with a median age of 51yrs with interquartile range 22 yrs. In the study done by Aslam et al. (2015),[11] among 158 patients of OP poisoning, mean age was 31.3 ± 11.8 years. Mahmoud et al., in his prospective cross sectional study done in 2021 among 100 patients found mean age was 27.06 ± 12.5 years.[12]

In the present study, the mortality rate was 9%, with 10 out of 106 individuals succumbed to death. Non survivors had a significantly higher RDW values (median 13.7 with IQR of 1.27) compared to survivors (median 12.8 with IQR 1.15, p=0.043).

Aslam et al. reported that non-survivors had significantly elevated RDW levels (13.87 ± 2.81) compared to survivors (12.99 ± 1.49) (p<0.05)11. Kang et al. (2014) also identified similar results - non survivors have higher RDW (13.9 ± 1.8) than survivors (12.9 ± 0.8).[13]

According to present study, RDW had a sensitivity of 60% and the specificity of 84 % with a cut-off value of 13.65 in predicting mortality in patients with OPI poisoning (Area Under the Curve is 0.69). Aslam et al in his study found that RDW with a cut off value of 13.5% had sensitivity of 57.1% and specificity of 68.1% in predicting mortality.[11] According to study done by Kang et al, RDW more than 13.5%, the sensitivity was 57.1%, and the specificity was 84.0 in predicting 30 day mortality.[13] In a study done by Mahmoud et al, RDW on admission had a sensitivity of 75% and specificity of 73.75% with a cut-off value of 14.3 in predicting mortality in patients with OPCs poisoning.[12]

In the present study, patients with RDW >14% had significantly longer hospital stays (median 14 with IQR 12 days) compared to RDW ≤14% (median 8 with IQR 5 days) with p value >0.05, indicating there was no statistically significant association. The duration of hospital stay and RDW had a moderate positive correlation, as indicated by correlation coefficient of 0.62. The duration of hospital stay tends to rise in tandem with RDW (p value : 0.001). According to the present study, pseudocholinesterase (PChE) levels were significantly lower in patients with higher RDW values (>14%). In this study, the median PChE level in the RDW ≤14% group was 4598 with IQR 5720 U/L, whereas in the RDW >14% group, it was significantly lower at 678 with IQR 359 U/L (p<0.05). In the study done by Arun Pranaav in 2019, patients with high RDW had mean PChE value 6107 ± 1841 and those with low RDW had mean PChE value of 6107 ± 1232.[10] In study done by Aslam et al Patients with high RDW had low PChE levels (4300 ± 4100) than those with low RDW (5500 ± 4300).[11] Kang et al. (2014) also reported that patients with RDW more than 13.5 had mean pseudocholinesterase levels 393.5 ± 189.8, and for those who have RDW ≤ 13.5 had levels 1611.4 ± 733.5).[13]

Influence of Other Factors on RDW – RDW can be influenced by pre- existing conditions, including infections, and inflammatory disorders, which were not fully controlled in this study. PChE Variability – Pseudocholinesterase (PChE) levels fluctuate based on multiple factors (including smoking, obesity) and their correlation with RDW might require further validation in multicentric studies.

CONCLUSION

RDW-CV at admission showed a significant association with the need for mechanical ventilation in patients with organophosphate poisoning. Patients with higher RDW-CV at admission were more likely to require mechanical ventilation. Higher RDW-CV values correlated with increased mortality. A positive correlation was observed between RDW-CV and duration of hospital stay. An inverse correlation was found between RDW-CV and pseudocholinesterase levels. An RDW-CV with a cut off of 12.95 %

predicts need of ventilation with sensitivity of 79.1 % and specificity of 77%. An RDW with a cut off of 13.65 % predicts mortality with sensitivity of 60% and specificity of 84%.

REFERENCES

1. Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. The Lancet. 2008 Feb 16;371(9612):597–607.
2. OECD. OECD Environmental Outlook to 2050: The Consequences of Inaction [Internet]. OECD; 2012 [cited 2025 Feb 15]. (OECD Environmental Outlook). Available from: https://www.oecd.org/en/publications/oecd-environmental-outlook-to- 2050_9789264122246-en.html
3. WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification, 2019 Edition. 2nd ed. Geneva: World Health Organization; 2020. 1 p.
4. Dobson S. PREVENTING DISEASE THROUGH HEALTHY ENVIRONMENTS.
5. Jeyaratnam J. ACUTE PESTICIDE POISONING: A MAJOR GLOBAL HEALTH PROBLEM.
6. Reigart JR. Recognition and Management of Pesticide Poisonings (5th Ed.). DIANE Publishing; 2009. 238 p.
7. Bardin PG, van Eeden SF, Moolman JA, Foden AP, Joubert JR. Organophosphate and Carbamate Poisoning. Arch Intern Med. 1994 Jul 11;154(13):1433–41.
8. Roberts DM, Aaron CK. Management of acute organophosphorus pesticide poisoning. BMJ. 2007 Mar 24;334(7594):629–34.
9. Balali-Mood M, Saber H. Recent Advances in the Treatment of Organophosphorous Poisonings. Iran J Med Sci. 2012 Jun;37(2):74–91.
10. Arun Pranaav S. Red Cell Distribution Width as Outcome Predictor in Organophosphate Poisoning [Internet] [masters]. Madurai Medical College, Madurai; 2019 [cited 2023 May 13]. Available from: http://www.repository-tnmgrmu.ac.in/11259/
11. Aslam S, Vadivelan A. Red Cell Distribution Width as Prognostic Marker in Organophosphorous Compound Poisoning. IOSR J Dent Med Sci. 2015 Sep 1;14:21– 4.
12. Mahmoud E, Abdel Salam M, Halawa H, Hafez R. Red cell distribution width as a predictor of severity and outcome of acute organophosphorus poisoned cases admitted to Poison Control Center Ain Shams University Hospitals (A prospective study). Ain Shams J Forensic Med Clin Toxicol. 2021 Jul 1;37(2):26–33.
13. Kang C, Park IS, Kim DH, Kim SC, Jeong JH, Lee SH, et al. Red cell distribution width as a predictor of mortality in organophosphate insecticide poisoning. Am J Emerg Med. 2014 Jul;32(7):743–6.