# Red Cell Distribution Width as Prognostic Marker in Organophosphorous Compound Poisoning

Shaikh Mohammed Aslam S<sup>1</sup>, Akhila Arcot Vadivelan<sup>2</sup>

<sup>1</sup> Associate Professor, Department of Medicine, M.S.Ramaiah Medical college, Bangalore, India <sup>2</sup> Junior Resident, Department of Medicine, M.S.Ramaiah Medical college, Bangalore, India

## Abstract:

**Introduction:** OPI poisoning is a major public health problem in developing countries like India. RDW is a simple and inexpensive test and elevated RDW is associated with acute inflammation and increased oxidative stress. Hence, this study was done to evaluate the prognostic value of RDW in OPI poisoning.

Aim: To evaluate the prognostic value of Red Cell Distribution Width in Organophosphorus insecticide poisoning.

**Methods:** A total of 158 patients of OPI were studied retrospectively from January 2005 to December2014. The diagnosis of a case of OPI poisoning was based on a clinical history of intentional ingestion of OPI and presence of characteristic signs and symptoms of OPI poisoning, and laboratory evidence of decreased serum cholinesterase activity.

**Result:** Mean age was  $31.32 \pm 11.84$  years and 58.2% of the patients were males. Mean serum pseudocholinesterase level was  $5.5\pm 4.3$  and mean RDW was  $13.07\pm 1.67$ . Mortality rate was 8.9%. Non survivors had higher RDW ( $13.87\pm 2.81$ ) when compared with survivors ( $12.99\pm 1.49$ ). RDW had a sensitivity of 57.1%, specificity of 68.1%, and negative predictive value of 94.3% with a cut-off value of 13.5% in predicting mortality in patients with OPI poisoning.

*Conclusion: RDW* levels on admission can be used a prognostic marker in patients with OPI poisoning. *Keywords:* Organophosphorous compound poisoning, Oxidative stress, Red cell distribution width.

## I. Introduction

Organophosphate insecticides (OPIs) are widely used in horticulture and agriculture in developing countries such as India. Due to easy availability, poisoning with these agents is very common. Suicidal poisoning by OPI is a major public health problem, and the annual number of mortalities is approximately 2000000 worldwide.<sup>[1]</sup> In India, these insecticides are among the most toxic of pesticides that cause poisoning in humans, mostly in farmers.

It has been reported that high values of Red Cell Distribution Width (RDW) has been associated with poor prognosis among patients with acute myocardial infarction, congestive heart failure, stroke, and sepsis.<sup>[2-5]</sup>

## Aims and Objectives

The aim of this retrospective study was to evaluate the prognostic value of RDW in patients with OPI poisoning.

## II. Materials And Methods

This was a retrospective observational study and was conducted between January 1, 2005 and December 31, 2014. We analysed 158 patients in the study. The diagnosis of a case of OPI poisoning was based on a clinical history of intentional ingestion of OPI and presence of characteristic signs and symptoms of OPI poisoning, and laboratory evidence of decreased serum cholinesterase activity. Cases involving patients younger than sixteen years of age, co-ingestion of OPI with other agents and those with pre hospital cardiac arrest were excluded from the study.

A standardized protocol for the treatment of OPI poisoning with atropine and pralidoxime was conducted in each case. If the patients presented with respiratory compromise, supportive care (including mechanical ventilation) was carried out.

#### **Data Collection**

All data was collected from case sheets. Demographic data, history, vital signs, level of consciousness and systemic examination findings were noted. Laboratory values of RDW, white blood cell count (WBC), haematocrit, platelet count, serum creatinine, serum albumin, and serum pseudocholinesterase were also noted.

#### Statistical analysis

All the continuous variables like age, pulse rate, platelet count etc were described using mean and standard deviation. All the qualitative variables were expressed as percentage. Students-t-test was used to compare the continuous variables which were normally distributed. Mann Whitney test was used to compare the continuous variables which were not normally distributed. Chi –Square test was used to test for difference in proportions in categorical data. ROC (Receiver operating curve) was used to determine the optimal cut off point for RDW for predicting mortality.

### III. Results

A total of 158 cases were studied. Basic details such as demography, clinical features on admission in the ED, laboratory characteristics were collected (Table 1). Mean age was  $31.32 \pm 11.84$  years. 58.2% of the patients were males. Mean heart rate was  $102.10\pm 21.33$  beats per minute and mean respiratory rate was  $22.34\pm16.13$  cycles per minute. Miosis was seen in 77 (48.7%) patients. Fasciculations was seen in 14(8.9%) patients and seizures was present in 7 (4.4%). 43 (27.2%) patients required ventilator support. Laboratory parameters revealed a mean WBC count of  $14153.15\pm17870.613$  cells/mm<sup>3</sup>, mean platelet count was  $285000\pm94000$  cells/mm<sup>3</sup>, mean serum albumin was  $3.96\pm0.74$  mg/dl, mean pseudocholinesterase was  $5.5\pm4.3$  U/ml and mean RDW was  $13.07\pm1.67\%$ . The morality rate was 8.9%.

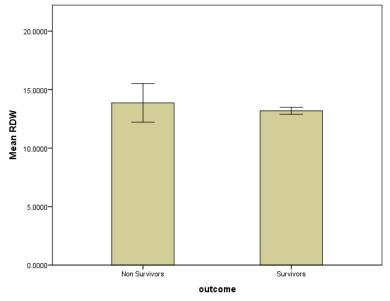
The patients were divided into two groups, using the cut-off point of RDW as 13.5%. A total number of 106 patients had RDW < 13.5% out of which 100 (94.31%) were survivors and 6 (5.7%) were non-survivors. The remaining 52 had a RDW > 13.5%, out of which 44(84.6%) were survivors and 8 (15.4%) were non-survivors. Patients with RDW > 13.5% had higher mortality (15.4%) compared to patients with RDW < 13.5% (5.7%) and was statistically significant (p=.043). Patients with RDW > 13.5% had significantly lower levels of pseudocholinesterase (p = 0.005) and albumin (p =0.004).

Patients who did not survive had higher levels of RDW ( $13.87\pm 2.86$  vs.  $12.99\pm 1.49$ , p= .060) (Fig 1) and were older ( $41.64\pm 17.75$  vs.  $30.32\pm 10.67$ ,p=.001).They also had significantly lower levels of albumin ( $3.57\pm .7522$  vs.  $4.008\pm .73$ , p=.034) and higher levels of creatinine ( $1.54\pm 1.30$  vs.  $.89\pm .26$ , p=.003), while haematocrit showed no significant difference ( $40.40\pm 5.26$  vs.  $40.80\pm 7.07$ , p=.954)

RDW had a sensitivity of 57.1 % and the specificity of 68.1% with a cut-off value of 13.5% in predicting mortality in patients with OPI poisoning. (Fig 2)

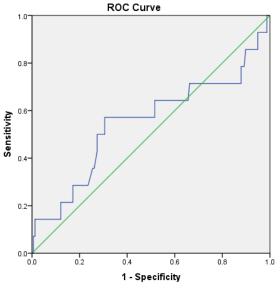
Variables	All Patients (n=	RDW <13.5	RDW > 13.5	P value
	158)	(n=106)	(n=52)	
Age (in years)	31.3±11.8	30.3±11.3	33.3±12.7	0.109
SBP (mmHg)	120.4±16.6	120.9±14.5	119.2±20.5	0.54
DBP (mmHg)	72.7±12.9	74.1±11.7	69.9±14.8	0.59
Pulse rate (per minute)	102.1±21.3	99.63±19.6	107.0±23.8	0.39
Respiratory rate (per minute)	22.3±16.1	22.5±19.1	21.8±7.0	0.614
SpO2 (%)	95.4±9.7	95.4±10.4	95.5±8.0	0.925
PCV (%)	40.77±6.9	41.2±6.1	39.7±8.1	0.184
WBC count ( cells/mm <sup>3</sup> )	14153.1±17870.6	13244.4±6941.4	16005.54±29643.0	0.731
Platelet count ( cells/mm <sup>3</sup> )	2.85±.94	2.9±.96	2.7±.90	0.297
Serum pseudocholinesterase (U/ml)	5.5±4.3	6.0±4.3	4.3±4.1	0.005
Creatinine (mg/dl)	0.95±.4	0.965±.56	0.92±.26	0.856
Albumin (gm/dl)	3.96±.74	4.0±.77	3.7±.61	0.004

Table 1: Baseline Characteristics and Laboratory findings of patients



Error Bars: 95% Cl

Figure 1: Mean RDW in survivors and non survivors



Diagonal segments are produced by ties.

Figure 2: Area under the ROC curve to determine the cut off point for RDW

#### IV. Discussion

The mechanism of action of the OPI is that it irreversibly inhibits acetylcholinesterase (AchE) and hence causes accumulation of acetylcholine at cholinergic synapses of the central and peripheral nervous systems. This leads to overstimulation of the muscarinic and nicotine receptors. Classical symptoms of OPI poisoning arise from muscarinic, nicotinic and central systemic effects, which include increased secretion like salivation and diarrhoea, bradycardia, muscle weakness, paralysis, confusion, and respiratory failure.<sup>[6]</sup> Apart from the cholinergic effects, organophosphates also change the balance between antioxidant defense mechanisms and free radical formation.<sup>[7]</sup>

The red cell distribution width (RDW) is a measurement derived from the red blood cell distribution curves generated on automated haematology analysers. It is a measure of the variability in the size of the erythrocytes that are circulating. It depicts anisocytosis and is usually a part of complete blood count. RDW is used during the differential diagnosis of anaemia.<sup>[8,9]</sup> It has been suggested that elevated RDW is associated with systemic inflammation and oxidative stress as the exact underlying mechanism is not well understood. There may be deformation of erythrocyte membranes by acute and chronic inflammation.<sup>[10,11]</sup> Similarly in OPI poisoning, there is acute inflammation and increased oxidative stress that can lead to a change

in the structure and size of the circulating erythrocyte. Hence, it is expected that RDW levels may be increased in OPI poisoning and can thus aid in prognosis.<sup>[12]</sup>

In our study 58.2% of the patients were males and mortality was 8.9%. Similar findings were noted in a study done by Zerrin Define Dundar et al where 55.66% of the patients were males and the mortality was 9.7%. Zerrin Define Dundar et al also noted that non survivors had higher median RDW than survivors 15.40(15.10-16.40) and 14.30 (13.30-16.00), respectively with a p value of 0.047. Similar findings were noted in our study, where non survivors had a higher level of RDW (13.87 $\pm$  2.86) compared to survivors (12.99 $\pm$ 1.49) with a p value of 0.060.<sup>[13]</sup> Studies done by Babu R Umesh et al and Changwoo Kang et al also concluded that RDW can be used as a predictor of mortality in patients with OPI poisoning.<sup>[14,15]</sup>

#### V. Conclusions

RDW is a simple and inexpensive test done as a part of complete blood counts in OPI poisoning. Hence we conclude that in developing countries like India, RDW levels measured on admission can be used as a prognostic marker in patients with OPI poisoning.

#### References

- [1]. Eddleston M, Buckley NA, Eyer P, et al. Management of acute organophosphorus pesticide poisoning. Lancet 2008; 371:597-607.
- [2]. Wang P, Wang L, Li H, Chen H. Relationship between the red cell distribution width and risk of acute myocardial infarction. J Atheroscler Thromb 2015;22(1):21-6.
- [3]. Tseliou E, Terrovitis JV, Kaldara EE, Ntalianis AS, Repasos E, Katsaros et al. Red blood cell distribution width is a significant prognostic marker in advanced heart failure, independent of hemoglobin levels. Hellenic J Cardiol. 2014 Nov-Dec;55(6):457-61.
- [4]. Söderholm M, Borné Y, Hedblad B, Persson M, Engström G. Red cell distribution width in relation to incidence of stroke and carotid atherosclerosis: a population-based cohort study. <u>PLoS One.</u> 2015 May 7;10(5):e0124957.
- [5]. Mahmood NA, Mathew J, Kang B, DeBari VA, Khan MA. Broadening of the red blood cell distribution width is associated with increased severity of illness in patients with sepsis. Int J Crit Illn Inj Sci .2014 Oct-Dec;4(4):278-82.
- [6]. Aardema H, Meertens JH, Ligtenberg JJ, Peters-Polman OM, Tulleken JE, Zijlstra JG. Organophosphorus pesticide poisoning: cases and developments. Neth J Med 2008 Apr;66(4):149-53.
- [7]. Rastogi SK, Satyanarayan PV, Ravishankar D, Tripathi S. A study on oxidative stress and antioxidant status of agricultural workers exposed to organophosphorus insecticides during spraying. Indian J Occup Environ Med 2009 Dec;13(3):131-4.
- [8]. Salvagno GL, Sanchis-Gomar F, Picanza A, Lippi G. Red blood cell distribution width: A simple parameter with multiple clinical applications. Crit Rev Clini Lab Sci 2015 Apr;52(2):86-105.
- [9]. Perlstein TS, Weuve J, Pfeffer MA, Beckman JA. Red blood cell distribution width and mortality risk in a community-based prospective cohort. Arch Intern Med 2009 Mar 23;169(6):588-94.
- [10]. Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G, Guidi GC. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Arch Pathol Lab Med 2009 Apr;133(4):628-32.
- [11]. Vidyasagar J, Karunakar N, Reddy M S, Rajnarayana K, Surender T, Krishna DR. Oxidative stress and antioxidant status in acute organophosphorous insecticide poisoning. Indian J Pharmacol 2004;36:76-9.
- [12]. Soltaninejad K, Abdollahi M. Current opinion on the science of organophosphate pesticides and toxic stress: a systematic review. Med Sci Monit.2009 Mar;15(3):RA75-90.
- [13]. Dündar ZD, Köylü R, Ergin M, Günaydın YK, Özer R, Cander B. Prognostic Value of Red Cell Distribution Width in Patients with Organophosphate Poisoning. JAEM 2015; 14: 65-9.
- [14]. Umesh BR, Prathima S, Murali MC. Can Red Cell Distribution Width (RDW) Predict the Mortality in Organophosphorus and Carbamate Insecticide Poisoning? JIST 2014 Jul; 10(2):19-22.
- [15]. 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.