

Study of Hyperglycemia and Its Association with Pseudocholinesterase Levels and Severity of Organophosphorus Poisoning

Dr. Ravi BN¹; Dr. Manmohan U S²; Dr. Phaneesh Bharadwaj B S³;
Dr. Pujitha S N⁴

¹Associate Professor, Department of General Medicine, A.I.M.S., Karnataka

²Postgraduate Resident, Department of General Medicine, A.I.M.S., Karnataka

³Senior Resident, Department of General Medicine, SDUMC., Karnataka.

⁴Postgraduate Resident, Department of General Medicine, SDUMC., Karnataka

Corresponding Author: Dr. Manmohan U S

ABSTRACT

Background: Random blood sugar (RBS) level is an important factor influencing the severity of organophosphorus (OP) compound poisoning. Here we studied RBS as a prognostic and mortality indicator in OP compound poisoning and its association with serum pseudocholinesterase levels.

Objectives

1. To study the clinical profile in patients who had consumed organophosphorus poison.
2. To determine the relation between glycemic status at admission and outcome in organophosphorus poisoning.

Methods: 100 cases of OP poisoning admitted to Adichunchanagiri Hospital and Research Centre, B.G.Nagar, Mandya, between Nov 2015- May 2017 were studied. Detailed history and clinical examination was done. RBS and pseudocholinesterase levels at admission were measured.

Results: 100 cases of OP poisoning admitted to SAH&RC were considered. Most patients were in the age group of 18-25 years. Males were more common (65%). Suicide was the most common motive (90%) and ingestion was the most common mode of poisoning (90%). Farmers were the main group involved in poisoning (55%). Dimethoate was the most common compound. Hyperglycemia was observed in 36% of patients with 80.6% developing complications and 72% requiring ventilator. Pseudocholinesterase was less than 4000U/L in 23% of patients and 91% of these patients required ventilator support. Overall mortality was 20%. Mortality was 33% in patients with hyperglycemia ($p < 0.009$) and 70% in patients with pseudocholinesterase < 4000 U/L ($p < 0.0001$). RBS negatively correlated with pseudocholinesterase levels. RBS > 200 mg/dl was associated with a mean pseudocholinesterase level 4355.36 (SD of 1520.86, $p < 0.001$). These observations suggest that admission hyperglycemia is a useful indicator of OP compound poisoning severity and its comparable to pseudocholinesterase levels.

Conclusion: Admission RBS > 200 mg/dl and pseudocholinesterase < 4000 U/L are reliable parameters to predict mortality and ventilator requirement in OP compound poisoning. A low pseudocholinesterase level and increase in blood sugar levels were associated for ventilator requirements, mortality and complications was found to be statistically significant according to chi square test.

Keywords: Organophosphorus; Hyperglycemia; Pseudocholinesterase; Dimethoate; RBS.

INTRODUCTION

Organophosphorus compound (OP) was synthesized by Von Hoffman. OP pesticide poisoning is common in developing countries. India being one of the

leading countries due to limited availability of facilities and finances, all patients cannot be managed in ICU. There is a need to identify at initial assessment, need for ventilatory support and assess the prognosis.

Serum pseudocholinesterase levels are known to be a useful predictor of prognosis in acute organophosphorus poisoning. ⁽¹⁾

The pharmacological action of all OPs is the inhibition of acetyl cholinesterase; cardiorespiratory failure is commonest cause for death. However, depending on the particular OP involved there is much variation in the timing of onset and clinical features. OP poisoning has high inpatient mortality and many patients have cardiorespiratory arrests after admission (40% of patients requiring intubation in this study). ⁽²⁾

Previous studies associating the severity or prognosis of organophosphorus poisoning with the estimation of plasma cholinesterase have been contradictory. Goswamy R et al, ⁽³⁾ in their study concluded that apart from clinical indicators, low plasma cholinesterase levels were of greatest predictive value in organophosphorus poisoning.

However Aygun D et al ⁽⁴⁾ found that plasma cholinesterase level estimations are useful in diagnosis of organophosphorus poisoning in acute phase but show no relation to severity of poisoning and also regarding morbidity and mortality of case. ⁽⁴⁾

Organophosphorus compounds inhibit cholinesterase allowing accumulation of acetylcholine at cholinergic sites resulting in continuous stimulation of cholinergic sites leading to marked increase in catecholamines which can lead to hyperglycemia. ⁽¹⁾

Nicotinic receptors function in brain pathways that increase the release of several pituitary hormones in crediting-vasopressin, ACTH and prolactin. In animal experiments changes in diurnal pattern of ACTH has been reported following organophosphorus poisoning. Persistent cholinergic stimulation could be causing changes in hormones and causes hyperglycemia. ⁽⁵⁻⁷⁾

In severe OP poisoning transient hyperglycemia and glycosuria are often found. ⁽⁶⁾

Mechanisms proposed are: OP compounds inhibit cholinesterase allowing accumulation of acetylcholine at cholinergic sites resulting in continuous stimulation of cholinergic sites leading to marked increase in catecholamines which can lead to hyperglycemia. Nicotinic receptors function in brain pathways that increase the release of several pituitary hormones in crediting-vasopressin, ACTH and prolactin. Persistent cholinergic stimulation could be causing changes in hormones and causes hyperglycemia.

It is common knowledge that high blood sugar levels are a poor prognostic factor in critically ill patients. This study was designed to evaluate RBS at admission as a prognostic indicator and to assess if it correlates with pseudocholinesterase levels.

MATERIALS AND METHODS

Study Design: Cross sectional analytical study

Study setting: Adichunchanagiri Hospital and Research Centre, B.G. Nagara during the period of November -2015 to May 2017.

Study period: November -2015 to May 2017

Sample size: Minimum number of 100 cases will be studied over the period of 18 months.

Sampling method: Purposive sampling

Instrument for data collection: A pretested structured pilot tested questionnaire.

Ethical clearance has been taken.

Written informed consent has been taken.

INCLUSION CRITERIA:

- 1) Patients with history of exposure to OP compound within previous 24 hours with characteristic clinical manifestations of organophosphorus compound poisoning.
- 2) Patients with age more than 18 years.

EXCLUSION CRITERIA:

- 1) Patients who had consumed alcohol, other poisons, drugs, mixed poisons.
- 2) Known cases of diabetes mellitus.
- 3) Patients of age less than 18 years.

Investigations:

Routine investigations: Blood: Hb%, TC, DC, ESR; Urine: albumin, sugar, microscopy, blood sugar, blood urea, serum creatinine, ECG.

Specific investigations: Serum pseudocholinesterase levels, Hba1c levels, ABG (arterial blood gas) analysis.

RESULTS

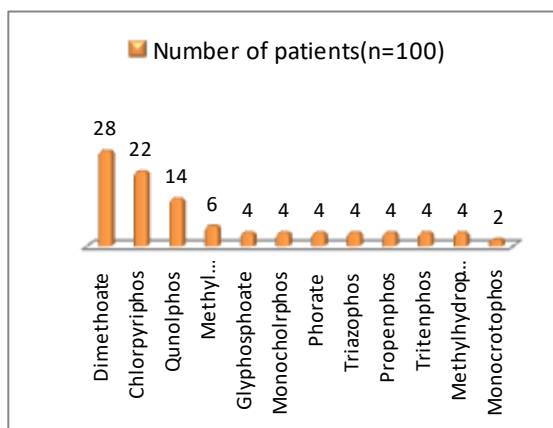
100 cases of OP poisoning admitted to Adichunchanagiri Hospital and Research Centre were considered. Commonest age group involved were between 18-25 years. Males were the most common victims (65%). Suicide was the most common motive of poisoning (90%) and ingestion was the most common mode of poisoning (90%). Farmers were the main group involved in poisoning (55%). Majority of patients admitted within 4 hours of exposure. Dimethoate was the most common compound in poisoning.

Table 1. Age Distribution Of Study Subjects

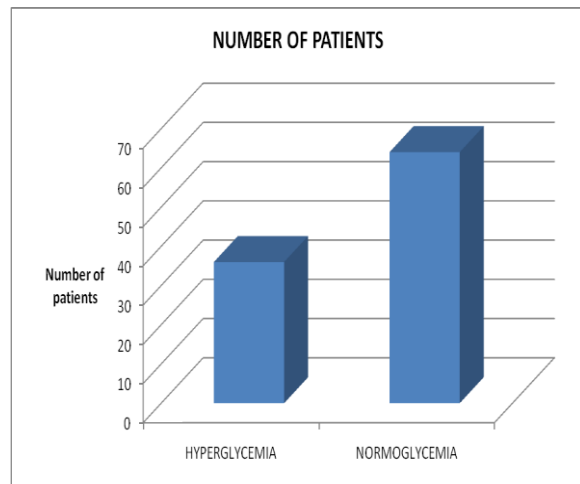
Age	No. of patients(n=100)
18 – 25	40
26 – 35	25
36 – 45	14
46 – 55	7
56–65	14

Table 2: Gender Distribution Of Study Subjects

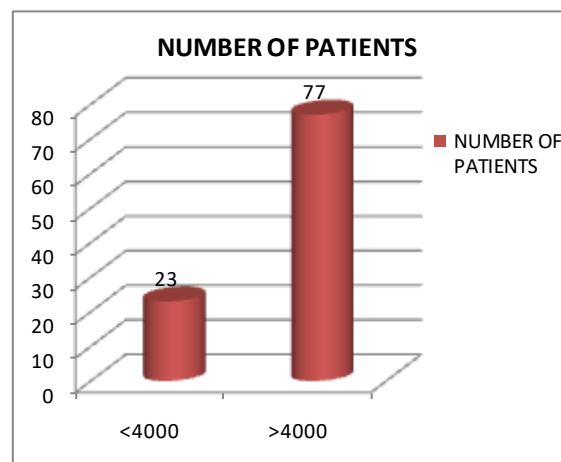
Sex	Number(n=100)	Percentage
Male	65	65
Female	35	35



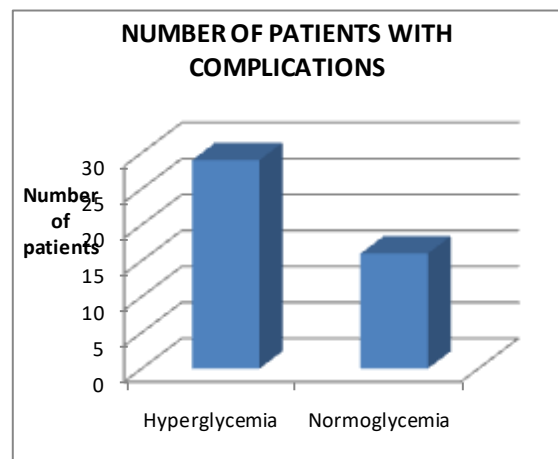
Graph 1: Organophosphorus Compound Of Study Subjects



Graph 2: Occurrence Of Hyperglycemia



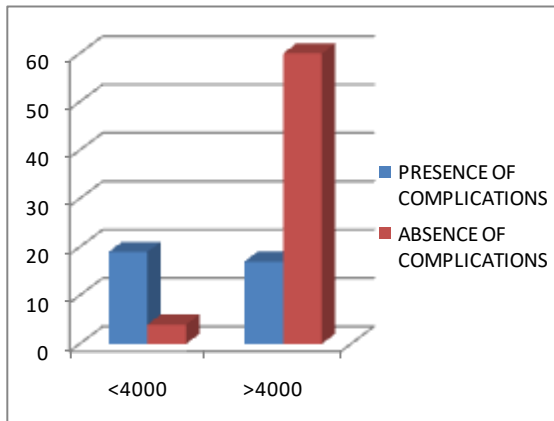
Graph3: Admission Pseudocholinesterase Levels



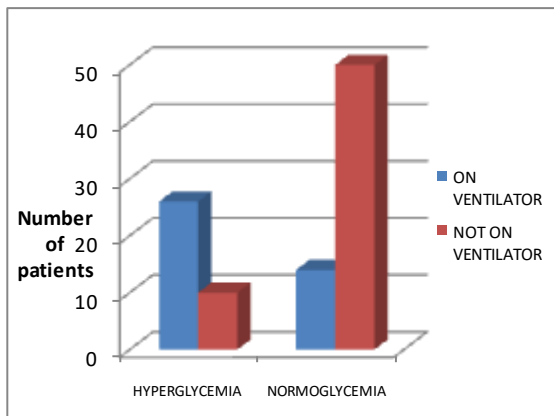
Graph 4: Association between admission RBS and complications (%)
 $\chi^2 = 20.22, P < 0.0001$

Organophosphorus compound: Dimethoate (28%) was the most common compound implicated in the poisoning. It was followed by Chlorpyrifos (22%) and quinalphos (14%). This was different from the study

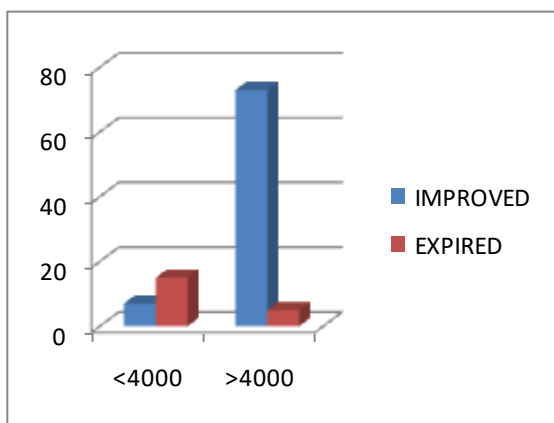
done by P Karki et al (8) Who found the most common compound as Methyl parathion (23%) followed by Propoxur (5%), which can be explained by the difference in availability of compound in a particular geographic location. In 6 patients (12%) the compound was not brought and the patient was diagnosed and treated on the basis of clinical features.



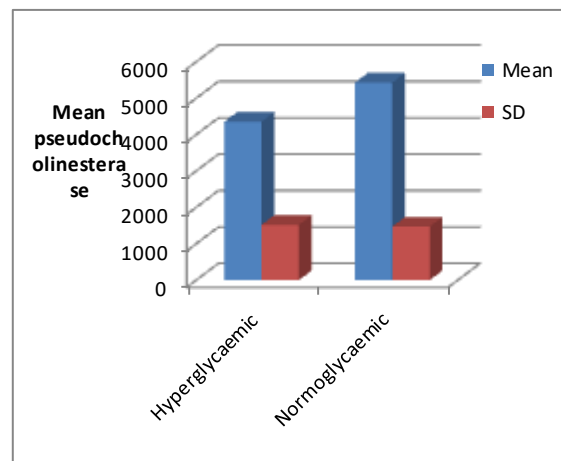
Graph 5. Admission Pseudocholinesterase and Complications



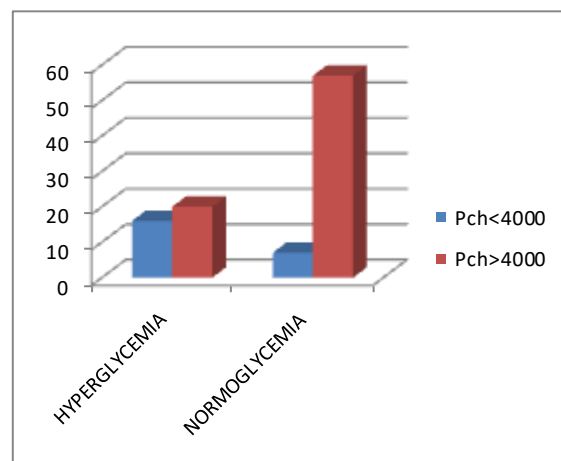
Graph 6. Admission RBS and Need For Ventilator



Graph 7. Relation of Pseudocholinesterase And Outcome



Graph8: Association Between Admission RBS And Mean Pseudocholinesterase Level



Graph 9: Correlating Admission RBS with Pseudocholinesterase Levels.

DISCUSSION

In the developing world acute Organophosphorus poisoning (OP) is widespread and its frequency is increasing. (1) WHO has estimated that lakhs of people worldwide die from pesticide poisoning. The commonest poisoning in India is OP poisoning owing to limited availability of facilities and finances in the developing countries as a result all OP patients cannot be managed in the intensive care unit. It is therefore important that clinical features and other factors which indicate severity of poisoning also predict the need for ventilatory support. It should be identified at the initial examination at admission in the emergency ward.

TABLE 3: STUDIES COMPARING SEX DISTRIBUTION

Sex	Goel et al (%) ^[9]	Vikram P et al (%) ^[10]	Shobha TR et al (%) ^[11]	Present study (%)
Male	72	75.1	56.5	65
Female	28	24.9	33.4	35

Males were the common victims in the present study which is in concurrence with the findings of Vikram P et al, Shobha TR et al, Goel et al. This could be attributed to the fact that they are exposed to more stresses of life and perhaps they are less efficient in managing the same when compared to women.

TABLE 4: STUDIES COMPARING MOTIVE OF POISONING

Motive	Goel et al (%) ^[9]	Bhattarai N et al (%) ^[12]	Vikram P et al (%) ^[10]	Present study (%)
Suicide	96.1	87.2	98.7	90
Accident	3.9	12.8	1.3	10

In the present study, majority of the cases of poisoning were suicidal in nature which is consistent with observation made by Vikram P et al, Bhattarai N et al.

In this study, maximum incidence of poisoning was among 18-25 years of age group (40%) which is consistent with the studies done by Logaraj M et al⁽¹³⁾ and Shankar PS et al.⁽¹⁴⁾ This age group in all probability is more vulnerable to the various emotional conflicts which occur during this phase of life.

Table 5: Age Distribution

Age	No. of patients(n=100)
18 – 25	40
26 – 35	25
36 – 45	14
46 – 55	7
56–65	14

Table 6: Studies Comparing Sex Distribution

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Table 7: Studies Comparing Motive of Poisoning

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In the present study, majority of the cases of poisoning were suicidal in nature which is consistent with observation made by Vikram P et al,⁽¹⁰⁾ Bhattarai poisoning is very common since these compounds are easily available for farmers and whenever there is impulse to commit suicide they are ready in hand.

Table 8: Studies Comparing Mode of Poisoning

Mode	SungurM et al (%) ^[15]	Present study (%)
Ingestion	93.6	90

Ingestion was the most common mode used for self poisoning by the patients, which is comparable with study done by Sungur M et al.^[15]

Table 9: Studies Comparing Clinical Features

Clinical features	Adlakha et al (%) ^[16]	Singh S et al (%) ^[17]	Goel et al (%) ^[9]	Present study (%)
Vomiting	56	90	97.08	94
Hyper salivation	36	80	28.15	90
Seizures	11	20	-	20

Vomiting was the commonest symptom in 94% followed by Hypersalivation 90% and above findings are comparable with following studies done by Adlakha et al, (16) Singh S et al, (17) Goel et al. (9)

Table 10: Studies Comparing Complications

Complications	Goel et al ⁽⁹⁾	Sungur ⁽¹⁵⁾	Present study
Respiratory Failure	34.95	29.7	40
ARDS	-	-	9
Pneumonia	-	-	5

Respiratory failure was the most common complication seen in 40% of patients which is comparable to studies by Goel et al, (9) Sungur et al. (15)

Table 11: Studies Comparing Hyperglycemia

Study	Hyperglycemia (%)
Present study	36
Sungur et al ⁽¹⁵⁾	31.9
Shobha et al ⁽¹¹⁾	26
Rao et al ⁽¹⁸⁾	12

Table 12: Studies Comparing Complications In Hyperglycemic Patients.

Study	Complications in hyperglycemic cases
Rao et al ⁽¹⁸⁾	67%
Present study	81%

In present study it was observed that admission hyperglycemia (RBS>200 mg/dl) was associated with complications in 81% as compared to 67% in Rao et al. (18) This showed a correlation that was highly significant (p<0.001). In addition hyperglycemia also showed a significant association with need for ventilator support (p<0.001). 72% of patients with hyperglycemia were found to need ventilator support as compared to 22% with normoglycemia.

In present study it was noted that Pseudocholinesterase values<4000U/L (p<0.001) was associated with complication in 91% (p<0.001) and all needed ventilator support and these observations were statistically significant.

The present study showed a overall mortality of 20% comparable with Bardin PG et al, (19) Singh S et al. (20) It was observed that there was mortality of 33% in patients with hyperglycemia which was statistically significant(p<0.009). Mortality among patients with

Pseudocholinesterase<4000U/L was 70% (p<0.001).

The above results indicate RBS value >200mg/dl is a good marker for predicting the mortality and also for assessing the need for ventilator support. Admission RBS was comparable to the low levels of pseudocholinesterase levels which is comparable with Rao et al. (18)

Further RBS was correlated with the Pseudocholinesterase levels RBS>200mg/dl was shown to be associated with a mean Pseudocholinesterase level 4355.36 with a SD of 1520.86 with a p<0.001 which was highly significant. These observations suggest that admission hyperglycemia is a useful indicator in OP compound poisoning and it is comparable to pseudocholinesterase. Further studies are needed in this area.

CONCLUSION

Admission hyperglycemia (RBS>200 mg/dl) was observed in 36% of patients associated with complications in 81% (p<0.001) as compared to 25% in normoglycemics.

- Pseudocholinesterase values <4000U/L(p<0.001) was associated with complication in 91%(p<0.001) and all needed ventilator support and these observations were statistically significant.
- Low levels of pseudocholinesterase level and increase in blood sugar levels were assessed for ventilator requirements, mortality and complications, and was found to be statistically significant.
- Overall mortality was 20%.Mortality was 33% in patients with hyperglycemia (p<0.009) and 70% in patients with pseudocholinesterase <4000U/L (p<0.0001).
- Admission RBS > 200 mg/dl along with low admission pseudocholinesterase levels can be considered as a useful factor in predicting the need for ventilator, morbidity and mortality of organophosphorus poisoning.

Recommendations - Study with follow up of study subjects is needed.

Limitations of the study

Bigger population with probability sampling technique ideally in community based study needed.

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