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## ASSESSMENT OF SEVERITY, TREATMENT AND OUTCOME OF ORGANOPHOSPHORUS POISONING: A DESCRIPTIVE STUDY

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### HOW TO CITE THIS ARTICLE:

Chandra Indira Priyadarsini, S. S. K. R. Bheemeshwara Rao, M. B. R. Sarma. "Assessment of Severity, Treatment and Outcome of Organophosphorus Poisoning: A Descriptive Study". Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 21, May 25, 2015; Page: 3194-3204.

**ABSTRACT: BACKGROUND:** Organophosphorous poisoning constitutes one of the most frequent poisoning in clinical practice all over the country and especially in this area where agriculture is the chief economic occupation. Acute organophosphorous poisoning ranks foremost in the list of agents which causes acute pesticide poisoning in the developing countries. Acute poisoning, accidental or due to deliberate ingestion or inhalation of these organophosphate chemicals is an important and one of the most common medical emergencies. Hence the present study is undertaken to assess severity of poisoning, management and outcome of organophosphorous poisoning cases admitted in Government General Hospital, Kakinada, A. P. **AIMS/OBJECTIVES:** 1. Assessment of severity of Organophosphorous poisoning according to Driesbach's criteria 2. To study the morbidity and mortality in these patients. **MATERIALS AND METHODS:** In this descriptive study fifty patients with organophosphorous insecticide poisoning were evaluated by clinical examination. They were investigated, treated and their treatment outcome were analyzed. **RESULTS:** 1. Chlorpyrifos and monocrotophos(together 66%) were the most commonly used pesticides. 2. 82% cases reached the hospital within 6 hours for commencement of treatment and were mostly of moderate to severe degree of OP poisoning while mild cases of accidental poisoning reached after 12 hours. Hence the mortality is high in the former group only. 3. When the severity of poisoning was graded by applying Driesbach's criteria at the time of admission 34% had severe degree of poisoning, 26% had moderate poisoning while 40% of cases presented with mild degree of poisoning. (Most of the cases were accidental inhalation and skin contact exposure.) 4. Among the patients belonging to moderate to severe degree of poisoning 30% of patients were put on assisted mechanical ventilation, indications being uncontrolled pulmonary secretions, continuing hypoxia, not relieved with routine Oxygen therapy and respiratory paralysis. 5. The mortality rate in the present study is 14% (7 cases out of 50). All of them expired despite good ventilatory support and intensive medical care. 6. In this study among 17 cases of severe degree poisoning, 5 patients expired and the remaining 12 cases recovered with Intensive medical care and mechanical ventilatory support.

**KEYWORDS:** Organophosphorus poisoning, Mechanical Ventilation, Cholinesterase.

**INTRODUCTION:** Acute organophosphorous poisoning constitutes one of the most frequent poisoning in clinical practice in developing countries like India and especially in this area where agriculture is the chief economic occupation. Organophosphates namely monocrotophos, chlorpyrifos are commonly used as pesticides for paddy and chilli crops. Paddy and chilli are widely cultivated in this area.

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## **The organophosphorous compounds clinically classified as;**

**Most dangerous:** TEPP, Disulfoton, Thiodemeton, Ditionsystox, Paraxon, BSI, Demeton (E 600), MevinPhos, ISD: EPN, Schradan, Metacide, Methyl Parathion, Monocrotophos, Dicrotophos.

**Dangerous:** Phosphamidon, Carbophenothion, Coumaphos, and Chlorpyrifos.

**Less dangerous:** Methyl Dimeton, Dimethoate, Phostex, Dicapthon, Orthophosphate, Trichlofor.

**Least dangerous:** Chlorthion, Ruelene, Malathion, and Runnel

**METABOLISM AND MECHANISM OF ACTION:** The organophosphorous compounds belong to the phosphorothionate class of chemicals. They are insecticidal and hence their toxic properties results from their ability to phosphorylate and inactivate certain esteratic enzymes in insects.

**MECHANISM OF PRODUCTION OF TOXICITY IN MAN:** In man, most cholinesterase in the nervous tissue and erythrocytes is acetylcholinesterase, whereas cholinesterase in the liver, plasma or serum is pseudocholinesterase. Inhibition of these enzymes by organophosphates is a result of firm binding of phosphate radicals of the organophosphates to the active sites of the enzymes, forming phosphorylated enzymes. The clinical features are due primarily, if not entirely, to inhibition of acetylcholinesterase of the nervous system, resulting in accumulation of acetylcholine at the synapses. This excess of acetylcholine initially stimulates, then paralyzes transmission in cholinergic synapses, sparing adrenergic synapses. The cholinergic synapses are in CNS, somatic nerves, ganglionic synapses of the autonomic nerves, parasympathetic nerve endings and sympathetic nerve endings to sweat glands.<sup>(1)</sup>

Majority of agents show some signs and symptoms of toxicity within 6 to 12 hours after exposure with the exception of the highly fat-soluble compounds (fenthion, difenthion, chlorfenthion).

With the exception of the fat-soluble agents, it was initially believed that most organophosphorous residues were eliminated within the first 48 hours after exposure. Newer data suggest these residues may remain for days to weeks, even after successful treatment of initial symptoms. ACHE, if not regenerated by nucleophilic oximes such as the antidote pralidoxime, must be generated at the nerve terminal, a process that may take several months.

Absorption of organophosphates in most instances of occupational poisoning has been through the skin and respiratory tract.

Poisoning by ingestion for the purpose of suicide, or rarely homicide, has been a most common cause of organophosphorous poisoning death. Self-poisoning with suicidal intent is a major problem in developing agricultural countries such as India and Sri Lanka, and is responsible for over 90% of exposures.

Because of easy and wide availability of organophosphates deliberate self-poisoning as well as occupational exposure with inadequate and inappropriate protective measures a good number of beds in medical ICU all over the country mostly developing countries are often occupied by organophosphorous poisoning cases. According to the WHO, one million serious accidental and two millions suicidal poisoning due to pesticides occur worldwide every year, of which 2,00,000 patients die, with most deaths occurring in developing countries.<sup>(2)</sup>

The Hospital management of pesticides poisoning often requires intensive care, particularly mechanical ventilation. Hence the present study is undertaken to assess the severity,

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management and outcome of organo-phosphorous poisoning cases admitted in Government General Hospital, Kakinada, and Andhra Pradesh.

**MATERIAL AND METHODS:** Fifty patients with alleged organo-phosphorous insecticide poisoning attending the department of medicine Rangaraya Medical College, Kakinada, A.P. were taken up for this study after informed and written consent.

Detailed history was taken in each case from patient and attendants. A meticulous physical examination was done on each of them at the time of admission. Appropriate investigations were done in all cases. Serum pseudocholinesterase levels estimation was done.

Characteristic symptoms and signs of the poisoning like frothing from mouth, miosis, fasciculations, pulmonary edema or respiratory paralysis were recorded.

The severity of poisoning was graded as mild, moderate, severe degree in all cases as per "DREISBACH'S CRITERIA"<sup>(3)</sup>

1. Mild- Anorexia, headache, weakness, anxiety, tremor of tongue and eyelids, miosis and blurred vision.
2. Moderate - Salivation, abdominal cramps, sweating, bradycardia, Fasciculations, crepitations but no pulmonary oedema.
3. Severe - Diarrhoea, loss of sphincteric control, Pin-point and non-reactive pupil, Respiratory difficulty and pulmonary oedema, cyanosis, convulsions, coma, heart block.

All these cases were immediately transferred to the Medical Intensive Care Unit.

The cases were treated with Intravenous Pralidoxime methyl iodide and Atropine depending upon the clinical picture.

**RESULTS:** In the present study of 50 cases of organophosphorous poisoning the following observations were found.

1. Chlorpyrifos and monocrotophos (together 66%) were the most commonly used pesticides of the organophosphorous group in the present study.
2. 82% of cases reached the hospital within 6 hours for commencement of treatment and were mostly of moderate to severe degree of OP poisoning while mild cases of accidental poisoning reached after 12 hours. Hence the mortality is high in the former group only.
3. When the severity of poisoning was graded by applying Dreisbach's criteria at the time of admission 34% had severe degree of poisoning, 26% had moderate poisoning while 40% of cases presented with mild degree of poisoning. (Most of the cases were accidental inhalation and skin contact exposure.)
4. All cases were administered injection Atropine, and injection PAM where indicated, apart from the supportive care.
5. Among the patients belonging to moderate to severe degree of poisoning 30 % of patients were put on assisted mechanical ventilation, indications being uncontrolled pulmonary secretions, continuing hypoxia, not relieved with routine Oxygen therapy and respiratory paralysis.
6. The mortality Rate in the present study is 14% (7 cases out of 50). All of them expired despite good ventilatory support and intensive medical care.
7. In this study among 17 cases of severe degree poisoning, 5 patients expired and the

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remaining 12 cases recovered with Intensive medical care and mechanical ventilatory support.

8. In our study out of 17 cases of severe poisoning 11 (64.70%) had signs of pulmonary edema and 6 had no signs of pulmonary edema. Among the 11 cases of pulmonary edema 5 patients were expired and 6 survived.
9. In our study, only 5 cases had neurogenic respiratory depression. However, 2 of them due to intermediate syndrome could be revived while the other 3 with central respiratory depression and coma expired despite ventilatory support.

**ETHICS:** The procedure followed were in accordance with ethical standards of the responsible committee on human experimentation.

**DISCUSSION:** In the present study of 50 cases of Organophosphorous poisoning admitted in Government General Hospital, Kakinada the peak incidence of this poisoning was in the age group of 16 to 30 years i.e., 62% and also there is gross male preponderance in the ratio of 4:1 (M: F) and 72% of our cases were from rural area while 28% cases were from urban area. Thus markedly higher incidence of O.P. poisoning was observed in young adult males mostly belonging to rural area and correlates well with and similar observations made in various studies, like Agarwal in 1993,<sup>(4)</sup> Yamashita et al 1997,<sup>(5)</sup> and Emerson et al in 1999.<sup>(6)</sup>

**Time lapse and survival:** Usually the time interval between exposure to the poisoning and commencement of appropriate therapy, apart from amount of poison exposed will decide the severity of poisoning and hence the survival. In our present study majority i.e., 60% of cases reached the hospital within 3 hours and 82% reached the hospital within 6 hours, in view of easy accessibility to better modes of transport in this region. However, 5 of these patients (4 out of 30, who reached the hospital within 3 hours, and 1 out of 11 who reached the hospital within 6 hours) presented with moderate to severe degree of poisoning expired despite reaching the hospital within 6 hours. Another 2 out of 5 cases who reached the hospital within 12 hours also expired in the present study; however the 4 cases who arrived after 12 hours were survived as all of them were cases of mild accidental inhalation only. Thus all the 7 cases who expired in the present study reached the hospital within 12 hours of exposure. This highlights the fact that patients with severe degree of poisoning brought to medical treatment immediately. Hence mild degree of inhalational exposures reached the hospital late. Hence, the disparity of mortality observed in the present study in relation to time of arrival.

**Nature of organophosphorous compound used:** In our study the commonest poison patients were exposed to is the chlorpyrifos, 24(48%), followed by monocrotophos 9(18%), as chlorpyrifos compound also used against termites during construction of new houses and also widely used for paddy crops. As this district is the rich paddy crop grower in the state, this compound is most widely used and hence it is easily accessible to rural population. Monocrotophos is also used by most agriculturists because it is an effective pesticide for rice and chilli pests.

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**Grading of severity of organophosphorous poisoning:** Grading was done according to Dreisbach's criteria, 20 patients had mild poisoning (40% cases), 13 patients (26%) had moderate poisoning, and 17 patients (34%) had severe poisoning.

**Mortality distribution according to severity:** In our study all mild case of poisoning recovered. Out of 13 cases of moderate poisoning 2 patients expired i.e. 15.38% mortality and 5 out of 17 cases of severe poisoning expired i.e 29.41% mortality. This study correlates with general observation that mortality is higher with increasing severity of poisoning.

**Serum Pseudocholinesterase level estimation:** Previous assumption that in patients with OP poisoning the Serum Pseudocholinesterase enzyme level supposed to correlates inversely with severity of poisoning. This aspect has also been studied in some of our cases as this investigation is not routinely done in our hospital and in view of its cost, we could study this enzyme level only in 1/3<sup>rd</sup> of cases i.e. 16 cases. But however, no correlation with drop in enzyme level and severity of poisoning was made out.

**Pattern of Treatment:** Intravenous Pralidoxime methyl iodide and Atropine formed the basis of therapy for these cases. In our study 30 cases (60%) of moderate to severe degree of poisoning were treated with Atropine and PAM for 3 days. 20 cases (40%) of mild degree of poisoning were treated with Atropine only.

In cases of severe degree of OP poisoning injection Atropine 5mg was given as Intravenous stat dose followed by slow continuous IV infusion of 100 mg Atropine bottles in 6 to 8 hours OR intermittent doses of 5-10 ampoules IV/ every 15 minutes until the pupils are moderately dilated or the patients are showing signs of Atropinisation. Then the intermittent doses were reduced to 2-5 ampoules/ hourly depending upon the pupil size, pulmonary secretions, tachycardia and restlessness (Atropine psychosis). This regimen continued for 24 - 48 hours and tapered depending upon the clinical profile and in most of the cases Atropine could be withdrawn by 7-10 days. In the present study, injection PAM was given IV/1 gm/ 6<sup>th</sup> hourly for 48-72 hours.

**Mechanical ventilatory support:** In our study 15 cases (30%) were put on ventilatory support. Out of them 8 cases recovered and 7 cases expired. Indications for mechanical ventilatory support are pulmonary secretions with hypoxia and respiratory depression. Those cases that expired despite ventilatory support were on mechanical ventilator for a period of duration varying from 12 hours to 96 hours.

## **MORTALITY:**

### **Factors influencing mortality:**

1. Chemical nature of compound i.e., highly dangerous or least poisonous.
2. Route of entry.
3. Quantity ingested.
4. Time lapse between ingestion and initiation of treatment and hospitalization.

In our study of 50 cases of OP poisoning, only 7 cases expired. 5 of them had severe poisoning and remaining two had moderate degree of poisoning at the time of admission. All of

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them also received mechanical ventilatory support and expired due to irreversible respiratory depression or uncontrolled respiratory secretions or cardiac arrest.

S. Singh et al 1984<sup>(7)</sup> reviewed acute poisoning cases and found that mortality rate in organophosphorous poisoning was 8.33%.

SB Siwach et al<sup>(8)</sup> in 1995 in their study found that mortality rate was 38.4% due to organophosphorous poisoning. Kabrawala and Solanki in 1971<sup>(9)</sup> reported mortality rate of 9.3%, Surjit Singh et al<sup>(10)</sup> in 1997 done a retrospective analysis of 867 cases of acute poisoning admitted during the period 1970 -89 in Nehru Hospital attached to PGIMER, Chandigarh, recorded mortality rate of 9.2% in 1970-79 and 11.5% in 1980-89 in cases of OP poisoning. Yamashita M et al 1997<sup>(5)</sup> in their study observed that the mortality following OP insecticides poisoning varies between 4-30%, G. Avasthi et al in 2001<sup>(11)</sup> observed 14% mortality rate in organophosphorous poisoning cases in 1999. The mortality rate of 14% observed in this study correlates with the observations found in studies done by Surjit Singh et al,<sup>(10)</sup> Yamashita M et al 1997<sup>(5)</sup> and G. Avasthi et al in 2001.<sup>(11)</sup>

In our study out of 17 cases of severe poisoning 11 (64.70%) had signs of pulmonary edema and 6 had no signs of pulmonary edema. Among the 11 cases of pulmonary edema 5 patients were expired and 6 survived. It was observed that in severe poisoning, patient with pulmonary edema and without pulmonary edema fared similarly in respect to morbidity and prognosis. Wadia RS et al in 1974<sup>(12)</sup> in their study found that patients with severe poisoning but without pulmonary edema had a greater morbidity and poorer prognosis. They had developed neurotoxicity.

In our study, only 5 cases had neurogenic respiratory depression. However, 2 of them due to intermediate syndrome could be revived while the other 3 with central respiratory depression and coma expired despite ventilatory support. In our study, only 4% had intermediate syndrome in the form of neck, proximal muscle weakness and mild respiratory paralysis observed on day 3 and were kept on mechanical ventilatory support and recovered by 7<sup>th</sup> day.

| Age group distribution | No. of patients | Percentage |
|------------------------|-----------------|------------|
| 1. 11-15               | 2               | 4          |
| 2. 16-20               | 13              | 26         |
| 3. 21-25               | 15              | 30         |
| 4. 26-30               | 3               | 6          |
| 5. 31-35               | 7               | 14         |
| 6. 36-40               | 3               | 6          |
| 7. 41-45               | 2               | 4          |
| 8. 46-50               | 3               | 6          |
| 9. 51-55               | 19              | 2          |
| 10. 56-60              | -               | -          |
| 11. 61-65              | 1               | 2          |

**Table 1: Age group distribution of 50 cases of organophosphorous poisoning**

In our study 62% of patients were in the age group of 16-30 years i.e., the poisoning is most common in adolescents and young adults than at extremes of age.

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| Sex    | No. of patients | Percentage |
|--------|-----------------|------------|
| Male   | 40              | 80         |
| Female | 10              | 20         |

Table 2: Sex Distribution

OP poisoning was consumed mostly by males i.e., 80% cases were males.

| Area  | No. of cases | Percentage |
|-------|--------------|------------|
| Rural | 36           | 72         |
| Urban | 14           | 28         |

Table 3: Demography (Rural/Urban distribution)

Most of these cases were from rural area. As this district is a rich agricultural area, there is easy availability of these pesticides.

| Portal of entry                | No. of patients | Percentage |
|--------------------------------|-----------------|------------|
| 1. Oral                        | 42              | 84         |
| 2. Inhalation                  | 5               | 10         |
| 3. Skin contact and inhalation | 3               | 6          |

Table 4: Portal of entry of OP insecticide observed in the present study

Oral ingestion is the most common mode of OP poisoning observed in the present study, most of them with suicidal intent. Inhalation while spraying is the next common mode.

**Table 5:** An attempt is made to know the exact nature of OP compound by identification of container at the consumption site and other enquiries. The following is the list of compounds identified.

| Organophosphate used | No. of patients | Percentage |
|----------------------|-----------------|------------|
| 1. Acephate          | 5               | 10         |
| 2. Monocrotophos     | 9               | 18         |
| 3. Triazophos        | 5               | 10         |
| 4. Chlorpyrifos      | 24              | 48         |
| 5. Malathion         | 1               | 2          |
| 6. Profenophos       | 1               | 2          |
| 7. Dimethoate        | 4               | 8          |
| 8. Phorate           | 1               | 2          |

Table 5

The above distribution shows Chlorpyrifos is the most widely used compound in this region, as this compound is also used as anti-termite agent during construction of new houses.

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| Grades of poisoning | No. of patients |        | Percentage |
|---------------------|-----------------|--------|------------|
|                     | Male            | Female |            |
| 1. Mild             | 14              | 6      | 40         |
| 2. Moderate         | 12              | 1      | 26         |
| 3. Severe           | 14              | 3      | 34         |
| Total               | 40              | 10     |            |

**Table 6: Patient distribution according to grades of severity of poisoning as per "Dreisbach's Criteria"**

20 patients had mild poisoning i.e., 40%- at the time of admission.

13 patients had Moderate poisoning i.e., 26%- at the time of admission.

17 patients had Severe poisoning i.e., 34%-at the time of admission.

**Table 7:** True Cholinesterase level (Erythrocyte acetyl Cholinesterase) and serum pseudo Cholinesterase level estimation are not available in this institution. However, 16 patients afford it and serum pseudo cholinesterase levels were estimated. The following table shows the results.

| Case No. | IP No.  | Name of the Op | Quantity | Time lapse after poisoning | Grades of poisoning | Duration of stay | BuChE value | Outcome  |
|----------|---------|----------------|----------|----------------------------|---------------------|------------------|-------------|----------|
| 1        | 1963323 | Chlorpyriphos  | 30 ml    | 1/2 hrs                    | Moderate            | 6 days           | 0.4U/ml     | Survived |
| 3        | 2044655 | Chlorpyriphos  | 20 ml    | 1 1/2 hrs                  | Severe              | 7 days           | 0.2U/ml     | Survived |
| 4        | 2048842 | Malathion      | 250 ml   | 3 hrs                      | Moderate            | 7 days           | 2.78 U/ml   | Survived |
| 10       | 240482  | Chlorpyriphos  | 100 ml   | 1.22 hrs                   | Severe              | 8 days           | 0.22 U/ml   | Survived |
| 11       | 242978  | Chlorpyriphos  | 10 ml    | 6 hrs                      | Mild                | 8 days           | 0.20 U/ml   | Survived |
| 12       | 244180  | Chlorpyriphos  | 250 ml   | 4 hrs                      | Severe              | 8 days           | 5 U/ml      | Survived |
| 23       | 250816  | Triazophos     | 20 ml    | 3hrs                       | Moderate            | 7 days           | 6.13 U/ml   | Survived |
| 26       | 252565  | Acephate       | 2 Lts    | 4 hrs                      | Moderate            | 5 days           | 4.6 U/ml    | Survived |
| 31       | 254892  | Acephate       | 100 ml   | 2 hrs                      | Moderate            | 3 hours          | 5.29 U/ml   | Expired  |
| 35       | 256102  | Chlorpyriphos  | 100 ml   | 3.15 hrs                   | Severe              | 7 days           | 0.32 U/ml   | Expired  |
| 37       | 257389  | Chlorpyriphos  | 100 ml   | 6 hrs                      | Mild                | 6 days           | 0.26 U/ml   | Survived |
| 43       | 259619  | Chlorpyriphos  | 200 ml   | 1.10 hrs                   | Severe              | 36 hrs           | 0.24 U/ml   | Expired  |
| 27       | 253345  | Chlorpyriphos  | 150m1    | 7 hrs                      | Severe              | 2 days           | 0.21 U/ml   | Expired  |
| 25       | 252495  | Triazophos     | 60m1     | 1 hrs                      | Moderate            | 6 days           | 0.36 U/ml   | Expired  |
| 46       | 238552  | Chlorpyriphos  | 200m1    | 8 hrs                      | Severe              | 1 days           | 0.28 U/ml   | Expired  |
| 50       | 261971  | Chlorpyriphos  | 100 ml   | 20min                      | Severe              | 4 days           | 4.6 U/ml    | Survived |

**Table 7**

Normal serum pseudo Cholinesterase level is 4.6 to 10.4u/ml. In five cases out of 16 it was within normal range and in the remaining 11 cases levels were decreased.



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| Treatment modalities                              | No. of patients | Percentage |
|---|-----------------|------------|
| 1. No. of cases treated with PAM and Atropine     | 35              | 70         |
| 2. No. of cases treated with Atropine without PAM | 15              | 30         |

**Table 8: Treatment modalities followed in the present study**

Moderate to severe degree of poisoning cases (35 cases) were treated with Atropine and PAM, mild cases (15 cases) were treated with Atropine only.

**Table 9:** All cases were closely monitored for any evidence of impending/ overt respiratory failure i.e., R.R.>30/ min, SpO<sub>2</sub><90% and pulmonary edema and endotracheal intubation and mechanical ventilation instituted wherever necessary. The following table shows the incidence of Mechanical ventilatory support in the present study.

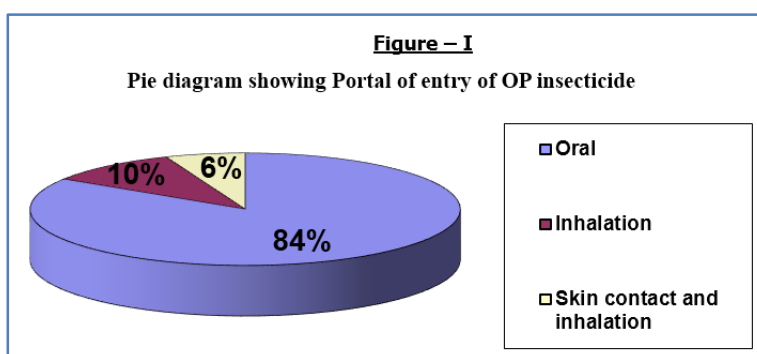
| Mode of treatment                      | No. of cases | Percentage |
|--|--------------|------------|
| 1. Treated with ventilatory support    | 15           | 30         |
| 2. Treated without ventilatory support | 35           | 70         |

**Table 9**

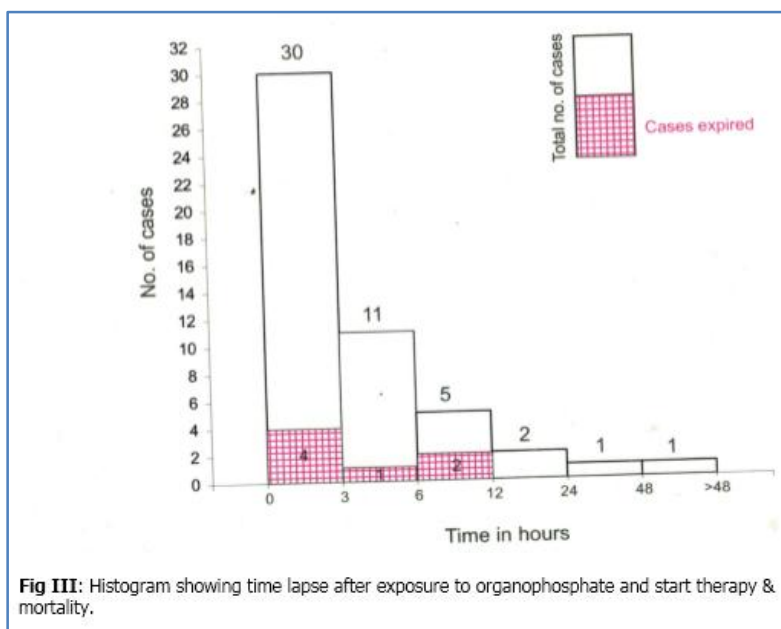
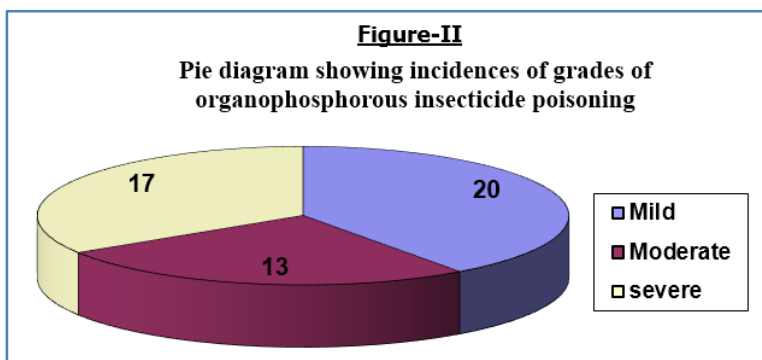
| Severity | Total No. of male cases | No. of cases expired | Percentage | Total No. of female cases | No. of cases expired | Percentage |
|----------|-------------------------|----------------------|------------|---------------------------|----------------------|------------|
| Mild     | 14                      | —                    | —          | 6                         | —                    | —          |
| Moderate | 12                      | 2                    | 16.66      | 1                         | —                    | —          |
| Severe   | 14                      | 4                    | 28.57      | 3                         | 1                    | 33.33      |
| Total    | 40                      | 6                    |            | 10                        | 1                    |            |

**Table 10: Mortality distribution according to severity of poisoning**

Most of the expired cases belong to moderate to severe degree of poisoning.



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**ACKNOWLEDGMENTS:** Thankful to Dr. M.V.V. Tirumal Rao, Dr. C.S.S. Sarma professor of medicine, Ranagarya Medical College, Kakinada,

Thankful to Dr. Yashodamma, M.D. Professor of Medicine. Ranagarya Medical College, Kakinada

I am thankful to my husband Dr. Saka Vinod Kumar, M.D., Professor & Head of Department of Pulmonary Medicine of Jawaharlal Institute of Postgraduate Medical Education and Research v(JIPMER), Pondicherry.

Thankful to Mr. M. Ganesan, Mr. P. Karunanithi staff working in Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry.

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Date of Submission: 19/05/2015.  
Date of Peer Review: 20/05/2015.  
Date of Acceptance: 23/05/2015.  
Date of Publishing: 25/05/2015.