

**Association between acute  
organophosphate and carbamate  
self - poisoning and development of  
hyperglycaemia**

**By**

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## **DECLARATION BY THE CANDIDATE**

The work described in this thesis was carried out by me under the supervision of Prof. U. Hettiaratchi, Prof. L. Athiththan, Prof. H, Peiris (Department of Biochemistry, Faculty of Medical Sciences, University of Sri Jayewardenepura) and Prof. S. Siribaddana (Department of Medicine Faculty of Medicine & Allied Sciences, Rajarata University of Sri Lanka) and a report on this has not been submitted in whole or in part to any university or any other institution for another Degree/Diploma.

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## LIST OF ABBREVIATIONS

|         |   |
|---------|---|
| ACh     | Acetylcholine   |
| AChE    | Acetylcholinesterase                                      |
| AGEs    | Advanced Glycated End products                            |
| ALP     | Alkaline Phosphatase                                      |
| ALT     | Alanine Aminotransferase                                  |
| AST     | Aspartate aminotransferase                                |
| ATP     | Adenosine Triphosphate                                    |
| BHT     | Bed Head Ticket   |
| CAT     | Catalase  |
| CNS     | Central Nervous System                                    |
| DM      | Diabetes Mellitus   |
| DMSO    | Dimethyl Sulfoxide  |
| DTNB    | Dithionitrobenzoic acid                                   |
| EDTA    | Ethylenediaminetetraacetic acid                           |
| ELISA   | Enzyme-Linked Immunosorbent Assay                         |
| ERC     | Ethics Review Committee                                   |
| ETU     | Emergency Treatment Unit                                  |
| FBS     | Fasting Blood Sugar                                       |
| FMS     | Faculty of Medical Sciences                               |
| GC      | Glucagon  |
| GP      | Glycogen Phosphorylase                                    |
| HbA1C   | Glycated Haemoglobin                                      |
| HOMA-IR | Homeostasis Model Assessment-estimated Insulin Resistance |
| HPA     | Hypothalamic-Pituitary-Adrenal axis                       |
| ICU     | Intensive Care Unit                                       |
| IGR     | Insulin to Glucagon Ratio                                 |
| IQR     | Inter Quartile Range                                      |
| IR      | Insulin resistance  |

|       |   |
|-------|---|
| LDH   | Lactate dehydrogenase                       |
| MDA   | Malondialdehyde                             |
| NADP  | Nicotinamide Adenine Dinucleotide Phosphate |
| OGTT  | Oral Glucose Tolerance Test                 |
| OP    | Organophosphates                            |
| PChE  | Plasma cholinesterase                       |
| PEPCK | Phosphoenol Pyruvate Carboxy Kinase         |
| POP   | Peradeniya Organophosphate Poisoning Scale  |
| RBC   | Red Blood Cell                              |
| RBS   | Random Blood Sugar                          |
| ROS   | Reactive oxygen species                     |
| RUSL  | Rajarata University of Sri Lanka            |
| SOD   | Super Oxide Dismutase                       |
| SPSS  | Statistical Package for Social Sciences     |
| T2DM  | Type 2 Diabetes Mellitus                    |
| THA   | Teaching Hospital Anuradhapura              |
| USJ   | University of Sri Jayewardenepura           |
| WHO   | World Health Organization                   |



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**ABSTRACT**

Intentional ingestion of pesticides has become a major health issue globally. Among the various types of pesticides, organophosphates (OPs) and carbamates, are commonly used for self-harm in the developing countries. In addition to adverse clinical outcomes of increased cholinergic manifestations, biochemical changes like hyperglycaemia have also been observed in acute exposure to OP and carbamate. Thus, the current study was designed to assess the glycaemic status and selected biochemical markers in acute OP and carbamate self-poisoned patients admitted to Teaching hospital Anuradhapura, (THA) with a follow-up study after 6 months of acute poisoning. This prospective longitudinal study was carried out in 157 patients. Severity of poisoning on admission was assessed using two methods; Peradeniya organophosphate poisoning (POP) scale and red blood cell (RBC) cholinesterase level. Venous blood sample was obtained to assess liver markers, RBC cholinesterase, and random blood sugar (RBS), on admission. On admission HbA1c was carried out to exclude the subjects with diabetes mellitus. Second blood sample was collected at the date of discharge after 8-10 hours of overnight fasting. Insulin, C-peptide, pancreatic amylase, phosphoenol pyruvate carboxy kinase (PEPCK), glucagon, liver markers, fasting blood sugar (FBS), Oral glucose tolerance test (OGTT), and homeostasis model assessment of insulin resistance (HOMA-IR) were assessed. Blood samples for the follow up study was taken after 6 months of poisoning and RBS, HbA1c, and liver markers were analyzed. Data were analyzed using SPSS version 21. Among the OP (62) and carbamate (95) self-ingested patients only 51 patients attended

the follow-up study. Mean age ( $\pm$ SD) of the total population, female and male groups were 33 ( $\pm$ 13), 28 ( $\pm$ 10) and 36 ( $\pm$ 13) years respectively. On admission 41.4% of the total study subjects were hyperglycaemic. The following parameters; RBS, AST and ALT on admission and ALT, AST, FBS, OGTT-I hour, OGTT 2-hour, insulin, C-peptide, glucagon and HOMA- IR at discharge, had a significant correlation with severity of poisoning. At discharge the biochemical parameters assessed, for median FBS, OGTT-1hour, OGTT-2-hour, insulin, C-peptide, glucagon, HOMA-IR, serum pancreatic amylase and AST showed significant differences ( $P < 0.01$ ) between POP mild and moderate poisoned groups. PEPCK was elevated in all three groups than the normal reference value. RBS and AST have significantly decreased in follow up study compared to the values on admission and discharge, whereas HbA1c did not show significant elevation in follow-up study. The findings of the present study indicate transient hyperglycaemia following acute OP and carbamate poisoning during the hospital stay which was normalized at the time of follow-up. Furthermore, FBS and HOMA-IR increased across the POP severity groups (mild to severe), and PEPCK was elevated above the cut off value in all three groups. Even though median pancreatic amylase values increased with the POP severity groups, the values were not elevated above the cut off value. Therefore, this transient change in glucose homeostasis might be attributed to the physiological stress, while excluding the pancreatic damage as an underlying mechanism of hyperglycaemia, which has been postulated in several studies. Further, larger sample size for follow-up study with severe poisoning patients would validate the findings.

**Key words:** Organophosphate, Carbamate, Peradeniya organophosphate poisoning scale, Hyperglycaemia, RBC cholinesterase