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# Electrolyte Concentrations and Liver Enzymes in Car Spray Painters Exposed to Car Spray Paints within Port Harcourt Metropolis, Rivers State, Nigeria

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#### Authors' contributions

This work was carried out in collaboration among all authors. Author ISK designed the study and performed the statistical analysis. Authors OOD, ACN and OG managed the literature review and analysis of the study. All authors have read and approved the final manuscript.

#### **Article Information**

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#### **ABSTRACT**

**Aim:** To determine the effect of car spray paint on electrolyte concentrations (sodium, potassium, bicarbonate and chloride), Anion gap, Total Protein, Albumin, liver enzymes (Alanine amino transferase and Aspartate amino transferase) of car spray painters.

**Place of Study:** The study was conducted within Port Harcourt metropolis, Rivers State Nigeria. **Methodology:** Twenty (20) male car spray painters age range between 25 and 61 years with 7-28 years work experience in car spray painting (test subjects) and twenty (20) apparently healthy male individuals aged between 25 and 61 years who work within an office setting far away from car

spray painting garage (non-exposed individuals) were used as control for the study. Plasma electrolyte concentrations were estimated using lon selective electrode method while Liver Enzymes Alanine amino transferase and Aspartate amino transferase were estimated using spectrophotometric method. Results obtained from the experiment were expressed as Mean  $\pm$  Standard Deviation. P < .05 were considered statistically significant.

**Results:** Sodium, Potassium, Bicarbonate and Chloride concentrations in plasma of car spray painters when compared to non-car spray painters did not showed any significant difference (P> .05). However, Anion gap was significantly increased (P<.05) in plasma of car spray painters when compared to non-car spray painters. Alanine amino transferase activity were significantly higher in plasma of Car spray painters (P<.05) when compared to non-car spray painters while Aspartate amino transferase activity, Total protein and Albumin concentrations remained relatively unchanged when compared between the studied groups. However, Aspartate amino transferase and Alanine amino transferase activities were affected by years of exposure to car paints.

**Conclusions:** This study suggest that car spray paint affects Anion gap and Alanine amino transferase activity in car spray painters hence safety apparatus should be worn while working. However further test on other liver enzymes should be done to validate the effect of spray paint on the liver.

Keywords: Electrolyte; liver enzymes; anion gap; albumin; total protein; car spray painting.

#### 1. INTRODUCTION

Car spray painting as an occupation involves the use of car paints on car surfaces for both protective and decorative purposes. It is a vocation which involves the use of special chemicals referred to as spray paints where a liquid coating substance is changed into a mist or aerosol, in order to apply a coating onto the body of cars. Spray paints used by car spray painters are water based paints such as primer, base coat, thinner and clear coat, the water based paints are usually used as a combination of two or more chemicals for spraying. The spray paints contain solvents such as xvlene. Isocvanates and styrene. Paint components also contain metals (Lead, Cadmium and Chromium) and pigments such as Acrylates and Methylates [1]. Water based paints generate a lot of aerosols which are inhaled within car spray painting workshops. According to research [2], car paints when sprayed disperse a lot of heavy toxic metals which can be suspended in the atmosphere long enough to be inhaled by car spray painters. In addition, the vapors from the car paints can be absorbed through the skin. Individuals who perform car spray painting without wearing appropriate personal protective equipment such as a respirator or gloves can be affected by the aerosols caused by the paints [3,4].

Furthermore, considerable inhalation and percutaneous absorption of solvents can occur within minutes of the onset of exposure. Most painting workshop within Port Harcourt Metropolis are poorly ventilated and painters

often enclose their spraying areas during and after the painting process with make shift items such as tarpaulin to prevent dust from settling on painted surfaces. This method exposes spray painters to extremely high levels of chemical hazards from paints used in working [5]. The procedure in which the spray painting is done itself offers the highest degree of exposure because the paint is aerosolized while being spread on the car parts. Likewise, the period which is allowed for the painted parts of the car to dry also releases some of the organic solvents in the form of volatile organic compounds [5]. Solvents such as Toluene, xylene, Benzene and isocyanates found in car paint are strong irritants to skin as they are volatile toxic materials [6]. Substances such as silica contained in car paints can be trapped in the lungs causing silicosis [6] while chromium another component of car spray paints can cause irritation of the eyes, skin, nose, lungs [7] and also cause lung cancer while Lead can cause elevated blood pressure which may indirectly influence electrolyte concentrations in workers exposed to it. Isocyanates in paint has been reported to cause occupational asthma [8] while toxicants such as xylene, acrylates and methyl acrylates cause respiratory depression, difficulty in breathing and respiratory tract irritation [9].

Toxicants from car paints may enter the human body through inhalation, skin contact and accidental ingestion [10]. Toxic materials and volatile substances when absorbed into the body may exert their effect on the system beyond the site of initial exposure and may be circulated and transported to organs such as the liver for

detoxification. The liver is an organ that metabolizes toxic substances and endogenous waste which influences metabolic and hemodynamic processes involving electrolyte balance and hepatic albumin synthesis. Alanine amino transferase (ALT) is an enzyme in the liver that increases in liver cell injury [11] while Aspartate Amino transferase is an enzyme associated with chronic liver tissue degeneration and necrosis.

Electrolytes are charged low molecular mass molecules present in plasma and cytosol, usually ions of sodium, potassium, calcium, magnesium, chloride, bicarbonate, phosphate, sulfate and lactate [12]. According to research [13], electrolytes maintain cellular tonicity and fluid balance between the various cellular components, they are involve in most metabolic processes, maintenance of pH, regulation of neuronal and muscular function. Sodium is the main extracellular cation. The plasma sodium level is a major factor in the control of water homeostasis and extracellular fluid volume. Potassium is the principal intracellular cation, 98% of which is maintained within the cells by the ATP dependent mechanism known as the Na<sup>+</sup>/K<sup>+</sup> -ATPase pump. Potassium plays a role in intracellular osmolality, enzymatic reactions, the regulation of the heart muscles and for the transmission of nerve impulses. Chloride is a major extracellular anion and occurs in the body mainly as sodium chloride. It helps to maintain proper water distribution, osmotic pressure and acid-base balance in the extracellular fluid of the body. Bicarbonate is the second most abundant anion in the extracellular fluid and is a major component of the buffering system of the blood. Anion gap is a measure of the acid base balance in the system. It is the difference between cations (sodium and potassium) and anions (chloride and bicarbonate) in an individual. Anion gap is requested in patients with acute illness and unknown exposure. Elevated levels of anion gap indicate acidiosis, renal failure and toxic ingestion while low values are as a result of gastrointestinal and renal bicarbonate losses [14] and may indicate bromide intoxication and monoclonal protein [15].

Car spray painters carry out their work using car spray paints which are aerosolized and these paints are inhaled into the body and also absorbed into the skin as they spray paints on cars. These car spray paints can be absorbed into the body and could interact and cause adverse side effects including disturbance in

cellular tonicity and fluid balance between the various cellular components. Most car spray painting in Port Harcourt metropolis is done in workshops and sheds within automobile mechanic areas without proper use of spraying booths and protective apparel [16]. This study therefore aimed to estimate the electrolyte concentrations and liver enzymes activity in car spray painters within Port Harcourt metropolis, Rivers state, Nigeria.

#### 2. MATERIALS AND METHODS

#### 2.1 Study Area

The study was conducted within Port Harcourt metropolis, Rivers State Nigeria. Car spray painters were recruited from Mile 3 mechanic garage and Ikokwu mechanic village within Port Harcourt metropolis, Rivers state, Nigeria.

#### 2.2 Study Population

A total of twenty (20) male car spray painters age range between 25 and 61 years with work experience of 7-28 years in car spray painting were used in this study. All the subjects have been directly exposed to car spray paints in the course of carrying out their work. Years of exposure was determined from years of working with car spray paint. Twenty (20) apparently healthy male individuals ages between 25 and 61 years who work within an office setting far away from car spray painting garage were used as non-exposed individuals who served as control for the study. Questionaires were given to each participant to obtain data on age, date of employment into the profession and years of working with car spray paint. Females were excluded from the study to avoid the influence of hormonal changes on the test results.

#### 2.3 Sample Collection

5mL of blood sample was collected from each participant by venipuncture from the antecubital vein into well labelled lithium heparin tubes. The blood obtained was separated after centrifugation at 2500rpm for 5 minutes using a Techmel & Techmel centrifuge. The plasma obtained were analyzed immediately after separation.

#### 2.4 Electrolyte Estimation

lon selective electrode (ISE) method of electrolyte estimation using ISE 4000 analyzer made by State Forest Research Institute (SFRI),

India was used for the determination of sodium, potassium, chloride and bicarbonate concentration in the blood samples collected from the car spray painters and controls.

#### 2.5 Principle of Ion Selective Electrode

When samples are mixed with high ionic strength ISE electrolyte buffer and passed through the flow cell, a potential is generated at the surface of the ion selective electrodes and thereby measuring the sodium, potassium, chloride and bicarbonate concentration present in the sample I17I.

#### 2.6 Procedure for Electrolyte Estimation

The ISE 4000 analyzer was switched on and cleaned using a cleaning solution. The ISE reagent was then connected to the packs and the analyzer. The ISE analyzer was calibrated to ensure a pass for sodium, potassium, chloride and bicarbonate. After the calibration, the screen displayed the main menu. The plasma sample was placed under the probe of the ISE analyzer and the "aspirate" button on the ISE analyzer screen was pressed. The probe aspirated the sample and was removed after a beep sound indicating the instruction from the analyser to remove the sample. The ISE analyzer measured each sample and the results were displayed on the screen within a minute.

# 2.7 Alanine Amino Transferase and Aspartate Amino Transferase Estimation

Spectrophotometric method was used to estimate Alanine amino transferase and Aspartate amino transferase [13].

### 2.8 Total Protein Estimation and Albumin Estimation

Biuret method was used to estimate Total protein while Albumin was estimated using Bromo Cresol Green method [13].

#### 2.9 Statistical Analysis

Results obtained from the study were analysed using Microsoft excel 2007 and SPSS version 20.0.Results were expressed as Mean  $\pm$  S.D for each group where applicable. P < .05 was considered statistically significant.

#### 3. RESULTS

The results obtained from Estimating the electrolyte concentration and liver enzymes of twenty (20) car spray painters(exposed) and twenty (20) non car spray painters (non exposed) are summarized in Tables 1-2 and Figs. 1 and 2.

## 3.1 Electrolyte Concentrations of All Studied Groups

Table 1 shows that Sodium, Potassium, Bicarbonate and Chloride concentrations were not significantly different in car spray painters exposed to car paint when compared to non-car spray painters who had no exposure to car paint, however, Anion gap showed significant increase in car spray painters when compared to non-car spray painters (P < .05).

#### 3.2 Liver Enzymes, Total Proteins and Albumin in Car Spray Painters (Exposed) and Non-Car Spray Painters (Non Exposed)

Table 2 shows significant increase in Alanine amino transferase concentration of car spray painters when compared to non-car spray painters, however, Aspartate amino transferase, Total protein and Albumin did not show any significant difference across the group.

# 3.3 Electrolyte, Total Protein, Albumin and Anion Gap in Car Spray Painter with Reference to Years of Exposure to Car Spray Paint

Fig. 1 shows that there were decrease in the concentrations of Protein and Anion gap as years of exposure to car spray paint increased while sodium, potassium, bicarbonate, Chloride and Albumin concentrations remained relatively unchanged.

#### 3.4 Alanine Amino Transferase (ALT) and Aspartate Amino Transferase (AST) Concentrations in Car Spray Painters With Reference To Years of Exposure to Car Spray Paint

Fig. 2 Shows that there were increase in the concentrations of Alanine amino transferase as years of exposure to car spray paint increased while Aspartate amino transferase concentrations decreased as years of exposure to car spray paint decreased.

Table 1. Electrolyte concentrations in car spray painters and non-car spray painters

Parameter	Exposed N=20	Non Exposed N=20	P value	Significance
	Mean ± S.D	Mean ± S.D		
Sodium (mmol/l)	144.00 ± 11.67	140.00 ± 2.52	0.1423	NS
Potassium(mmol/l)	$4.10 \pm 0.66$	4.00 ± 0.31	0.5433	NS
Bicarbonate(mmol/l)	24.00 ± 2.46	23.00 ± 2.11	0.1757	NS
Chloride(mmol/l)	104.00 ± 4.56	105.00 ± 3.03	0.4191	NS
Anion gap (mmol/l)	18.00 ± 11.01	12.00 ± 3.31	0.0250	S

S= Significant, NS= Not Significant. P< .05 is considered statistically significant

Table 2. Liver enzymes, Total proteins and Albumin in car spray painters(exposed) and non-car spray painters (non exposed)

Parameter	Exposed N=20 Mean ± S.D	Non Exposed N=20 Mean ± S.D	P value	Significance
ALT (IU/L)	20.00 ± 4.50	5.20 ± 3.50	0.0001	S
AST (IU/L)	8.00 ± 5.30	6.70 ± 2.56	0.3295	NS
Total protein (g/l)	69.00 ± 14.46	68±5.94	0.7764	NS
Albumin (g/l)	38.00 ± 6.39	40±2.07	0.1909	NS

S= Significant, NS= Not Significant. P< .05 is considered statistically significant. ALT= Alanine amino transferase, AST= Aspartate amino transferase

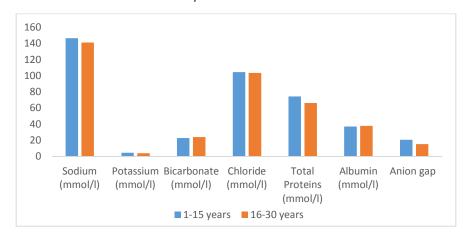


Fig. 1. Electrolyte, Total protein, Albumin and Anion gap in car spray painter with reference to years of exposure to car spray paint (1-15 years and 16-30years of exposure)

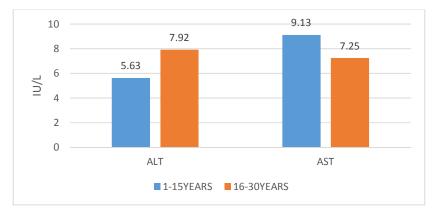


Fig. 2. Alanine amino transferase (ALT) and Aspartate amino transferase (AST) concentrations in car spray painters with reference to years of exposure to car spray paint

#### 4. DISCUSSION

Electrolyte (sodium, potassium, bicarbonate and chloride) concentrations in car spray painters when compared to non-car spray painters did not show any significant difference in this study (Table 1). Electrolytes which are charged compounds in the body help to maintain water balance and osmotic pressure in intracellular and extracellular fluid compartments by interacting with each other in tissues, nerves and muscles which makes them a vital component for healthy function. The results obtained in this study suggested that electrolytes of car spray painters are not affected by the chemical constituents in car spray paints such as lead, cadmium and isocyanate,this suggest that redistribution of electrolytes to action sites within the body are not affected by car spray constituents. Chemical constituents in car paints such as cadmium when inhaled or absorbed through skin contact are transported in the blood bound to albumin. The bound complex is taken into the liver where metallothionein is induced and bound to the chemical constituents of paints. The bound complex is easily filtered through the glomeruli. Cadmium a constituent of car spray paint is transported to the gut and excreted in feaces while some are eliminated through the hair [18]. Other car paint constituents such as isocyanates have been reported to conjugate macromolecules at site of contact and systemic absorption which makes them easily eliminated in urine [19]. This could suggest the reason why electrolytes of car spray painters were not affected by the chemical constituents in car paint as observed in this study because inhaled or absorbed chemical constituents are easily removed from circulation through various means of elimination. This is in contrast with previous work done by some researchers [20] where adverse effects of volatile organic compounds were seen to cause elevated serum electrolytes among paint factory workers.

Anion gap was significantly increased in car spray painters when compared with non-car spray painters (Table 1). Anion gap is the difference between primary measured cations and anions. Anion gap is useful in the interpretation of acid-base disorders and the diagnosis of conditions such as ketoacidosis and poisoning. The high anion gap in the car spray painters may be attributed to metabolic acidosis which may be as a result of exposure to car spray paints. This result is in agreement with

previous study done [21] where elevated values of anion gap indicated metabolic acidosis.

study showed that Alanine amino This transferase (ALT) was significantly increased in car spray painters when compared with non-car spray painters (Table 2) and Alanine Amino transferase concentrations increased as years of exposure to car spray paint increased (Fig 2). Long term exposure to toxic substances affect organs such as the liver which metabolize toxic substances hence the effect on liver enzyme production. Alanine amino transferase helps to convert alanine, an amino acid found in the cells of the liver and the kidney. The level of Alanine amino transferase in the blood can help evaluate liver function or determine the underlining cause of liver problem. Alanine amino transferase test may be performed to monitor the progression of liver diseases such as hepatitis or liver failure. Toxic solvents absorbed in the body are metabolized by the liver and may generate liver damage which affects liver enzyme production Similar reports [23] demonstrated physiological damage to glomerular membrane.

This study also showed that Aspartate amino transferase was not significantly different in car spray painters when compared to non-car spray painters (Table 2). However, decrease in the concentrations of Aspartate amino transferase were observed in car spray painters as years of exposure to car paints increased (Fig. 2). Aspartate amino transferase is an important enzyme in Amino acid metabolism, it is found in the liver, it can also be found in red blood cells. heart, muscle tissue, pancreas and kidneys. Aspartate amino transferase levels are valuable in the diagnosis of liver disease, although not specific for a particular liver disease; it can be used in combination with other enzymes to monitor the cause of various liver diseases. Increased in the activity of AST can cause myocardial infection [24]. This study is in contrast to some research study which reported elevated liver enzymes in painters [25]. The liver metabolizes toxic organic solvents which can cause damage to membranes in the liver, this could account for low levels of Aspartate amino transferase as years of exposure to car paint increased. Similar studies [23] also reports physiochemical damage to body organs by reactive metabolites from paint. They attributed damage caused by metabolites from paints to high lipophilicity which can occur after long duration of exposure to car paint.

Total protein and albumin were also not significantly different between car spray painters and non-car spray painters in this study (Table 2) however, Total protein decreased as years of exposure to car paints increased (Fig. 1). Proteins are important building blocks of all cells and tissues; they are important for body growth, development and health. They form the structural part of most organs and make up enzymes and hormones that regulate body functions. This is in agreement with reports [13] which stated that Total protein and Albumin levels are rarely raised except in dehydration and artefactually by prolonged venous stasis.

#### 5. CONCLUSIONS

This study was able to establish that Anion gap and Alanine Amino transferase were affected by exposure to car spray paints in car spray painters while concentrations of Total protein, Sodium and Aspartate amino transferase and Alanine Amino transferase were affected by years of exposure to car spray paint.

#### 6. RECOMMENDATIONS

It is advised that car spray painters should adhere to safety procedures by wearing safety wears and nose mask while working to avoid the influence of car spray paints on their Alanine amino transferase and anion gap. Car spray painters should also rehydrate their system by drinking a lot of fluid to reduce the increase in anion gap and avoid future acid base disorders. Further study on other liver enzymes is also recommended.

#### CONSENT

The participants used for the study were recruited after obtaining informed consent. Each participant was duly informed about the research before obtaining informed consent.

#### ETHICAL APPROVAL

Well written approval was obtained and kept by the Authors (CHST/RJC/002/2020).

#### **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

#### **REFERENCES**

 Tornling G, Alexanderson R, Plato N. American Journal of Industrial Medicine. 1990;17:299-310.

- Abidemi OO. Levels of Pb, Fe, Cd and Co in Soils of automobile workshops in Osun state, Nigeria. Journal of Applied Sciences and Environmental Management. 2011; 15(2):279-282.
- 3. Semple S, Brouwer DH, Dick F, Cherrie JW. A dermal model for spray painters. Part II: estimating the deposition and uptake of solvents. Annals of Occupational Hygiene. 2011;45(1):25-33.
- 4. Chen W, Li T, Zou G, Li X, Shi L, Feng S, Shi J, Zhou F, Han S, Ling L. Study protocol: A cluster randomized controlled trial to access the effectiveness of a multipronged behavioural intervention to improve use of personal protective equipment among migrant workers exposed to organic solvents in small and medium-sized enterprises. BioMed Central Public Health. 2016;16:580.
- Ojo TO, Onayade AA, Akinyemi PA, Adesanmi AJ. Environmental working conditions, Lung function and Total serum bile acids of Spray painters exposed to organic solvents in Ile-Ife, Nigeria. Journal of Health and Pollution. 2017;7(13):2-10.
- 6. Health, Safety & Environment (HSE), HSG 261. Health and safety in motor vehicle repair and associated industry. London, ISBN 978 0 7176 63 08 8: 2009.
- Occupational Safety and Health Administration, (OSHA). Safety and health topics/ Chromium; 2019c. Available:https://www.osha.gov/SLTC/chromium/index.html
- 8. Bernstein IL, Chan-Yeung M, Malo JI, Bernstein DI. Asthma in the work place. Marcel Dekker, New York. 1993;1-4.
- Kandyala BIL, Chan-Yeung M, Malo JI, Bernstein DI. Asthma in the work place. Marcel Dekker, New York. 1993;1-4.
- Glindmeryer HW, Lefante JJJr, G, Rando RJ, Freyder L, Hnizdo E, Jones RN. American Journal of Industrial Medicine. 2004;6(2):104-111.
- Tzong-His L, Yung-Hsuan S, Wei-Shiung Y. et al. Bright liver and Alanine Aminotransferase are associated with metabolic syndrome in Adults. 2005; 13:1238–1245.
- Scott MG, LeGrys VA, Klutts JS. Electrolytes and blood gases. Tietz Fundamentals of Clinical Chemistry, 6<sup>th</sup> edition. St. Louis: Elsevier Saunders. 2008; 431-438.
- Cheesbrough M. District Laboratory Practice in Tropical Countries, Part 1

- (Second edition update). Cambridge: Cambridge University Press. 2010;355-369.
- Kraut J, Madias N. Serum anion gap: it uses and limitations in clinical medicine. Clinical Journal of the American Society of Nephrology. 2007;2(1).
- Kalio IS, Hanson AH. Evaluation of Anion Gap in Petrol Attendants in Port Harcourt Metropolis. World Journal of Pharmaceutical Research. 2016;(5)3: 1499-1506.
- 16. Aribo EO, Antai AB. Lung function parameters in spray painters in Calabar, Nigeria. Annals of Biological Research. 2014;5(11):32-35.
- 17. D'Orazio P, Meyerhoff ME. Ion-selective electrodes. Tietz Fundamentals of Clinical Chemistry, 6<sup>th</sup> edition. St. Louis: Elsevier Saunders. 2008;87.
- Nordberg M. General apect of Cadmium: Transport, uptake and metabolism by the kidney. Environ. Health Perspect. 1984; 54:13-20.
- John Cocker. Biological monitoring for isocyanates. Occupational Medicine. 2007; 57(6):391-393.

- Orisakwe OE, Nwachukwu E, Osadolor HB, Afonne OJ, Okocha CE. Liver and Kidney function amongst paint factory workers in Nkpor, Nigeria. Toxicology and Industrial Health. 2007;23(3):161-165.
- 21. Kraut JA. Serum anion gap: Its uses and limitations in clinical medicine. Clinical Journal American Society of Nephrology. 2007;2(1):162-174.
- Malaguarnera G, Cataudella E, Giordano M, Nunnari G, Chisari G, Malaguarnera M. Toxic hepatitis in occupational exposure to solvents. World Journal of Gastroenterology. 2012;18:2756-66.
- 23. Al-Ghamdi SS. Occupational exposure to paints causes impairment of kidney function. Journal of Environmental Protection. 2011;2:533-536.
- Thapa BR, Anuj W, Michel FS. Liver function tests and their interpretation. Indian Journal pediatrics. 2007;74:663-671.
- Aziz TA. Effect of painting products on liver function, Hematological markers, Heavy Metals and GSH levels among painters in Sulaimani city. World Journal of Pharmceutical Sciences. 2015;3:2081-7.

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