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Water contamination: A culprit of serum heavy metals concentration, oxidative stress and health risk among residents of a Nigerian crude oil-producing community

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ABSTRACT

Niger Delta has become popular for crude oil extraction for the past few decades. This uncoordinated activity has made it a hotspot for xenobiotics exposure and water bodies remain the environmental matrix significantly affected. One of the most deleterious components of crude oil is heavy metals (HMs). This study investigates HMs concentration in water and serum of humans residing in an oil-host community with the consideration of systemic effects, pollution status, carcinogenic and non-carcinogenic health risks and comparison made with residents from a non-oil-producing community. Heavy metal analysis, serum electrolytes, Urea, Creatinine, and liver enzymes were assessed using standard procedures; malondialdehyde, catalase, SOD, glutathione reductase, GPx and total antioxidant capacity (TAC) by spectrophotometry and TNF-α and 8-OHdG assessed via ELISA method. We found altered serum electrolytes; increased serum Pb and Cd levels; increased AST, ALT, ALP and lipid peroxidation; and decreased enzymes antioxidants including TAC among Ugbegugun community residents compared with control. We observed an association between environmental crude oil contamination, ecological and health risks in the community. We concluded that protracted exposure to HMs induces multi-systemic toxicities characterized by DNA damage, depletion of the antioxidant system, and increased free radical generation culminating lipo-peroxidation with significant ecological, carcinogenic, and non-carcinogenic risks characterize crude oil water contamination.

1. Introduction

Aquatic and soil pollution, secondary to crude oil bunkering, spillage, and other crude oil extractive activities such as gas flaring and fracking, has been the bane of environmental pollution in many oil-rich countries, globally. Nigeria's Niger Delta region is remarkable for crude

Abbreviations: 8-OHdG, 8-hydroxy-2-deoxyguanosine; ABS, Fraction of the applied dose dermally absorbed; $ADI_{dermal\text{-}water}$, Average daily intake via skin exposure to water; ADI_{ing}, Average daily intake Ingestion; $ADI_{ing\text{-}water}$, Average daily intake of water; AAS, Atomic absorption spectrophotometry; AF, Adherence factor; ALP, Alkaline phosphatase; ALT, Alanine aminotransferase; As, Arsenic; AST, Aspartate aminotransferase; AT, Average time of exposure; ATSDR, Agency for Toxic Substances and Disease Registry; BW, Body Weight; CAT, Catalase; Cd, Cadmium; CF, Contamination factor; CF, Conversion factor; C_{hm}, concentration of heavy metal in the soil; CO, Carbon monoxide; Cl^-, chloride ion; Cr, Chromium; CR, Cancer risk; CSF, Cancer slope factor; Cu, Copper; DNA, Deoxyribonucleic acid; ED, Exposure duration; EDTA, Ethylene diamine tetraacetic acid; EF, Enrichment factor; EF, Exposure frequency; ELISA, Enzyme-linked immunosorbent assay; ER, Ecological risk; ET, Exposure time; FAD, Flavin Adenine Dinucleotide; FE, Fraction of the dermal exposure ratio to soil; Fe, Iron; GPx, Glutathione Peroxidase; GR, Glutathione reductase; HI, Hazard index; H_2O_2, Hydrogen peroxide; HCO_3, Bicarbonate ion; HQ, Hazard quotient; I_{geo}, Geo-accumulative index; IR, Ingestion rate; K^+, Potassium ion; Kp, Permeability coefficient; LGA, Local government area; MDA, Malondialdehyde; Mn, Manganese; MC_d, Modified degree of contamination; Na^+, Sodium ion; NADPH, Nicotinamide adenine dinucleotide phosphate hydrogen (NADPH; PAH, Polycyclic aromatic hydrocarbon; Pb, Lead; PCB, Polychlorinated biphenyl; PLI, Pollution load index; RFD, Reference dose; ROS, Reactive Oxygen Species; SA, Surface Area; SOD, Superoxide Dismutase; TAC, Total antioxidant capacity; TBA, Thiobarbituric Acid; TCA, Trichloroacetic Acid; TNF- α, Tumor Necrosis Factor- Alpha; Tr, Toxic response; TPTZ, tripyridyltriazine; WHO, World Health Organisation; Zn, Zinc.

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oil exploration-an activity that has transformed it into a hotspot for pollution of water bodies. Sequel to this, aquatic and terrestrial food sources such as fish, goat, chicken, and cow meats from the region had been reported to be contaminated particularly with heavy metals [1,2]. Corroboratively, several statistically motivated rankings have positioned Nigeria ahead of most countries known to be affected by oil pollution. Civil upheaval and militant agitation emanating from the Niger Delta area targeted against the Nigerian state, are partly due to the significant environmental pollution that leaves a deteriorated water body, perturbed aquatic life, and a deranged ecosystem [3]. The two (2) decades between 1976 and 1996 witnessed about 4840 oil spills with about 2.5 million barrels of crude oil [4]. Worst still, the half decade between 2015 and 2021 witnessed count of spills growing to approximately 5000 in the Niger Delta region. This considerable spate of pollution targets the water bodies and leaves them undrinkable while significantly disrupting aquatic life and ecosystem [5,6] because surface water is the common sink for environmental contaminants [7]. Several *in-situ* [1,8] and *ex-situ* studies [9,10] have poised human exposure to environmental pollutants as the culprit of bioaccumulation of toxic substances in the body.

One of Niger Delta communities known for active crude oil exploration is the Ugbegugun community. Localized in Warri North local government, it is an Itsekiri village sharing a boundary with Escravos and lying between 5° 36' 49.2"N, 5° 10' 30.0"E and 5° 36' 43.7"N, 5° 10' 42.4"E. Located in Warri North Local Government Area in Delta State, Nigeria, Ugbegugun community is an oil-rich community hosting headquarters of oil-producing companies.

Serological analysis is an important aspect of environmental toxicology used for monitoring systemic translocation, abundance, and protoxicosis of xenobiotics. Serum biochemistry plays a vital role as a reliable biomarker for a number of disorders of chronic origins [11], particularly in exposure to toxicants and physiological response in disease prognostication [12,13]. Oxidative stress, inflammation, liver, and hepatic alterations in chronic exposure to toxicants all have a strong link with serum biochemistry.

Pollution indices, carcinogenic and non-carcinogenic risk assessments have become an integral part of the toxicological assessment [14,15]. Since invasive research is not an ethically permissible protocol in research involving human subjects, the development of models of toxicity estimation has become an acceptable investigative method in toxicology. Carcinogenic and non-carcinogenic risks assessment has become a very handy and dependable tool for the consequential risk associated with the actual or potential environmental exposure to xenobiotics particularly toxic metals [16,17]. While several reports of pollution activities emanating from the detrimental crude oil exploitation in the Niger Delta environment have been documented, the direct implication on the health of residents has been very scarce considering the level of pollution entrenched in the region. Meanwhile, detrimental and deleterious crude oil explorative activities such as gas flaring, fracking, bunkering, oil smuggling, oil theft, and illegal refinery which are all commonplace in the Niger Delta environment precede exposure to hazardous crude oil components. According to Scientific Committee on Health, Environmental and Emerging Risks (SCHEER), there are over 1300 of these hazardous components including Volatile Organic components, Heavy metals, Polycyclic Aromatic Hydrocarbon (PAHs), particulate matter, etc [18]. which may constitute health risk to vulnerable residents.

Heavy metals such as Lead (Pd), Nickel (Ni), Vanadium (V), Zinc (Zn), Chromium (Cr), Arsenic (As), and Cadmium (Cd), classified by the Agency for Toxic Substances and Disease Registry as carcinogens [19] are known to be consistently detected in crude oil and co-exposed in environmental samples during crude oil spillage [20,21]. Several components of the Niger Delta environment have been reported contaminated with heavy metals borne out of stimulation fluid, venting, diesel exhaust, flaring, drilling mud, storage pit, and pond. These heavy metals are not only distributed into the Niger Delta environment but also, they constitute a significant source of systemic toxicosis and are implicated in the etiology of cancer. Okoye and colleagues found significant bioconcentration of heavy metals in the soil, and vegetation within the oil-rich Niger Delta [8]. In another study, soil, feed, and food materials within the area were also reported to be contaminated with heavy metals [1,2]. The aforementioned reports are in consonance with that of Thomas and his colleagues who found significant heavy metal contamination in the water resources within the Niger Delta environment despite remediation [22]. The latter is synonymous with the study of [23] who analytically compared the groundwater quality statuses, associated health risks due to heavy metal pollution and total hydrocarbon in Delta state, Nigeria. They found significant carcinogenic risk, particularly in adult and children, following crude oil contamination. More recently, heavy metal pollution of the Niger Delta environment was demonstrated to induce serum and neuropathological changes through heavy metal bioaccumulation and oxidative stress in Africa giant rats [24]. This kind of study deciphering the level of contaminants and pollution in crude oil-polluted environments is common. The height of most of the studies is the ecological risk assessment which is a probabilistic analysis of the potential health risk. However, studies investigating actual human exposure typical of the crude oil-producing Niger Delta and quantifying the extent of the systemic hazard of the exposure are very scarce. Hence, this work, in a holistic approach, evaluated the level of heavy metals, the extent of their distribution, associated health risk, and eventual systemic impact of crude oil-induced heavy metal contamination by assessing pollution indices, serum and surface water heavy metals status, serum oxidative (including liver and kidney functional analysis), biochemical and genetic alterations on a gender basis including the carcinogenic and non-carcinogenic health risk among residents of the Niger Delta region.

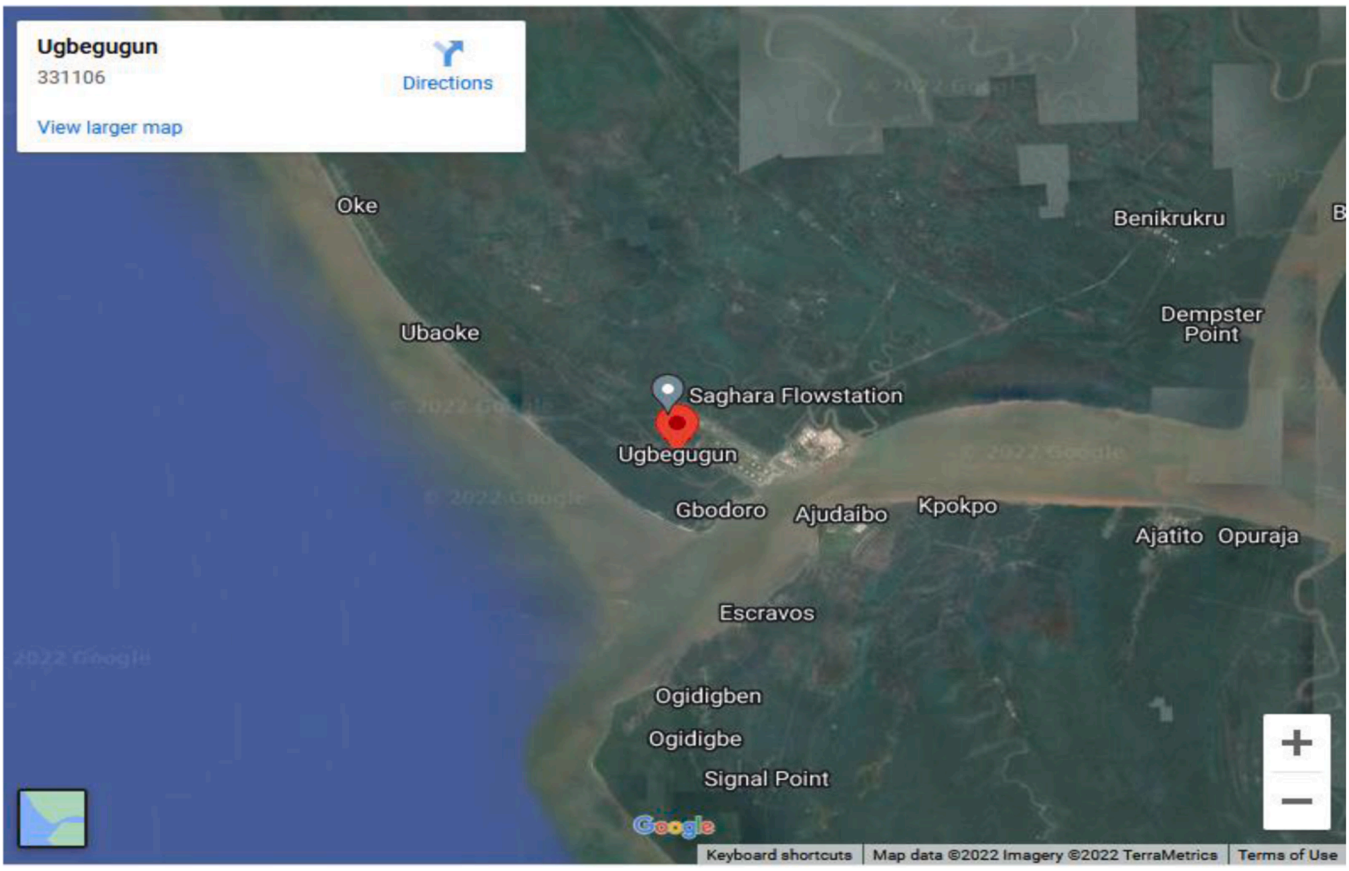
2. Materials and method

2.1. Geographical analysis of the sites

Ugbegugun community is one among the Niger Delta communities in Warri North local government known for active oil explorative activities. It is a riverine Itsekiri village with a boundary to Escravos lying between 5° 36' 49.2"N, 5° 10' 30.0"E and 5° 36' 43.7"N, 5° 10' 42.4"E in Warri North Local Government Area in Delta State, Nigeria. The localization of the community on the national map is represented in Fig. 1. It is an oil-rich community playing host to the headquarters of oil-producing companies. Okada community is located in the North-East Local Government Area (LGA) of Edo State, which lies between 6° 43' 57.8"N, 5° 23' 23.6"E, and 6° 42' 48.4"N, 5°23'24.3"E. It is a habitable and serene environment that plays host to several secondary/high schools and Nigeria's premier private University (Igbinedion University).

2.2. Human sample collection and Ethical approval

The series of studies conducted in this work were carried out on fifty (50) adult residents in Ugbegugun community, Niger Delta (25 each of males and females) between 20 and 50years old and compared with a similar number of residents from Okada community- a non-oil-producing community (about 152 km away from Ugbegugun) also within the Niger Delta environment. The data analyzed included a well-structured questionnaire for the collection of demographic data such as gender, lifestyle, age, occupation, health challenge and drug of intervention, etc to determine inclusion and exclusion. Following the satisfaction of the inclusion criteria, blood samples were collected. Inclusion criteria involve sound physical and mental health and willingness to participate only among residents of the duo communities who have resided for 10 years and above while residents below 20 years of age or above 50 years of age were excluded. Also, individuals with underlying illnesses such as cardiovascular disease, poor eyesight, poor memory,



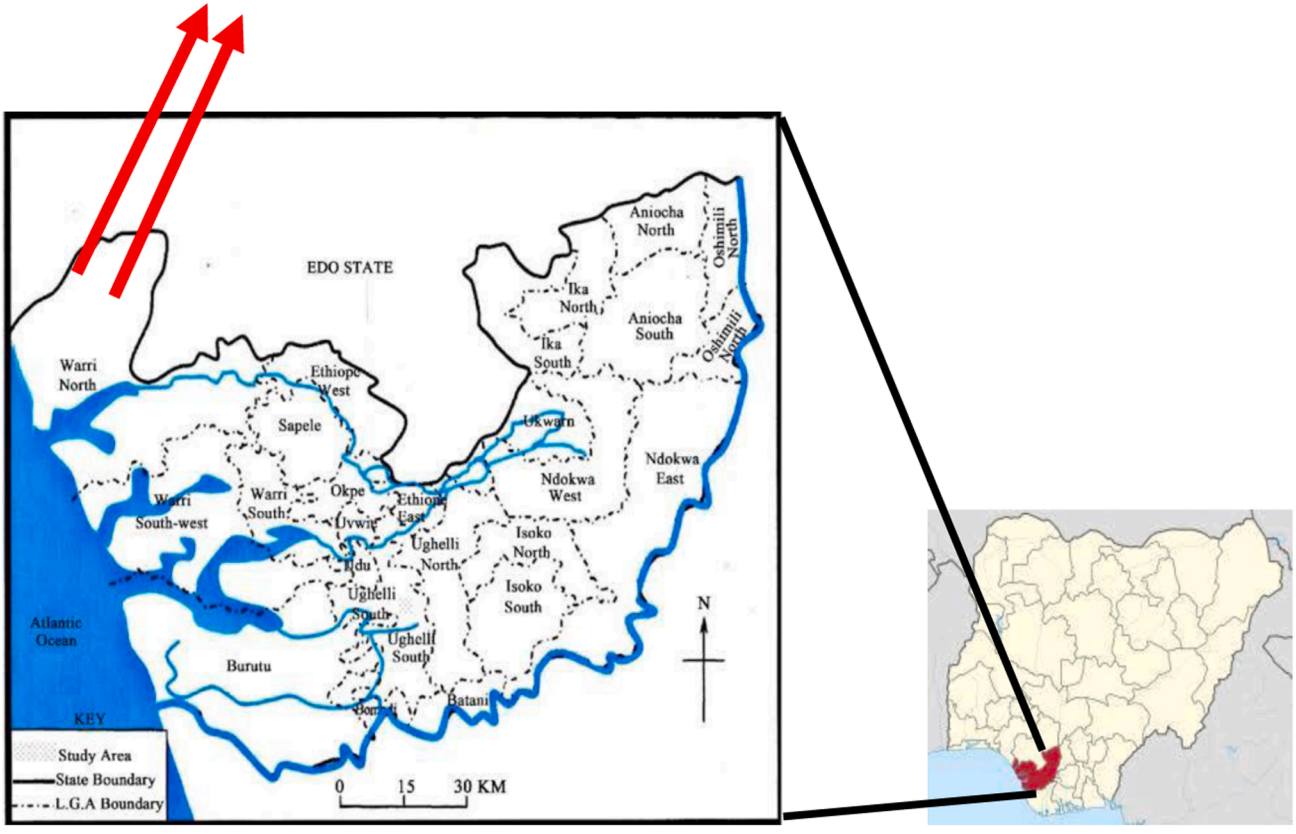


Fig. 1. The Google image describing the geographical site of the study community.

amnesia, and insomnia were exempted from the study. Included participants each signed an informed consent having met all the inclusion criteria.

Prior to the commencement of this study, ethical approval was obtained from the Delta State Ministry of Health, Nigeria. The study got express approval due to its importance and approval number HM/596/T/156 was allotted. The study was thereafter conducted in accordance with the provision of the confidentiality and privacy of respondents. Careful explanation of the purpose, consent, and implication were made known to participants before data collection and therefore no disclosure of information as the data obtained were treated as personal and private. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments while the research proposal was also duly approved by the Igbinedion University research ethical committee.

The total number of study participants was one hundred (100). Fifty (50) participants (25 males; 25 females) were recruited from the oil host community (Ugbegugun, Delta state), and Fifty (50) participants (control; 25 males; 25 females) from the non-oil host community (Okada, Edo State) Nigeria. Following the completion of the structured questionnaire, blood (6 mL) was carefully collected under sterile conditions via venipuncture into two (2) separate plain tubes; 1 mL into one tube and 5 mL into another for each participant. The first one (1 mL) was subjected to digestion for toxic elements analysis, the other (5 mL) was cryo-centrifuged at −4°C (Centurion Scientific Model K241R) and 5000 rpm for 5 minutes to obtain the serum which was immediately used for biochemical assays as given below.

2.2.1. Blood digestion and heavy metal content analysis

Blood samples were digested using the wet acid digestion method [25] with slight modification. 1 mL of blood samples was taken from the volunteers each into sample bottles. 3 mL of a freshly prepared mixture of concentrated nitric acid (HNO_3) and Hydrogen peroxide (H_2O_2) (2:1, v/v) was aliquoted into the bottle and allowed to stand for 15 min. Conc. HNO_3 (CAT No:7697–37–2) and H_2O_2 (CAT No: 7722–84–1) used were of analytical grades from Sigma-Aldrich Chemie and Qualikem respectively. The mixture was then digested for 2 hours at 70 °C. This procedure was repeated till a clear solution was precipitated. The set-up was allowed to cool after excess acid was allowed to escape by evaporation. Levels of trace elements Pb and Cd in the digested blood from the residents of the duo communities were analyzed using Atomic Absorption Spectrophotometry (AAS; ICE 3000, Thermo Fisher Scientific, Waltham, MA) using 217.0, 228.9 wavelengths respectively.

2.2.2. Serum electrolyte and Hepato-renal physiological analyses

Renal physiological tests carried out in this study involved the assessment of serum levels of electrolytes such as potassium (K^+), sodium (Na^+), chloride (Cl^-), and HCO_3^-, urea, creatinine and serum levels of hepatic enzymes including Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), and Alkaline phosphatase (ALP) were analyzed in the serum using commercially available kits with respective CAT Nos UR220, CR510, AL1200, AS1202, AP542. The procedure was as described by the manufacturer and other instructions of the manufacturers were stringently followed.

2.3. Oxidative stress assessment

2.3.1. Protein and Lipo-peroxidation

Total protein in the serum of the residents of the communities was determined in compliant with earlier method [26]. with the use of Bovine serum albumin as the standard while the level of lipid peroxidation in the serum was determined by the above-stated protocol using the method described by [27]. 50 μL of serum sample was dispensed into a clean test tube, 100 μL of Trichloroacetic acid (TCA)/ Thiobarbituric acid (TBA) working solution was added followed by 1.85 mL of distilled water was added. The mixture was placed in a boiling water bath for 15 minutes and allowed to cool thereafter. The mixture was then centrifuged and the absorbance read at 535 nm using a microplate reader.

2.3.2. Superoxide dismutase

Superoxides scavenging superoxide dismutase (SOD) is an enzyme whose level corresponds to cellular bioprotection. In this study, the level of the activity was determined by the kinetic method [28] with slight modification. Ability of the enzyme to prevent epinephrine autoxidation in a basic medium was spectrophotometrically determined when 0.2 mL serum sample was added to 2.5 mL phosphate buffer (50 mM) at pH 10.4 and the reaction initiated by the addition of 0.3 mL Adrenaline (Sigma-Aldrich Chemie; Cat No: 51–43–4). The solution was read at 420 nm. Calculation of the enzyme activity was in terms of nanomoles of unoxidized adrenaline per minute of protein using molar extinction coefficient of 4.02×103 per M/cm.

2.3.3. Catalase

Hydrogen peroxide (H_2O_2) is a dangerous reactive oxygen species whose systemic clearance depends on the level of the antioxidant enzyme catalase present in the cytochrome system. Serum catalase activity was evaluated according to [29,30]·H_2O_2 decomposition rate was measured in the mixture of 0.019 M H_2O_2, 50 μL of serum sample and1.95 mL of 0.05 M phosphate buffer (pH 7.0), and absorbance was determined spectrophotometrically at 240 nm, and at 0 sec, 20 sec, 40 sec, 60 sec, and 80 sec for each sample as the nmol H_2O_2 consumed/min/mg protein at 240 nm.

2.3.4. Glutathione peroxidase (GPx)

Glutathione Peroxidase activity (GPx) was determined by kinetic method [31]. The disappearance of NADPH at 37 °C was monitored and recorded from the mixture of 1 mM each of ethylene diamine tetraacetic acid (EDTA), sodium azide, and glutathione; 0.05 M phosphate buffer (pH 7.0), 1 EU/mL glutathione reductase, 0.2 mM nicotinamide adenine dinucleotide phosphate hydrogen (NADPH), 0.25 mM and 0.1 mL of serum sample. The quantity (in Nanomoles) of oxidized NADPH per minute per milligram of protein was evaluated using the molar extinction coefficient of 6.22×10^{-3}/M/cm.

2.3.5. Glutathione reductase (GR)

Glutathione reductase, an antioxidant enzyme that complements the biological action of glutathione peroxidase was assayed by monitoring the disappearance of NADPH at 37 °C from the mixture of 0.5 mM EDTA, 1 mM oxidized glutathione; 0.1 M phosphate buffer (pH 7.6), 0.1 mM (NADPH), and 0.05 mL of serum sample at a set wavelength of 340 nm in accordance with [31] modified by [32]. The quantity (in Nanomoles) of oxidized NADPH per minute per milligram of protein was evaluated using the molar extinction coefficient of 6.22×10^{-3}/M/cm.

2.3.6. Total antioxidant capacity (TAC)

TAC is the assessment of the wide range of systemic agents capable of chelating oxidant molecules [33]. Its level when compared with the ROS level can be used to effectively determine systemic oxidative damage. In this study, it was assayed in the serum samples and analyzed using the Ferric reducing antioxidant power (FRAP) assay method [34]. FRAP was made from a mixture of buffer acetate, tripyridyltriazine (TPTZ) solution, and hydrochloric acid (HCl) and served as the working solution. $FeCl_3$ was later added and gently mixed. 240 μL of the working solution was added to the pre-aliquoted 8 μL of the serum sample and incubated for 10 minutes at 37 °C. The mixture was read at 532 nm for the detection of total antioxidant capacity and expressed as mmol/L.

2.3.7. Serum tumor necrotic factor-alpha (TNF-α)

The quantitative sandwich enzyme-linked immunosorbent assay (ELISA) technique was used to determine serum tumor necrotic factor-alpha (TNF-α) levels. The human TNF-α ELISA kit Quantikine, R&D

System, Inc. Minneapolis, USA (Cat No: DTA00D; No: 898914) was used with total compliance with the manufacturers' instruction with results expressed as pg/mL.

2.3.8. 8-hydroxy-2-deoxyguanosine (8-OHdG)

ELISA-based quantification was used in the estimation of the 8-OHdG in serum samples. A quantitative sandwich enzyme-linked immunosorbent assay (ELISA) technique was used to determine serum 8-hydroxy-2-deoxyguanosine levels. The human 8-OHdG ELISA kit Quantikine, R&D System, Inc. Minneapolis, USA (Cat No: 4380–096-K; No: 4380–096) was used with complete compliance with the manufacturer's instruction and results were expressed in ng/L.

3. Water contamination assessment

Enrichment factor (EF) was estimated according to equation 1 relative to Iron (Fe) as the reference material using the equation below

$$EF = (C_i \times C_{Fe}) \div (B_{Fe} \times B_i) \tag{1a}$$

C_i is the concentration of i^{th} element in the sample, C_{Fe} is the concentration of the reference metal. Fe was used as the reference metal in this study because of its abundance in Shales and high toxicity threshold. B_i is the background value of the i^{th} element and B_{Fe} is the background value of Fe. The continental shale metal levels were used as the background metal content in this study where Pb, Cd, Zn, and Cu have values 0.015, 16, 0.005, 0.5, 0.7, and 1.3 mg/L respectively [35]; Fe and Mn were according to [36,37] respectively.

Contamination factor (CF) was determined using the equation below:

$$CF = \frac{C_i}{C_b} \tag{1b}$$

Where Ci is the mean concentration of i^{th} metal in the sample, C_b is the background value according to [38]. The background value was according to [35].

Contamination degree (C_d) was calculated based on the equation below

$$C_d = \sum_{i=1}^{n} CF^i \tag{1c}$$

CF^i is the contamination factor of the i^{th} element. Values less than 1.5 is considered "unpolluted"; within 1.5–2.0 is "slightly polluted"; 2–4, moderately polluted; 4–8, "moderately to heavily polluted"; 8–16, "severally polluted", 16–32, "heavily polluted", and values higher >32 are usually considered "extremely polluted".

Pollution load index (PLI) was calculated according to [39] as shown in equation E below. The scale is as shown in Table S2

$$PLI = (CF_1 \times CF_2 \times CF_3 \ldots CF_n)^{1/n}. \tag{1d}$$

Where CF_1 is the contamination factor with respect to the first element, CF_n is the contamination factor with respect to the n^{th} element.

Er^i is the Enrichment factor of the i^{th} element

Ecological Risk (ER) was calculated according to [40] using the equation

$$Er = Tr^i \times CF^i \tag{1e}$$

Where Tr^i is the toxic-response of the i^{th} metal. The Toxic response of Zn=Mn=1; Fe=Nil; Pb=Cu=5; Cd=30 [41] and CF^i is the contamination factor of the i^{th} heavy metal. Ecological risk was scaled according to Table S1.

The geo-accumulation index (I_{geo}) proposed by [41] was used to describe metal contamination by comparing current concentrations with pre-industrial levels and rated based on the scale described by Quingje et al., [42]

$$I_{geo} = \log_2 \frac{C_n}{1.5 \times B_n} \tag{1f}$$

C_i is the concentration of n^{th} element in the sample, B_i is the background value of the n^{th} element in the average Shale value. I_{geo} is scaled on seven (7) distinct categories according to table S2.

4. Health risk analysis

The level of carcinogenic and non-carcinogenic health risks of residents of Ugbegugun community was calculated on the Chronic daily intake (CDI) of toxic metals via the prandial and dermal adsorption routes using Eqs. 2a and 2b according to the United States Environmental Protection Agency [43].

4.1. Non-carcinogenic risk

Hazard quotients and Hazard index were calculated and used to evaluate the potential non-carcinogenic health risk via ingestion of surface water and dermal exposure routes with the adult and children as the target groups. The assessment of anthropogenic exposure dose via ingestion and dermal routes absorption of the metals such as Pb, Cd, Mn, Cu, Fe, and Zn in the river supplying the oil-host community, Ugbegugun was conducted by deploying the Chronic daily intake (CDI) using the equation described by [43].

$$CDI_{ing-water} = \frac{C_{hm} * IR * EF * ED * CF}{BW * AT} \tag{2a}$$

$$CDI_{derm-water} = \frac{C_{hm} * SA * Kp * ABS * ET * EF * ED * CF}{BW * AT} \tag{2b}$$

$$HQ = \frac{CDI}{RFD} \tag{2c}$$

$$\mathrm{HI} = \sum_{i=1}^{n} (CDI/RFD)ing + (CDI/RFD)derm \tag{2d}$$

Where $CDI_{ing\text{-}water}$ is the chronic daily intake of the ingestion of the water, $CDI_{derm\text{-}water}$ represents chronic daily intake due to heavy metal exposure via skin route (μg kg^{-1} day^{-1}). Hazard index (HI) values higher than 1.0 denote non-carcinogenic health risk while HI values lower than 1.0 usually denote the absence of non-carcinogenic risk. Other acronyms are presented in Table S3

4.2. Carcinogenic risk analysis

Since carcinogenesis is known to be preceded by time-dependent exposure to carcinogens, carcinogenic risk due to exposure to contaminated water in the linear equation below, is therefore estimated as an incremental probability of any exposed individual developing cancer throughout the lifetime.

$$CANCER\ RISK_{total} = \sum Cancer\ Risk = \sum_{i=1}^{n} ADI_i * CSF_i \tag{3}$$

Calculated values of cancer risk higher than 1×10^{-4} were considered to be of significant health risk, values between 1×10^{-6} and 1×10^{-4} are within acceptable range, while the risk values below 1×10^{-6} are not considered sources of adverse health effect [44-46]. Pb and Cd are the only known heavy metals capable of inducing cancer via ingestion route, their respective cancer slope factors (CSF) are 8.5 mg/kg/day and 6.1 mg/kg/day while there is none of the heavy metals assessed in this study known to be carcinogenic via the dermal route, hence there is no CSF available for them [47,48].

4.3. Statistical analysis

Statistical analysis was done with GraphPad Prism version 8.0.1 (244). Data were analyzed with Student's independent t-test and a p-value less than 0.05 ($p<0.05$) was considered significant. Data are presented in Mean ± Standard Error of Mean (SEM).

5. Results

5.1. Water pollution indices

Water bodies constitute the environmental matrix most vulnerable to pollution from crude oil exploitation in the Niger Delta environment. We, therefore, assessed the water from Ugbegugun community for heavy metal content and results show that Zn, Fe, Pb, Cd, Cu, and Mn were present in varying quantities. Pollution analysis of the water was carried out according to the equations stated above.

Enrichment factor (EF) was estimated according to Eq. 1a. Results show Cd as the most enriched heavy metal in water from the community followed by Pb with values of 2102.12 and 619.98 respectively which are well above "extreme pollution" category. The community water is severely polluted with Fe and Zn; moderately polluted with Cu and unpolluted with Mn. The order of EF for all the assessed metals is given as Cd>Pb>Fe>Zn>Cu>Mn

The contamination factor (CF) was assessed according to Eq. 1b and according to the scale in Table S2. Cd and Pb have the highest contamination factor in the community water with "extreme" level of contamination. This is followed by Fe which was found to have "severely" contaminated the water. Zn moderately contaminated while Cu and Mn fall under the "uncontaminated/unpolluted" category.

This pattern is similar to the enrichment factor indices which equally presented metals in the same order of Cd>Pb>Fe>Zn>Cu>Mn.

Contamination degree (CD) was assessed according to Eq. 1c. The value of CD of the water from the community is 669.13, a value which is significantly higher than the "extreme pollution" category of scale. Pollution load index (PLI) was estimated according to Eq. 1d. Result of PLI is 7.02; a value which falls above the "extreme pollution".

CF-dependent index, ecological risk (ER), was assessed according to Eq. 1e with result presented in Table 1. Cd constitutes the most ecological risk in the community water followed by Pb and least by Cu and Mn. The hierarchical order of ecological risk is given as Cd>Pb>Fe>Zn>Cu>Mn while enrichment factor index shows that Cd is the most enriched heavy metal and Mn, the least, with the same order Cd>Pb>Fe>Zn>Cu>Mn. Geoaccumulative index (Igeo) was determined according to Eq. 1f. Result of the Igeo showed a diminuendo pattern from Cd, Pb, and Fe to Zn with all metal existing at "extreme" pollution level. The water was considered moderately polluted with Cu and "unpolluted" with respect to Mn.

Humans can be exposed to contaminated water via the gastrointestinal and dermal routes. The result of the non-carcinogenic risk among the community residents (adults and children) is presented in Table 2 below. The chronic daily intake (CDI) of heavy metals via oral and dermal routes among adults share similarity in pattern with the highest risk found with Fe and lowest in Cu with the order Fe>Cd>Pb>Mn>Zn>Cu; the CDI among children differ in pattern when the risks of the gastrointestinal and dermal routes are compared. Fe generated the highest risk via oral route while Pb generated the highest risk via the dermal route. Cu generated the least risk in the duo exposure routes. The order of the risk generated via the oral route is given as Fe>Cd>Pb>Mn>Zn>Cu while Pb>Zn>Fe>Cd>Mn>Cu is the order of the risk with respect to the dermal route. Hazard quotients (HQ) were estimated according to Eq. 2c. HQ both in adult and children is presented in Table 2. The adults and children HQ via the oral route exhibit similar pattern of expression. It was found highest in Cd and least in Fe with the order Cd>Pb>Cu>Mn>Zn>Fe while the dermal route in adult and children exhibited different pattern of expressions. The highest HQ in adult via the dermal route is found with Fe and least in Cu with the order Fe>Cd>Pb>Zn>Mn>Cu while the order found in children was Pb>Mn>Cd>Zn>Cu. The dermal reference dose for Fe is not available, hence, the HQ for Fe was neither estimated nor included. Hazard index (HI) was estimated in both adults and children according to Eq. 2d. The value was higher in the oral route among the children with the value of 6.97E+02 than in adult (1.82E+02). Similarly, the HI via the dermal exposure route (HI_{dermal}), in children was found to be higher (with the value 8.06E+00) than that of the adult, with the value 2.21E-04. The values of HI in this study are significantly greater than 1, both in the adult and children categories except in adult HI_{dermal}.

This study found CR to be 1.09 in exposure via the oral route and 0.0002 via dermal exposure for adult while we observed 4.171 via ingestion exposure route for children. No CR was reported in this study for children via the dermal route because slope factors for the assessed metals are not available.

We progressed to assess the serum physiological status among the residents of the community and we made comparison with another Niger Delta region with low environmental contamination, Okada

5.1.1. Serum electrolyte and heavy metal status

Serum levels of both electrolytes and heavy metals were monitored among the two communities. Figs. 3a and 3b show the result of the

Table 1
Pollution indices result of Ugbegugun community water analysis.

HEAVY METAL	Contamination factor (CF)	ER	Igeo	Enrichment Factor (EF) average
Zn	2.97	2.97	6.61	12.25
Fe	4.12	-	9.15	16.96
Pb	150.53	752.67	334.52	619.98
Cd	510.40	15312.00	1134.22	2102.12
Cu	0.97	4.87	2.16	4.01
Mn	0.13	0.13	0.29	0.54

Igeo: Geoaccumulative index; CF: Contamination Factor; ER: Ecological Risk, TR: Toxic-response or Toxicity coefficient;

Table 2
Analysis of non-carcinogenic health risks following gastrointestinal and percutaneous exposure to water in Ugbegugun community.

Potentially Toxic elements	ADIing	ADI derm	HQing	HQderm
ADULT				
Zn	4.67E-02	2.13E-04	1.56E-01	3.54E-05
Fe	9.06E-02	4.12E-04	1.29E-01	5.89E-05
Pb	7.10E-02	3.23E-04	2.03E+01	4.04E-05
Cd	8.02E-02	3.65E-04	1.60E+02	4.05E-05
Cu	3.98E-02	1.81E-04	9.94E-01	1.81E-05
Mn	6.58E-02	2.99E-04	4.70E-01	2.72E-05
HI			**1.82E+02**	**2.21E-04**
CHILDREN				
Zn	1.78E-01	3.76E-03	5.95E-01	6.27E-02
Fe	3.46E-01	1.22E-03	4.94E-01	-
Pb	2.71E-01	3.81E-03	7.74E+01	7.26E+00
Cd	3.06E-01	1.08E-03	6.12E+02	2.15E-01
Cu	1.52E-01	5.34E-04	3.80E+00	4.45E-02
Mn	2.51E-01	8.83E-04	1.79E+00	4.80E-01
HI			**6.97E+02**	**8.06E+00**

Fig. 2. Relics and artifacts of pollution from Ugbegugun community with black arrows showing crude oil pollution at the bank of the Ugbegugun community river.

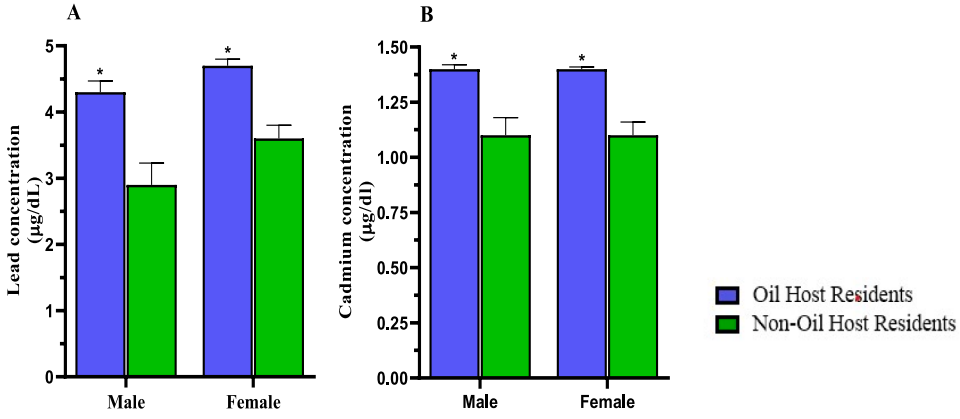


Fig. 3. (A) Serum Lead concentration and (B) Serum Cadmium concentration among residents of an oil host community in Delta State and a non-oil host community in Edo State, Nigeria. *p<0.05 was considered significant when compared with the residents of a non-oil host community.

serum heavy metal status while Fig. 4a-d show the effect of serum electrolytes among male and female residents of Ugbegugun community following protracted residence in oil-polluted and non-oil-polluted environments compared to the control community. There were significant sex-independent differences in Pb level between the oil host community and non-oil host community residents. Values of oil host community residents were significantly higher in both sexes when compared with their respective controls (non-oil community residents; Fig. 3a). Similar

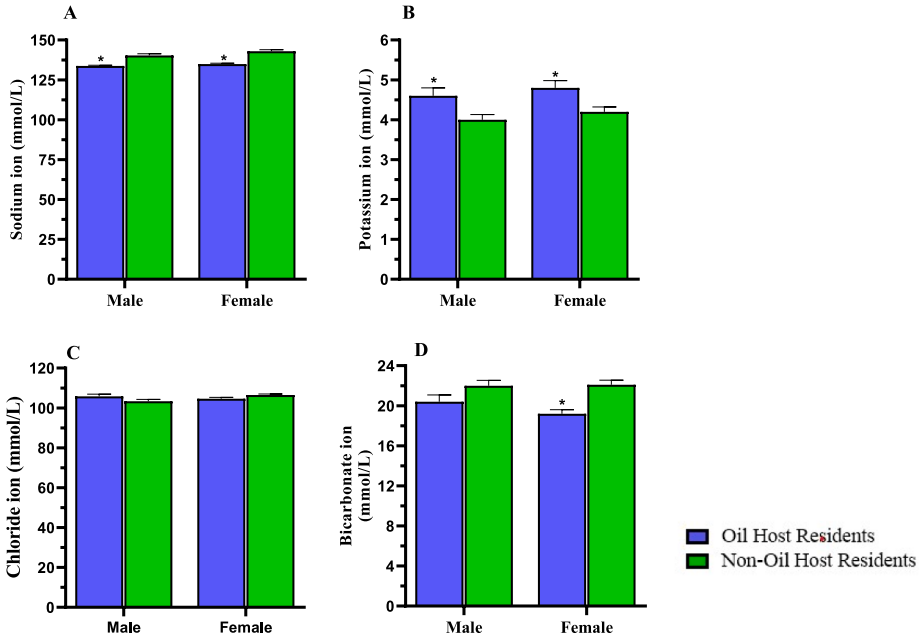


Fig. 4. (A) Serum sodium ions level (B) Serum Potassium ion level (C) Chloride ion level and (D) Bicarbonate ion level among residents of an oil host community in Delta State and non-oil host community in Edo State, Nigeria. *p<0.05 was considered significant when compared with the residents of a non-oil host community.

pattern was observed for cadmium levels as the oil host resident levels in both males and females were significantly higher than non-oil community residents (Fig. 3b).

Fig. 4a depicts the serum level of sodium in male and female residents between the oil-host community and the control community. There was a significant reduction in serum sodium in the male and female categories of oil-host community residents when compared with their non-oil community residents. Also, there was significant increase in serum potassium levels in male and female oil-host community residents when compared with their counterparts in non-oil-host community (Fig. 4b). Fig. 4c is the graph showing the serum level of chloride ion study participants. The result shows that there is no significant difference in the male and female categories of the oil host community residents when compared with the control. There was no significant difference between the males in oil-host and non-oil-host communities residents. However, there was a significantly decrease in serum bicarbonate of the female residents of the oil host community when compared with the non-oil host community (Fig. 4d).

5.1.2. *Serum hepatorenal biochemical analysis*

This study assesses kidney function tests through the measurement of urea and creatinine levels and liver function tests by measurement of serum levels of liver enzymes. There were significant increases in creatinine (Fig. 5a) and Blood Urea Nitrogen (Urea; Fig. 5b) in the oil-host community residents when compared with their control in the non-oil host community residents. These increases were consistent in both sexes. All the liver enzymes (ALT, AST, and ALP) in the male and female categories were significantly higher than their counterparts in the non-oil host community residents (Figs. 6a, b, and c respectively).

5.2. *Lipid peroxidation and antioxidative enzyme level*

There was a significant increase in the level of malondialdehyde (MDA) among both the male and female categories of oil-host community residence when compared with their counterparts from the non-oil community (Fig. 7a).

The enzyme antioxidant levels including CAT and SOD significantly reduced in both males and females in oil-host community residents than their respective counterparts in non-oil host community residents. The results are shown in Figs. 7b and c respectively. There is also a significant reduction in glutathione reductase and glutathione peroxidase levels in the oil-host community residents than in the non-oil host community. This is consistent with the male and female categories (Fig. 7d and e). Fig. 7f shows the effect of environmental pollution due to

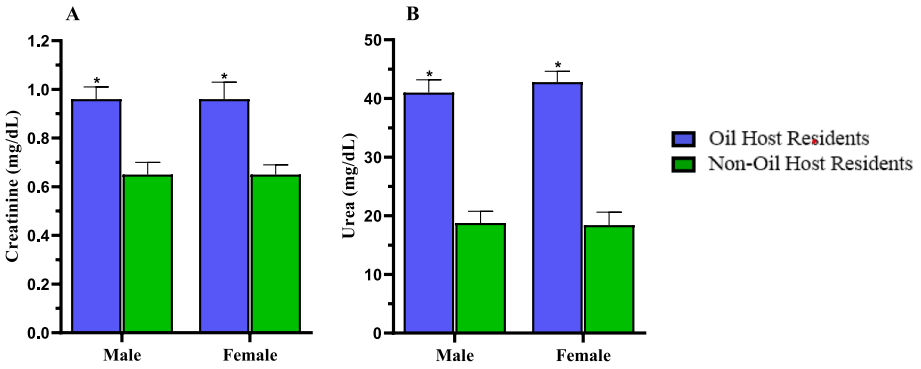


Fig. 5. (A) Serum creatinine level and (B) Serum urea level among residents of the oil host community in Delta State and non-oil host community in Edo State, Nigeria. *p<0.05 was considered significant when compared with the residents of a non-oil host community.

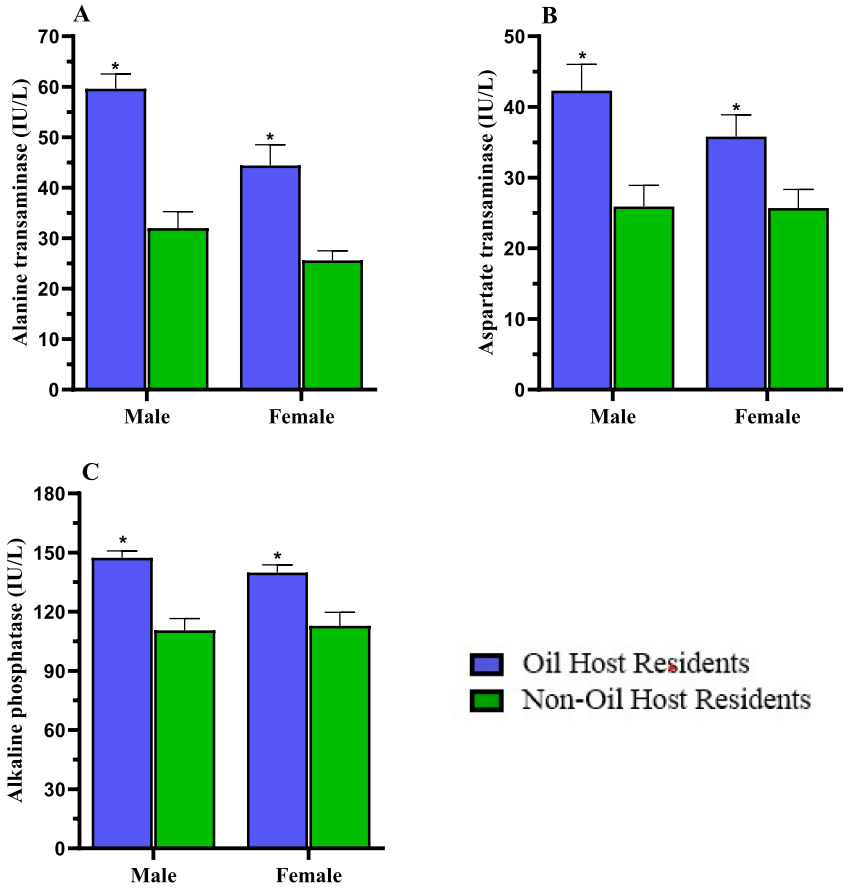


Fig. 6. (A) Alanine transaminase, (B) Aspartate transaminase, and (C) Alkaline phosphatase activity among residents of an oil host community in Delta State and non-oil-host community in Edo State, Nigeria. *p<0.05 was considered significant when compared with the residents of a non-oil host community.

crude oil on serum total antioxidant capacity (TAC) among oil host community residents. TAC significantly decreased in the oil-host community residents when compared with the non-oil host residents. The decrease was consistent in both sexes. However, the values of the antioxidants including SOD, CAT, glutathione and TAC were found to be lower in males when compared with females.

5.2.1. Inflammatory and DNA base damage

Tumor necrosis factor-α (TNF- α) tumor necrotic factor-alpha level was significantly higher ($p<0.05$) in male (23.8 ± 2.22 pg/mL) and female (35.4 ± 6.98 pg/mL) residents of the Oil Host community when compared with both male (14.4 ± 1.69 pg/mL) and female (16.8 ± 1.22 pg/mL) of the non-oil host Community (Fig. 8a). Fig. 8b shows that 8-hydroxy-2-deoxyguanosine level was significantly higher ($p<0.05$) in male (23.4 ± 2.37 ng/L) and female (25.9 ± 2.47 ng/L) residents of the Oil Host community when compared with both male (15.2 ± 1.49 ng/L) and female (17.8 ± 1.34 ng/L) of the non-oil host Community.

6. Discussion

Communities close to the coastal region in Nigeria are particularly known for dependence on the rivers with such activities as swimming, bathing, fishing, and washing. This is particularly the case in most Niger Delta communities which are known to host multi-national oil exploration companies. The Niger Delta environment is a hub of multiple sources of crude oil-characterized toxicants to which an average resident is exposed. Several legal and illegal activities involving crude oil extraction, distribution, mining, theft, bunkering, and pipeline vandalism occasion the spilling and flaring that culminate in soil and water contamination making the soil, water, and air significantly unsafe for habitation. Oil firms within the Niger Delta environment were reported to spill a total of 23, 896 barrels of crude oil amounting to #711bn in 2021 alone. Such massive anthropogenic activities involving crude oil exploration in the Niger Delta have therefore been considered a major factor culminating in the exposure of humans and other biotic components in the environment. Crude oil is composed of contaminants notably Polycyclic Aromatic Hydrocarbons (PAHs) and heavy metals. Most of the toxicological studies from the Niger Delta region focus on the assessment of PAH content while there had been a dearth of information on the heavy metal environmental distribution and the associated risks, particularly on water bodies. Hence, this study evaluated the level of heavy metals and the extent of their distribution, the associated health risk, and crude oil-induced heavy metal contamination. Moreover, the toxicosis of crude oil in humans is sex-dependent [49], the null hypothesis we tested in this study is that there is no difference in the health status of the male and female residents of Ugbegugun, a Niger Delta community, and that of Okada, a community found at the outskirt of the Niger Delta with significantly low pollution.

The pollution analysis of the water and the health risk of exposure to the heavy metal content depict that Cd is the most enriched heavy metal followed by Pb. This study also found that Cd and Pb have the highest contamination factor. The contamination degree is considerably higher than the “extreme” category of pollution. Also, we found that the PLI (7.02) exceeds the extreme pollution scale. Cd constitutes the most ecological risk followed by Pb while Mn is the lowest ecological risk when compared with all other assessed heavy metals. For non-carcinogenic risk assessment, HQ_{oral} in children and adults were found to be highest with respect to Cd while HQ_{dermal} was found highest with respect to Fe in adults and found highest with respect to Pb in children. Children within the environment of Ugbegugun community are at more

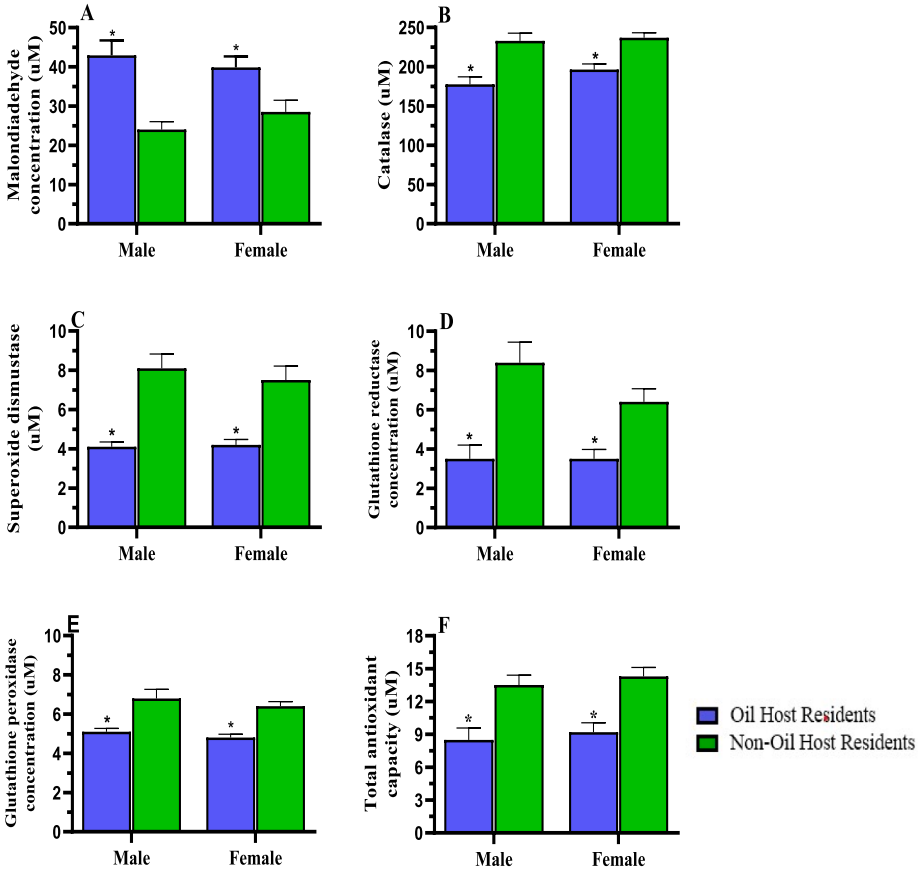


Fig. 7. (A) Serum malondialdehyde concentration, (B) Catalase, (C) Superoxide dismutase, (D) Glutathione reductase, (E) glutathione peroxidase activities, and (F) Total antioxidant capacity among residents of an oil host community in Delta State and non-oil host community in Edo State, Nigeria. *p<0.05 was considered significant when compared with the residents of a non-oil host community.

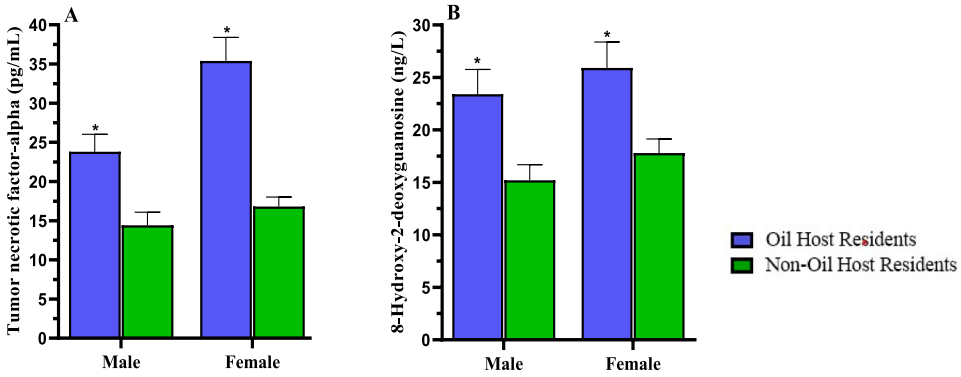


Fig. 8. (A) Serum tumor necrotic factor-alpha and (B) 8-hydroxy-2-deoxyguanosine concentration among residents of an oil host community. Bars represent Mean ± SEM. *p<0.05 was considered significant when compared with the residents of a non-oil host community.

risk with higher HI_{oral} than adults. We found that the non-carcinogenic HI_{oral} for children is 281.81% of the adult's HI_{oral}. This suggests that there is a significant non-carcinogenic health risk for the community residents, particularly among the children. Like most studies that consider the pattern of risk among adult and children [50,51], this series of studies found considerable risk among the children more than the adult with a percent increase of 76% (Table 2). Studies associated with heavy metal-induced aquatic pollution and health risk within the Niger Delta are limited as most studies focus on soil, sediment, vegetation, and food materials [52] confirmed the contamination of heavy metals such as Pb, Ni, Cu, Mn, Cr, Zn, and Cd in water samples from various Niger Delta states including Rivers, Delta, and Bayelsa. Ejike and his colleagues evaluated the concentration of Arsenic (As), Cd, and Pb in underground water samples from the Niger Delta environment and found non-carcinogenic risk level between 1.614 and 5.043-values that shows significant risk [53]. Results from this study are at par with the Chinese environmental study that assessed heavy metals pollution in an oil-based drill cutting at a shale gas drilling field which found contamination from heavy metals such as Cd, Cu, Cr, Mn, Hg, Ni, Pb, and Zn and reported non-carcinogenic risk associated with the occupational exposure [54]. Their study differs from this study having found higher non-carcinogenic risk through the dermal route than the oral route while

ours found the reverse.

Carcinogenic risk has been estimated as the product of Chronic daily intake and slope factor according to Eq. 3 above. This study found CR in adults and children particularly via the ingestion route while the dermal route generates no carcinogenic risk.

The abundance and serum distribution of electrolytes and heavy metals differ considerably. Increases in serum levels of the heavy metal are indicative that it is of geogenic sources as corroborated by water pollution analysis. Both Pb and Cd constitute the most considerable ecological, geo-accumulative, and health hazard risks in the community (Table 1). Observing their serum abundances among the residents of the community when compared with the control community is confirmatory that the interaction of the residents with the polluted environment precipitated the biocontamination of their body fluids. The Niger Delta environment is polluted with xenobiotics from multiple sources and environmental matrices including air, water, and soil are at the receiving end. Although it may be difficult or almost impossible to decipher the relative percentage contributions of the different crude oil toxicant fragments sources such as gas flaring, fracking, bunkering, accident spillage following defunct or abandoned equipment or spillage due to oil theft, in the water body, however, this study observed that the water matrix was significantly polluted and that the pollution is crude oil exploration-borne (Fig. 2; Table 1 and Table 2). This is evidenced by ubiquitous oil sheens seen at the river bank and widely distributed as shown by the black arrows in Fig. 2. This study exposes the fact that the water body is the ultimate contaminants sink after unregulated crude oil activities in the Niger Delta region. Fishing, swimming, and washing are the human activities that predispose Niger Delta residents to the toxic effect of crude oil pollution. This study considers the status of serum electrolytes owing to the role they play in systemic physiology and pathology as components of homeostasis. They are known to play crucial roles in inflammation and loss of cellular enzymatic activities following biotransformation [55]. We observed alterations in serum electrolyte levels including Cl, HCO_3^-, Na, and K.

This study observed decreased serum Na levels and increased serum K levels (both in the male and female categories) while there was a lower bicarbonate ion in the female category of the oil-host community residents when compared with the non-oil host community residents. These conditions of electrolyte imbalance can result from a wide range of etiologies including hepatorenal dysfunctions and are known to be associated with deleterious health statuses such as abnormal gait, osteoporosis, seizures, nausea, and cognitive derangement [56,57].

Higher biochemical hepatorenal indices including urea, creatinine, AST, ALP, and ALT observed across the sexes of Ugbegugun community residents when compared with the control Okada community is indicative of histotoxic crude oil effect. While the liver detoxifies and metabolizes, the kidney maintains homeostasis of the body fluid via clearance and elimination making the duo organs germane to systemic functional maintenance via a number of functions which warrant their huge blood supply from the arterial tray. Significant perfusion of these organs with heavy metal-contaminated blood volume culminates generation of reactive oxygen species (ROS) which attacks the organs making them vulnerable to functional impairment. This may be responsible for the increase in the levels of Urea, creatinine, and liver enzymes. This result confirms the possible rationale for the electrolyte imbalance observed in this study and also represents a follow-up and confirmation of earlier report of Thomas et al., [22] which found heavy metal-induced hepato-renal toxicities among Agbidiama community residents in Kolokuma/Opokuma local government of Bayelsa state, due to crude oil contaminated water. Experimental investigation conducted on Wistar rats also corroborated the result in this study following the report of significantly high AST and ALT after exposure to the hydrophilic portion of Bonny light crude oil [58].

MDA is the product of attack of electrons on polyunsaturated fatty acids due to the release of ROS. Metrics of MDA have been a reliable oxidative stress biomarker for the assessment of the toxicosis of many toxicants, etiology, and prognosis of diseases [59-62]. It has been used for the experimental toxicological screening of crude oil [63]. High level of MDA among the males and females of the participants of this study when compared with the control community is indicative of high degree of lipid peroxidation induced by the toxic components of crude oil to which the community residents are exposed through the water.

Glutathione peroxidase (GPx) is a group of enzyme antioxidant species which biochemically functions to reduce products of lipid peroxidation into their respective alcohols and H_2O_2 into water [64], a function catalyzed by another intracellular enzyme catalase which is known for the catalysis of disintegration of H_2O_2; glutathione reductase (GR) is an antioxidant enzyme glutathione disulfide to glutathione using flavine Adenine Dinucleotide (FAD) and Nicotinamide Adenine Dinucleotide Phosphate Hydrogen (NADPH) [65] with glutathione eventually mopping up the system of ROS. While catalase (CAT) catalyzes the biotransformation of H_2O_2, SOD is an enzyme that detoxifies the cell by dismutating superoxides generated cytosolically. Serum total antioxidant capacity (TAC) is the measure of the entirety of antioxidants that subserves a reductive role in the serum following exposure to toxicants including crude oil. Metrics of TAC remain a litmus test for the confirmation of the entirety of antioxidants beyond those measured in this study. The significant reduction in the levels of these antioxidants including GPx, GR, CAT, SOD, and TAC in male and female categories as observed in this study when compared with the contrasting significant increase in the level of lipid peroxidation as measured by MDA is indicative that exposure to crude-oil-contaminated water induces oxidative stress. This status prolongs the cytotoxic effect of intracellularly generated oxidative stress among the residents of the community. Although depletion of some antioxidants measured in this study had earlier been reported in human subjects and experimental conditions to be reduced by crude oil contamination, however, this study used multiple models of toxicological screening including serum hepato-renal integrity, oxidative stress, inflammomutagenicity, water pollution status, and health risk assessment to investigate crude oil toxicosis and its associated carcinogenic and non-carcinogenic risks in crude-oil-polluted Niger Delta community.

Guanine nitrogenous base of DNA is susceptible to attacks from free radicals due to its low oxidative potential among other nitrogenous bases. 8-hydroxy-2-deoxyguanosine (8-OHdG) adduct production is the result of such attacks and has become a useful index of DNA damage from xenobiotics in an oxidative stress-dependent mechanism. It has been suggested as the reliable biomarker for toxicity [66,67], cancer progression screenings [68] and has recently been used to screen DNA damage in Chinese children exposed to acetaminophen [69]. The significant increase in the level of 8-OHdG adduct in both males (65% increase) and females (69% increase) of the community residents when compared with the control community shows that crude oil contamination induces oxidative DNA damage.

Tumor necrosis factor-alpha (TNF-α) regulates immune cells by inducing apoptosis, inflammation, and carcinogenesis. The level of serum TNF-α has been closely linked with several human disorders including cancer [70], inflammatory bowel disease [71], and neurodegeneration [72]. This study found an increase in serum levels of TNF-α both in male and female genders among Ugbegugun community residents when compared with the control. The increase is suggestive that the toxicosis of xenobiotic components of crude oil may be inflammatory, apoptotic, and carcinogenic-dependent. Pathologies such as reproductive toxicity and hepato-renal damage have been linked to crude oil exposure, particularly from the Niger Delta region [73,74]. The pathophysiological mechanism that has been responsible is largely oxidatively mediated. We made a synopsis of the systemic pathologies reported in the literature on crude oil toxicity and presented the mechanism involved in Fig. 9 above. When toxic components of crude oil such as Polycyclic Aromatic Hydrocarbon (PAH), polychlorinated biphenyl (PCB), carbon monoxide, heavy metals, etc. are absorbed into the body, they are sequestered into the cells where they attack the

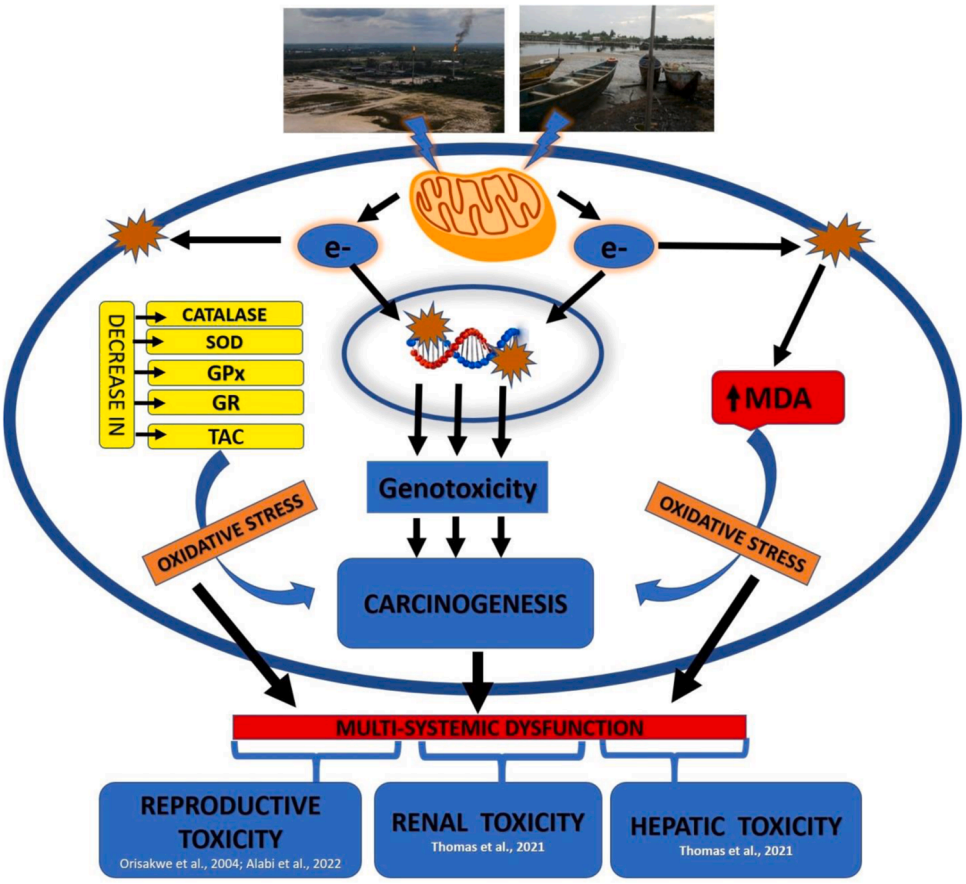


Fig. 9. Putative mechanism of crude oil-induced systemic pathology and carcinogenic risk.

mitochondrion causing leakage of electrons from the electron transport chain. These reactively labile electrons attack the cell membrane and permeate the nucleus where they also attack the nitrogenous bases of the DNA causing cytogenotoxicity. These mechanisms have been considered as the etiology of crude oil-induced carcinogenesis and a number of systemic pathologies have already been reported in the literature (Fig. 9).

Conclusively, water contamination from crude oil induced oxidative stress via depletion of systemic antioxidant capacity and increased free radical generation which evidently attacks plasmalemma and nuclear genetic material culminating in lipid peroxidation and DNA base lesion among male and female residents of Ugbegugun community. There are significant ecological, carcinogenic, and non-carcinogenic risks associated with crude oil exploration in the community. Evidence of pathological indices observed among the residents of this community significantly implicates crude oil contamination of the water matrix in the community. We, therefore, recommend a pragmatic clean-up process and stringent regulation of crude oil explorative activities in the Niger Delta particularly in areas hosting oil company headquarters like Ugbegugun community.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.toxrep.2024.03.006.

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