International Research Journal of Medical Sciences _____ ISSN 2320 –7353
Vol. **1(11),** 9-16, December **(2013)** *Int. Res. J. Medical Sci.*

Impact of Prolonged Exposure to Oil and Gas Flares on Human Renal Functions

Egwurugwu J.N.[1], Nwafor A. [2], Oluronfemi O.J. [2], Iwuji S.C.[3] and Alagwu E.A.[1]
[1]Department of Human Physiology, College of Medicine and Health Sciences, Imo State University, Owerri, NIGERIA
[2]Department of Human Physiology, College Health Sciences, University of Port Harcourt, Choba, NIGERIA
[3]Department of Biomedical Technology, School of Health Technology, Federal University of Technology, Owerri, NIGERIA

Available online at: www.isca.in, www.isca.me
Received 8th October 2013, revised 25th October 2013, accepted 27th November 2013

Abstract

This study evaluated the effects of prolonged exposure to oil and gas flares on the renal functions of some residents of the Niger Delta region of Nigeria in the vicinity of the oil and gas flares continually in the order of ten (10) years and above compared to the control subjects drawn from non oil and gas production environments. The subjects were matched for age, sex, educational status and socioeconomic status. Of the 3150 adult volunteers screened, 790 (475 exposed groups and 315 control groups) met the inclusion criteria and participated in the study. Blood samples were collected from all subjects and analyzed for serum concentrations of urea, creatinine, potassium, uric acid and inorganic phosphate. The results showed that the exposed to environmental pollutants of oil and gas origins had statistically significantly increased serum concentrations of urea, creatinine, potassium, uric acid and inorganic phosphate compared with control ($p<0.05$). Our result suggests therefore that individuals exposed to chronic – low level of oil and gas flared associated-environments had raised levels of renal dysfunction biomarkers and thus are more predisposed to developing kidney diseases.

Keywords: Prolonged exposure, gas flares, renal function, kidney disease, Niger Delta.

Introduction

The Niger Delta Region, in Southern Nigeria, is the center of oil and gas production and allied activities in Nigeria[1-2] and the richest part of Nigeria in terms of natural resources such as oil and gas deposits, extensive forests, suitable agricultural lands and abundant fish resources[2-3.] It has the largest natural gas reserve in Africa, has the second largest oil reserve in Africa and is the African continents primary oil producer[4]. The Niger Delta region of Nigeria has about 606 oil fields with 355 situated onshore; 251 situated offshore with 5,284 drilled oil wells and 7,000km of oil and gas pipelines[5-6]. Furthermore, it has more than 123 flaring sites, thereby making Nigeria one of the highest emitter of green house gases in Africa[6.] Exposure to hazardous chemicals, emissions and pollutants associated with oil and gas production is likely to be more in those that reside close to the facilities[8].

Flared gas is one of the generated wastes in the oil and gas industry that could be turned into wealth but allowed to not only waste but pose unquantifiable health, social, economic and cultural hazards to man. Gas Flaring is a common practice of burning off unwanted, flammable gases via combustion in an open atmosphere, non-premixed flame[9]. According to the World Bank[1] gas flaring is one anthropogenic activity, defined as the "wasteful emission of greenhouse gases (GHGs) that causes global warming, disequilibrium of the earth, unpredictable weather changes and major natural disasters because it emits a cocktail of benzene and other toxic substances that are harmful to humans, animals, plants and the entire physical environment"

The reasons for continued gas flaring in the Niger Delta Region of Nigeria include lack of necessary technology for gathering and conserving the gas flared, on the one hand, and market for the gas, on the other hand[9]. Others include lack of political will by the government and its agencies, lack of cohesion among the exposed citizens concerned, hence cant forge a common front to fight for their fundamental human rights.

During gas flaring, complete combustion though rarely achieved, releases relatively innocuous gases such as carbon dioxide and water[11] whereas incomplete combustion emits various compounds such as methane, propane, and hazardous air pollutants such as volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons (PAHs) and soot[12] benzene, naphthalene, styrene, acetylene, fluoranthene, anthracene pyrene, xylene and ethylene[13].

Representatives of volatile organic compounds (VOCs) released during production, storage and transportation associated with the oil and gas industry are benzene and toluene[14]. These in particular, are hazardous due to their inherent toxicity in mammals and their wide use in industry and high volume of production lead to substantial environmental releases[15]. Flaring can also produce other pollutant emissions such as particulate matter (PM) in the form of soot or black carbon[9.] Flaring can also produce soot and other pollutant species that have negative effects on air quality and the environment[16-18]. These volatile hydrocarbons, which can be absorbed into the blood via the respiratory tract, as well as through the food chain,[19] have various potential health effects[20].

It is evident that gas flared environment is polluted with contaminants not only from gas and oil flare but also from other sources such as industries(e.g. petrochemical, fertilizer industries), diesel fuel/exhaust chemicals, radiations and climate change[21].

It has been observed that about 45.8 billion kilo watts of heat is discharged into the atmosphere from 1.8 billion cubic feet of gas everyday in the Niger Delta region, leading to temperatures that render large areas inhabitable[22]. The heat generated from gas flaring kills vegetation around flaring area, destroys mangrove swamps and salt marshes, suppresses the growth and flowering of some plants, induces soil degradation and diminishes agricultural productivity[23-24.] Furthermore, increased ambient thermal conditions have also been noted in oil and gas flared environments[25-26.] Increased ambient temperature can cause chronic and persistent dehydration. Chronic and persistent dehydration can affect lead to increased serum urea and reduced renal perfusion[27].

Water bodies from gas and oil flared environments tend to have increased levels of heavy metals such as lead, cadmium, copper, manganese, magnesium, nitrates compared with non-gas flared areas[28-30].

The kidney is the primary organ of cadmium toxicity especially following chronic exposure[31.]. Increases in mortality from renal diseases have been observed among populations living in cadmium polluted areas of Belgium[32], England[33-34], and Japan[35-38.] with elevated levels of bio markers of renal dysfunction.

To the best of our knowledge, no work has been done to assess the possible effects of prolonged exposure of oil and gas flares on human renal function in the Niger Delta Region of Nigeria and this necessitated this research.

Material and Methods

Research design: This is a case controlled research, comparing some residents of the Niger Delta region of Nigeria, chronically exposed to low dose emissions of oil/gas flaring with non-exposed persons from another community within the same region.

Study areas: The study was conducted in two different communities in the Imo East Senatorial zone of Imo State, one of the nine, oil producing states in the Niger Delta of Nigeria. The two communities, have similar socioeconomic and cultural characteristic features. Egbema, an oil and gas producing community with active gas flaring by Shell Petroleum Development Company (SPDC) for more than 45 years, constitute the test group. This community is located in between many other active oil and gas flaring sites such as Ossu, Oguta and Izombe oil and gas fields operated by Addax and Akri and Ebocha oil and gas fields run by Nigeria Agip Oil Company. Thus, the residents are well exposed to the effects of oil and gas flaring. Alaoma Owerre Ebeiri autonomous community, a non oil and gas producing area, constitute the control group population.

Selection of subjects: Of the 3150 apparently healthy volunteers between the ages of 18 and 80 years screened, 790 subjects (475 test groups and 315 control groups) met the inclusion criteria and therefore participated in the study. All known cases of hypertension, diabetes mellitus, metabolic syndrome, dyslipidemia, renal disease, atherosclerosis and contraceptive users were excluded from the study. All selected participants consented to in writing and /or thump printed to participate in the study. All subjects must have lived in their various communities consistently for more than 5 years. The Ethics Committee on Human Biomedical Research of the University of Port Harcourt, Nigeria gave approval to the work and the study conforms to the Helsinki Declaration on Biomedical Research.

Analyses of the Clinical Chemistry indices: Determination of serum urea: Principle: Urea in serum is hydrolyzed to ammonia in the presence of urease. The ammonia is then measured photometrically by Berthelot's reaction[39-40.]

$$\text{Urea} + H_2O \xrightarrow{\text{Urease}} 2NH_3 + CO_2 .$$

$$NH_3 + \text{hypochlorite} + \text{phenol} \longrightarrow \text{indophenols (blue compound)}$$

Procedure: 10µL of the serum sample was added to 100µL of reagent 1, mixed and incubated for 10 minutes at 37°C. 2.5 ml of reagents 2 and 3 were added, mixed immediately and incubated at 37°C for 15 minutes. The absorbance was taken at 546 nm against the reagent blank. The serum urea concentration of the serum sample was determined and the results expressed in mg/dl. This was later converted to mmol/L using standard methods.

Determination of Serum creatinine: Principle: Creatinine in alkaline solution reacts with picric acid to form a colored complex. The amount of the complex formed is directly proportional to the creatinine concentration.

Procedure: 100µL of the serum sample was added with 1000µL of the working reagent and then mixed. After 30 seconds, the absorbance A_1 of the standard and sample were taken. Exactly 2 minutes later, the absorbance A_2 of the standard and sample were taken. The creatinine concentrations in the samples were determined and expressed in mg/dL. This converted to µmol/l using standard methods.

Determination of serum potassium: Principle: The amount of potassium is determined by using sodium tetraphenylboron in a specifically prepared mixture to produce a colloidal suspension[41]. The turbidity of which is proportional to potassium concentration in the range of 2-7mEq/L

Procedure: 10µL of the sample was added to 1ml of potassium reagent, mixed and allowed to sit for 3 minutes at room temperature, thereafter, the absorbance was taken at 500 nm against the reagent blank. The potassium concentration of the samples were determined and expressed in mmol/l.

Determination of serum calcium: Principle: Calcium with Arsenazo 111 [2,7-{bis(2-arsonophenyfazo)}-1,8-dihydroxynaphthalen-3,6-disulphuric acid], at neutral pH yields a blue colored complex, whose intensity is proportional to the calcium concentration. Interference by magnesium is eliminated by the addition of 8-hydroxyquinoline-5-sulfonic acid.

Procedure: 10µL of the serum sample was added to 1000µL of the working reagent, mixed and incubated for 10 minutes. The absorbance was taken at 630 nm against the reagent blank. The calcium concentration of the samples were determined and expressed in mg/dl. This was later converted to mmol/l. Conversion factor: Calcium(mg/dl) x 0.2495m = calcium(mmol/l).

Determination of Uric acid: Principle: Uric acid is oxidized to allantoin by uricase. The generated hydrogen peroxide reacts with 4-aminoantipyrine and DHPS to quinoneimine

$$\text{Uric acid} + H_2O + O_2 \xrightarrow{\text{Uricase}} \text{Allantoin} + CO_2 + H_2O_2.$$

$$\text{DHPS} + \text{4-aminoantipyrine} + 2H_2O \xrightarrow{\text{POD}} \text{Quinoneimine} + 3H_2O.$$

Procedure: 25µL of the serum sample, standard and control were added to 1000µL of the working reagent, mixed and incubated for 10 minutes. The absorbance was taken at 510 nm against the reagent blank. The uric acid concentration of the samples were determined and expressed in mg/dl.

Determination of inorganic phosphorous: Procedure: Inorganic phosphorous was determined by the method of Drewes[42]. 50µL of samples, standard and control were added to 2.0 ml of working reagent and incubated for 1 minute at 25°C. 1 ml of developer was added to all tubes and the mixture allowed to stand at room temperature for 10 minutes. Absorbances of sample, standard and control were determined at 680 nm using a RA-50 spectrophotometer (Ames/Techinicon, France).

Statistical analysis: Statistical Package for Social Sciences (SPSS) (version 17 for windows, SPSS Inc., Chicago, USA) was used to analyze the data. The differences in the various parameters studied between the test and control groups were evaluated using Kolmogorov-Simirnov Z statistic. Anova was used to assess differences within the groups. Statistically significant values were determined at $p < 0.05$ or 95% confidence level.

Results and Discussion

Of the 3150 volunteers, 790 subjects met the inclusion criteria and participated actively in this study. There were 267 (34%) males and 523 (66%) females, with a male: female ratio of 1:2.

Table 1 compares the Clinical Chemistry indices of the general population between the control and test group subjects. There was statistically significant increase in the serum concentrations of uric acid, potassium, creatinine, urea and inorganic phosphate in the test group subjects compared with the control ($p<0.05$), with percentage differences of 24.49, 11.94, 13.09, 14.35 and 41.77% respectively. Conversely, statistically significant decrease in the serum concentration of calcium was observed in the test group subjects compared with the control($p<0.05$), with percentage differences of 8.13%.

Figure 1 shows the percentage differences of the Clinical Chemistry indices studied. All the parameters studied except calcium were statistically significantly increased in the test subjects compared with the control, while calcium statistically increased in the control subjects compared with the test subjects($p<0.05$).

Table 2 compares the Clinical Chemistry indices between the males and females of the entire population. There is statistically significant increase in the serum concentrations of calcium, inorganic phosphate, uric acid and potassium in the male test subjects compared with the female test subjects($p<0.05$). No significant differences between the control males and females studied ($p>0.05$).

Table 2 compares the Clinical Chemistry indices between the males andfemales of the entire population. There is statistically significant increase in the serum concentrations of calcium, inorganic phosphate, uric acid and potassium in the male test subjects compared with the female test subjects($p<0.05$). No significant differences between the control males and females studied ($p>0.05$).

Table-1
Clinical Chemistry indices of the general population

Parameter	Control group	Test group	P Value	% difference
Urea (mmol/L)	4.27±0.16	4.93±0.09	0.01°	14.35
Creatinine(µmol/L)	97.98±1.46	111.70±1.54	0.01°	13.09
Potassium (mmol/L)	4.18±0.06	4.71±0.06	0.01°	11.94
Calcium(mmol/L)	2.17±0.02	2.00±0.02	0.01°	-8.13
Inorganic phosphate(mmol/L)	1.97±0.04	3.01±0.05	0.01°	41.77
Uric acid (mg/dl)	5.21±0.07	8.59±0.13	0.01°	24.49

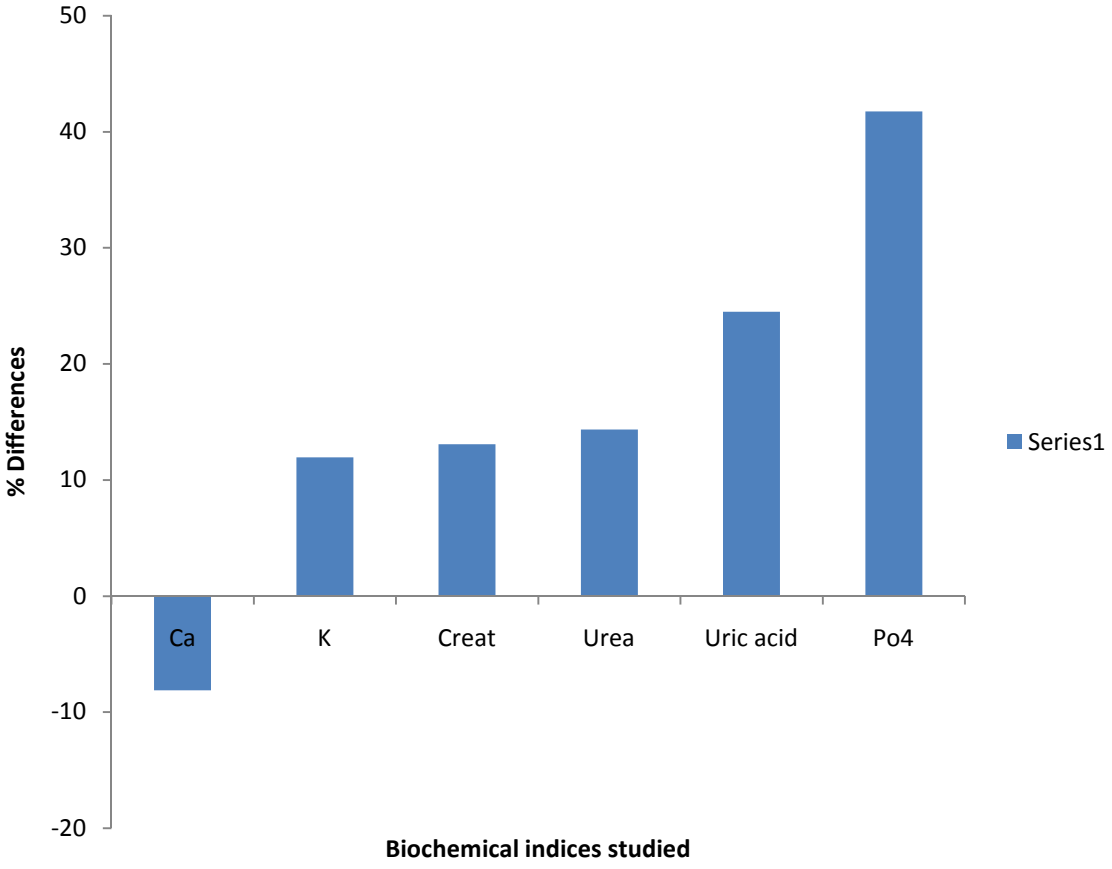

Figure-1
Percentage differences between the control and test group biochemical indices studied.

Table-2
Comparison of Clinical Chemistry Indices between males and females in the population

Parameter	Research group	Sex group		P value	% difference
		Male	Female		
Urea (mmol/l)	Control	4.08±0.22	4.40±0.23	0.96	7.55
	Test	4.70±0.14	5.03±0.12	0.37	6.59
Creatinine (umol/l)	Control	96.47±2.26	99.00±1.91	0.29°	2.58
	Test	113.11±2.63	111.11±1.88	0.18	1.78
Calcium (mmol/L)	Control	2.15±0.03	2.17±0.03	0.823	0.93
	Test	2.05±0.05	1.98±0.02	0.01	3.47
Inorganic phosphate (mmol/L).	Control	1.94±0.05	1.99±0.05	0.37	2.54
	Test	3.22±0.13	2.93±0.06	0.01	9.42
Uric acid(mg/dl)	Control	5.90±0.03	5.65±0.02	0.33	2.16
	Test	9.45±0.09	7.24±0.03	0.01	13.24
Potassium (mmol/L).	Control	4.12±0.09	4.21±0.08	0.604	2.14
	Test	4.92±0.16	4.62±0.07	0.01°	6.29

Discussion: The results showed that the serum concentrations of urea, potassium, creatinine, inorganic phosphate and uric acid were significantly higher in the test subjects compared with control ($p < 0.05$). Prolonged exposure to gas flares impacted negatively on serum concentrations of urea, creatinine, potassium, inorganic phosphate and uric acid on the test subjects. The kidney can greatly be damaged before losing sufficient function to modify the normal clinical indication of renal disease such as serum creatinine concentration[43.] And it has also been noted that about 5 0 % of renal capacity may be

lost before serum creatinine become abnormal and disease is detected clinically[44]. Low level chronic exposure to oil and gas flares can affect the kidneys in a number of ways:

Gas flaring causes increased ambient temperature[26]. About 45.8 billion kw of heat are discharged into the atmosphere of the Niger-Delta from 1.8 billion cubic feet of gas everyday[22, 25.] Increase in ambient temperature can cause persistent and chronic dehydration among residents of gas flared environments. Chronic dehydration can cause reduced blood volume, increase in blood viscosity, and increase in blood pressure. Dehydration is further worsened by the poor water quality in the Niger Delta Region[29-30]. Furthermore, chronic and persistent dehydration can lead to reduced glomerular filtration rate (GFR) and increase in serum creatinine. Elevated levels of serum creatinine and urea can arise from persistent dehydration and reduced renal perfusion[27]. Increase in serum concentration of creatinine in the exposed subjects may also be due to vigorous exercises[27] as majority of them are farmers and they use bicycle as their main means of transportation.

Serum uric acid (SUA) in man is derived from the breakdown of purines and is essentially the product of the action of the enzyme, xanthine oxidase on xanthine and hypoxanthine. The increased SUA in those exposed to prolonged gas and oil activities compared to the non exposed may be due to i. excessive caloric intake, increased societal stress and genetic predisposition, ii. increased levels of serum uric acid is constant finding in lead toxicity and it may cause damage to renal tubules[43], iii. Hypertension may increase SUA via elevated serum lactate levels. Hypertension initially produces renal microvascular diseases and local tissue hypoxia, as evidenced by increase in serum lactate. The lactate decreases tubular secretion of uric acid, leading to increased serum levels. Intrarenal ischaemia can also contribute to generation of uric acid via xanthine oxidase. It is also possible that metabolic alterations or disturbances (hyperinsulinemia) or sympathetic activity may produce changes in renal sodium handling, leading to increased arterial pressure, decreased renal blood flow and decreased uric acid secretion. This, in turn, increases purine oxidation resulting in increased production of reactive oxygen species (ROS), subsequent vascular injury, and reduced nitric oxide[45-46]. Hyperuricemia is a known cause of kidney disease and cardiovascular diseases[47-51]. Increased serum uric acid level is involved in the progression of chronic kidney disease[52] and chronic kidney disease is a known cause of anaemia[53]. Elevated serum uric acid level is an independent predictor of the development of both microalbuminuria[54] and renal dysfunction in subjects with normal renal function[55-56].

Hypertension can greatly affect the kidneys. Olanrewaju *et al*[57] has observed that increased systolic blood pressure may predict kidney damage. Gas flaring affects sleep-wake cycle[58.] Sleep deprivation is associated with high prevalence of hypertension[59-60.] Sleep deprivation causes significant increase in serum norepinephrine and sympathetic activity, venous endothelial dysfunction and hypertension[61]. Paradoxical sleep deprivation reduced plasma angiotensin 11 concentrations, increased renal sympathetic nerve activity and possibly increase in blood pressure[62]. Modesti and co-workers[63] have demonstrated that for every hour of extra daylight experienced, the average nighttime systolic blood pressure rose by 0.63 mmHg. Hypertension is both an important cause and consequence of chronic kidney disease[64]. Chronic kidney disease is the most common form of secondary hypertension and its also an independent risk factor for cardiovascular morbidity and mortality[65-66].

Role of heavy metals: The Nigerian crude oil is known to contain heavy metals such as Al, Zn, As, Ba, Fe, Pb, Co, Cu, Cr, Mn, Ga, Sb, Ni and V[28]. Furthermore, surface and underground waters in gas flared environments tend to have more concentrations of heavy metals such as lead, barium, cadmium, selenium, manganese, magnesium and copper than non gas flared area[28,31]. The residents of the Niger Delta Region are therefore exposed not only to the various air and soil pollutants but also to water contaminants especially the heavy metals. And some heavy metals such as lead, arsenic, xylene, Chromium, zinc and cadmium, present in oil and gas flares, can affect the kidneys adversely.

Increases in mortality from renal diseases have been observed among populations living in Cd polluted areas of Japan[35-38], Belgium[32], and England[33]. Lead nephrotoxicity is characterized by proximal tubular nephropathy, glomerular sclerosis and interstitial fibrosis[43, 67-68]. Renal failure have been noted in individuals exposed to varying doses of chromium[69-71]. Epithelial cell damage in the glomerulus and proximal convoluted tubules and increased plasma creatinine and urea levels were noted in rats exposed to zinc acetate[72].

Orisakwe et al[44] reported increase in serum concentrations of creatinine and potassium with degeneration and necrosis of glomeruli in rats treated with crude oil. **Arsenic** intoxication has been associated with tubulointerstitial nephritis[73.] Benzene, toluene, ethlybenzene, and xylene (BTEX)BTEX have been linked to leukemia, kidney failure, and negative effects on the cardiovascular system[74].

Conclusion

In conclusion, prolonged exposure to low dose emissions of oil and gas flares caused increase in serum concentrations renal dysfunction biomarkers such as urea, creatinine, potassium, inorganic phosphate and uric acid, suggesting that residents of oil/gas flared environments are more prone to developing kidney diseases than the un-exposed.

References

1. World Bank, Defining and Environmental Strategy for the Niger Delta. West Central Africa Department, World Bank, Washington DC, P 150 **(1995)**

2. Ukpaka C.P. Characteristics of produced water from an oil terminal in Niger Delta area of Nigeria, *Journal of Research in Environmental Science and Toxicology*, **1(5)**, 115-130 **(2012)**

3. Ana G.C., Air Pollution in the Niger Delta Area: Scope, Challenges and Remedies, The Impact of Air Pollution on Health, Economy, Environment and Agricultural Sources, Dr. Mohamed Khallaf (Ed.),ISBN: 978-953-307-528-0**,** (2011) InTech, Available from: http://www.intechopen.com/books/the-impact-of-airpollution-on-health-economy-environment-and-agricultural-sources/air-pollution-in-the-niger-delta-area-scopechallenges-and-remedies. Accessed on January 23, **(2013)**

4. Kadaya A.A., Oil exploration and spillage in the Niger Delta of Nigeria, *Civil and Environmental Research*, **2(3), (2012)**

5. Anifowose B., Assessing the Impact of Oil & Gas Transport on Nigeria's Environment, U21 Postgraduate Research Conference Proceedings 1, University of Birmingham UK **(2008)**

6. Onuoha F.C., Oil Pipeline Sabotage in Nigeria: Dimensions, Actors and Implications for National Security L/C, African Security Review Institute for Security Studies, **17(3)** (**2008**)

7. Uyigue E. and Agho M., Coping with Climate Change and Environmental Degradation in the Niger Delta of Southern Nigeria. Community Research and Development Centre Nigeria (CREDC) (**2007**)

8. Witter R., Stinson K., Sacket H., Putter S., Kinney G., Teitelbaun D. and Newman L., Potential exposure-related human health effects of oil and gas development: a literature review (2003-2008), (**2008**) www.ccag.org.au/images/stories/pdfs/literaturereviewwitter et al2008.pdf. accessed 04/01/13 **(2013)**

9. McEwen J.D.N. and Johnson M.R., Black carbon particulate matter emission factors for buoyancy driven associated gas flares, *Journal of Air Waste Management Association*, **62(3),** 307-321 (**2010**)

10. Kaldany R., Gblobal Gas Reduction Initiative, a paper presented at the IFC Informal Launch Conference of the Global Gas Reduction Initiative, Marakesh, November 8, 2001, Slides 3-7. www.ifc.org/ogc.globalgas.htm. (**2001**)

11. Leahey D.M. and Preston K. Theoretical and observational assessments of flare efficiencies, *Journal of the Air and Waste Management Association*, **51,** 1610-1616 (**2001**)

12. Kindzierski W.D. Importance of Human environmental exposure to Hazardous air pollutants from Gas flares, *Environmental Review*, **8,** 41-62 (**2001**)

13. Strosher M.T., Investigation of Flare Gas Emissions in Alberta; Calgary, Alberta (**1996**)

14. Olsgard M.L., Bortolotti G.R., Trask B.R. and Smits J.E.G., Effects of inhalation exposure to a binary mixture of benzene and toluene on vitamin A status and humoral and cell-mediated immunity in wild and captive American kestrels, *Journal of Toxicology and Environmental Health,* Part A, **71,** 1100-1108 (**2008**)

15. Robinson S.N., Shah R., Wong V.A. and Farris G.M., Immunotoxicological effects of benzene inhalation in male Spraque-Dawley rats, *Toxicology,* **119,** 227-237 (**1997**)

16. Strosher M.T., Characterization of emissions from diffusion flare systems. Journal of Air Waste Management Association, **50(10)**, 1723-1733 (**2000**)

17. Johnson M.R. and Kostiuk L.W., Efficiencies of low-momentum jet diffusion flames in crosswinds, *Combustion and Flame*, **123,** 189-200 (**2000**)

18. Johnson M.R., Wilson D.J. and Kostiuk L.W., A fuel stripping mechanism for wake-stabilized jet diffusion flames in crossflow, *Combustion Science and Technology*, **169,** 155-174 (**2001**)

19. Eyong E.U., Biochemical and toxicological implications following ingestion of shellfish exposed to crude oil polluted water, Ph.D Thesis submitted to the Department of Biochemistry, University of Calabar, Calabar, Nigeria, 329 (**2000**)

20. USEPA, United States Environmental Protection Agency (USEPA) (2004): Volatile organic compounds, http://www.epa.gov/volatile organic compounds, Washington DC. **(2004)**

21. Nwafor A., Life under assault: no where to hide. University of Port Harcourt Inaugural Lecture Series No 102, (**2013**)

22. Agbola T. and Olurin T.A., Landuse and Landcover Change in the Niger Delta Excerpts from a Research Report presented to the Centre for Democracy and Development (**2003**)

23. United Nations Development Programme,. Niger Delta Human Development Report. Abuja, Nigeria, 185&186 **(2006)**

24. Mba C.H., Environmental Protection and National Development: Towards Optimal Resolution of Conflicting Measures and Strategies. in: Aja Akpuru-Aja and Emeribe Augustine C., Policy and Contending Issues in Nigerian National Development Strategy, John Jacob's Publishers, Ltd, Enugu, Nigeria (**2000**)

25. Aaron K.K., Human Rights Violation and Environmental Degradation in the Niger-Delta, In Elizabeth Porter and Baden Offord(eds), *Activating Human Rights*, Oxford, Barne, New York (**2006**)

26. Oseji O.J., Environmental impact of gas flaring within Umutu-Ebedei gas plant in Delta State, Nigeria, *Archives of Applied Science Research*, **3(6),** 272-279 (**2011**)

27. Rosner M.H. and Bolton W.K., Renal function testing, *American Journal of Kidney Diseases,* **47(1),** 174-183 **(2006)**

28. Idodo-Umeh G. and Ogbeibu A.E., Bioaccumulation of the Heavy Metals in Cassava Tubers and Plantain Fruits Grown in Soils Impacted with Petroleum and Non-Petroleum Activities, *Research Journal of Environmental Sciences*, **4,** 33-41 (**2010**)

29. Nwankwo C.N. and Ogagarue D.O., Effects of gas flaring on surface and ground waters in Delta State Nigeria, *Journal of Geology and Mining Research*, **3(5)**, 131-136 (**2011**)

30. Egwurugwu J.N., Nwafor A., Nwankpa P., Olorufemi O.J., Okwara J.E., Prolonged gas flaring and water quality in Obiakpu, Egbema Imo State Nigeria, *International Research Journal Environmental Science,* **2(4),** 1-5 (**2013**)

31. Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profile for Benzene (update). US Department of Health and Human Services, Atlanta, Georgia, 200-2004-09793,1-415 (**2007**)

32. Lauwerys R. and De Wals P.H., Environmental pollution by cadmium and mortality from renal diseases, Lancet, **1(8216)**, 383 (**1981**)

33. Inskip H., Beral V., McDowall M. Mortality of Shipham residents: 40-year follow-up, *Lancet,* 896-899 (**1982**)

34. Thomas L.D., Hodgson S., Nieuwenhuijsen M. and Jarup L., Early kidney damage in a population exposed to cadmium and other heavy metals, *Environ Health Perspect,* **117(2**), 181-184 (**2009**)

35. Arisawa K., Nakano A., Saito H., Liu X.J., Yokoo M., Soda M., Koba T., Takahashi T. and Kinoshita K., Mortality and cancer incidence among a population previously exposed to environmental cadmium, *Int Arch Occup Environ Health,* **74,** 255-262 (**2001**)

36. Arisawa K., Uemura H., Hiyoshi M., Dakeshita S., Kitayama A., Saito H. and Soda M., Cause-specific mortality and cancer incidence rates in relation to urinary β2-microglobulin: 23-Year follow-up study in a cadmium-polluted area, Toxicol Lett, **173(3),** 168-174 (**2007**)

37. Nishijo M., Nakagawa H., Morikawa Y. et al., Mortality in a cadmium polluted area Japan, *Biometals*, **17(5)**, 535-538 (**2004**)

38. Nishijo M., Morikawa Y., Nakagawa H., Tawara K., Miura K., Kido T., Ikawa A., E., Kobayashi E. and Nogawa K., Causes of death and renal tubular dysfunction in residents exposed to cadmium in the environment, *Occup Environ Med.,* **63,** 545-550 (**2006**)

39. Chaney A.L. and Marbach E.P., Modified reagents for determination of urea and ammonia, *Clin. Chem*., **8,** 130 (**1962**)

40. Tobacco A., *Clinical Chemistry,* **25(2),** 336 (**1979**)

41. Terri A.E. and Sesin P.G. Determination of serum potassium by using sodium tetraphenylboron, *Am. J. Clin. Path,* **29,** 86- 90 (**1958**)

42. Drewes P.A., Determination of inorganic phosphorus in serum or plasma without deproteinization, *Clin. Chem. Acta*., **39,** 81-83 (**1972**)

43. Loghman-Adham M., Renal effects of environmental and occupational lead exposure, *Environmental Health Perspective*, **105,** 928-939 (**1997**)

44. Orisakwe O.E., Njan A.A., Afonne O.J., Akumka D.D., Orish V.N. and Udemezue O.O. Investigation into the nephrotoxicity of Nigerian Bonny light crude oil in albino rats, *International Journal of Environmental Research and Public Health*, **1,** 106-110 (**2004**)

45. Alderman M.H., Cohen H. and Madhavan S., Distribution and determinants of cardiovascular events during 20 years of successful antihypertensive treatment, *Journal of Hypertension*, **16,** 761-9 (**1998**)

46. Bickel C., Rupprecht H.J., Blankenberg S., Rippin G., Hatner G., Daunhauer A. et al., Serum uric acid as an independent predictor of mortality in patients with angiographyically proven coronary artery disease, *American Journal of Cardiology*, **89,** 12-7 (**2002**)

47. Satarug S., Nisho M., Lasker J.M., Edwards R.J. and Moore M.R. Kidney dysfunction and hypertension: Role for Cadmium, P450 and Heme Oxygenases, *Tohoku Journal of Experimental Medicine*, **208,** 179-202 (**2006)**

48. Siu Y.P., Leung K.T., Tong M.K., Kwan T.H. Use of allopurinol in slowing the progression of renal disease through its ability to lower serum uric acid level. *American Journal of Kidney Diseaes;* **47,** 51-59 (**2006**)

49. Talaat, K.M, el-Sheikh, A. R. The effect of mild hyperuricemia on urinary transforming growth factor beta and the progression of chronic kidney disease. American Journal of Nephrology, **27,** 435-440 (**2007**)

50. Feig D.I, Kang D.H, Johnson R.J. (2008): Uric acid and cardiovascular risk. *New England Journal of Medicine*, **vol 359 (17**), 1811-1821 (**2008**)

51. Resl M., Clodi M., Neuhold S., Kromoser H., Riedl M., Vila G., Prager R., Pacher R., Strunk G., Luger A. and Hulsmann M. Serum uric acid is related to cardiovascular events and correlates with N-terminal pro-B-type natriuretic peptide and albuminuria in patients with diabetes mellitus. Diabetes Medicine, **29(6),** 721-5 (**2012**)

52. Ito S., Naritomi H., Ogihara T., Shimada K., Shimamoto K., Tanaka H., Yoshike N. Impact of serum uric acid on renal function and cardiovascular events in hypertensive patients treated with losartan. *Hypertension Research*, **35,** 867-873 (**2012**)

53. Guyton A.C. and Hall J.E. *Textbook of Medical Physiology*, 12th Edition, Sanders, An Imprint of Elsevier, Philadelphia, Pennsylvenia (**2010**)

54. Lee J.E., Kim Y.G., Choi Y.H., Huh W., Kim D.J. and Oh H.Y. Serum uric acid is associated with microalbuminuria in prehypertension, *Hypertension,* **47(5),** 962-7 (**2006**)

55. Iseki K., Oshiro S., Tozawa M., Iseki C., Ikemiya Y. and Takishita S. Significance of hyperuricemia on the early detection of renal failure in a cohort of screened subjects. *Hpertens.Research*, **24,** 691-697 (**2001**)

56. Tomita M., Mizuno S., Yamanaka H., Hosoda Y., Sakuma K., Matuoka Y., Odaka M., Yamaguchi M., Yosida H., Morisawa H., and Murayama T., Does hyperuricemia affect mortality? A prospective cohort study of Japanese male workers, *Journal of Epidemiology*, **10,** 403-409 (**2000**)

57. Olanrewaju T.O., Aderibigbe A., Chijioke A., Dada S.A. and Rafiu M.O. Predictors of kidney damage in newly-diagnosed hypertensive Nigerians, *Tropical Journal of Nephrology*, **5(1),** 29-34 (**2010**)

58. Gobo A.E., Richard G. and Ubong I.U. Health Impact of Gas Flares on Igwuruta/Umuechem Communities in Rivers State, *Journal of Applied Science and Environmental Management,* **13(3),** 27-33 (**2009**)

59. Legramante J.M. and Galante A., Sleep and hypertension: a challenge for the autonomic regulation of the cardiovascular system, *Circulation*, **112,** 786-788 (**2005**)

60. Gottlieb D. J., Redline S., Nieto F.J., Baldwin C.M., Newman A.B., Resnick H.E. and Punjabi N.M., Association of usual sleep duration with hypertension: the Sleep Heart Health Study. *Sleep*, **29(8**), 1009-14 (**2006**)

61. Dettoni J.L., Consolim-Colombo F.M., Drager L.F., Rubira M.C., Cavasin de Souza S.B.P., Irigoyen M.C., Morstarda C., Borile S., Krieger E.M., Moreno H. and Lorenzi-Filho G., Cardiovascular effects of partial sleep deprivation in healthy volunteers, *Journal of Applied Physiology*, **113(2),** 232-6 (**2012**)

62. Perry J.C., Bergamaschi C.T., Campos R.R., Andersen M.L., Montano N., Casarini D.E. and Tufik S. Sympathetic and angiotensinergic responses mediated by paradoxical sleep loss in rats, *Journal of Renin-Angiotensin-Aldosterone System,* DOI: 10.1177/1470320310391504 (**2011**)

63. Modesti P.A., Morabito M., Massetti L., Rapi S., Orlandini S., Mancia G., Gensini G.F. and Parati G. Seasonal blood pressure changes: an independent relationship with temperature and daylight hours, *Hypertension,* **61(4),** 908-14 (**2013**)

64. Tedla F.M., Brar A., Browne R. and Brown C., Hypertension in chronic disease: Navigating the Evidence, *International Journal of Hypertension*, Doi:10, 4061 /2011/132405 (**2011**)

65. Anavekar N.S., Mc Murray J.J.V., Velazquez E.J.et al., Relation between renal dysfunction and cardiovascular outcomes after myocardial infacrction, *New England Journal of Medicine*, **351(13**), 1285-1295 (**2004**)

66. Go A.S., Chertow G.M., Fan D., McCulloch and Hsu C.Y., Chronic kidney disease and risks of death, cardiovascular events, and hospitalization, *New England Journal of Medicine*, **351(13)**, 1296-1305 (**2004**)

67. Diamond G.L. Risk assessment of nephrotoxic metals, In: Tarloff J, Lash L, eds. The toxicology of the kidney, London: CRC Press, 1099-1132 (**2005**)

68. Goyer R.A., Mechanisms of lead and cadmium nephrotoxicity, *Toxicol Lett,* **46,** 153-162 (**1989**)

69. Wasser W.G., Feldman N.S. and D'Agati V.D., Chronic renal failure after ingestion of over-the-counter chromium picolinate, *Ann Intern Med,* **126(5),** 410 (**1997**)

70. Wani S., Weskamp C., Marple J. and Spry L., Acute tubular necrosis associated with chromium picolinatecontaining dietary supplement, *Ann Pharmacother,* **40,** 563-566 (**2006)**

71. Barešić M., Gornik I., Radonic R., Zlopasa O., Gubarev N. and Gasparovic V., Survival after severe acute chromic acid poisoning complicated with renal and liver failure, *Intern Med*., **48(9)**, 711-715 **(2009)**

72. Llobet J.M., Domingo J.L, Colomina M.T., Mayayo, E. and Corbella J., Subchronic oral toxicity of zinc in rats, *Bull Environ Contam Toxicol.,* **41**, 36-43 **(1988)**

73. Prasad G.V. and Rossi N.F., Arsenic intoxication associated with tubulointerstitial nephritis, *American Journal of Kidney Diseases*, **26**, 373-376 **(1995)**

74. Colborn T., Kwiatkowski C., Schultz K. and Bachran M. "Natural Gas Operations from a Public Health Perspective," *International Journal of Human and Ecological Risk Assessment,* www.endocrinedisruption.com/files/Oct2011HERA10-48forweb3-3-11.pdf. (**2010**)