RESEARCH PAPER | Medical Science | Volume : 4 | Issue : 12 | Dec 2014 | ISSN - 2249-555X

Impact of high level of Aluminum on Parathyroid hormone in Bauxite dust exposed mine workers

KEYWORDS: Aluminium, Bauxite dust, Biomarker, ELISA, Parathyroid Hormone.

Aruna A. Jawade
National Institute of Miners' Health, Wadi, Nagpur 440 023, India,

Ruchika K. Jain
National Institute of Miners' Health, Wadi, Nagpur 440 023, India,

Pravin N. Soni
National Institute of Miners' Health, Wadi, Nagpur 440 023, India,

Rajani G. Tumane
National Institute of Miners' Health, Wadi, Nagpur 440 023, India,

Lucky R. Thakkar
National Institute of Miners' Health, Wadi, Nagpur 440 023, India,

B. B. Mandal
National Institute of Miners' Health, Wadi, Nagpur 440 023, India,

Shubhangi K. Pingle
National Institute of Miners' Health National Institute of Miners' Health, JNARDDC Campus, oppo. Wadi Police station, Amravati Road, wadi, Nagpur, Wadi, Nagpur 440 023, India,

ABSTRACT *Bauxite ore is a major source of aluminium mineral. Dust particles of bauxite ore may be deposited in parathyroid gland and ultimately interrupt the secretion of parathyroid hormone (PTH) and calcium metabolism. In the present exploratory and stratified randomized study, 273 subjects were selected from three different bauxite producing mines. Whole blood and serum samples were used for measurement of Aluminium, PTH and calcium level respectively. The result shows that there is a negative correlation between levels of Al, Ca and PTH. It was also observed that PTH level is significantly decreased ($p < 0.0001$) in experimental group as compared to both the groups. It was also observed that PTH level decreases as the duration of exposure increases. Our preliminary findings suggest that PTH may be used as a potential biomarker for early detection of bauxite dust toxicity among exposed workers. Evaluation of PTH with panel of biomarkers may be helpful for further research on the bauxite toxicity among bauxite dust exposed workers.*

Introduction

Bauxite ore is mined all over the world because of industrial importance and presence of ample amount of Aluminium (Al) in ore (1). Al is the third most abundant element present in Earth's crust (8.3% by weight) (2). Occupational and environmental exposure of Bauxite dust occurs mainly during the process of mining, smelting and beneficiation of Bauxite (3). Bauxite dust exposure causes serious health problems by interaction with human biological systems like metabolic alterations in the biochemical and hormone regulatory processes (4). The effects of aluminum containing Bauxite dust can lead to interference with the disturbance in parathyroid hormone (PTH), bone metabolism and changes in serum essential elements as calcium and phosphorus (5).

PTH is the most important endocrine regulator of calcium and phosphorus concentration in extracellular fluid. PTH is a calcium regulatory hormone secreted by parathyroid gland which is regulated by hypothalamus axis. Al being major competitor of calcium, its overload leads to PTH suppression (6) however it is unclear whether decrease in synthesis or release of the hormone is mainly involved in PTH suppression. Number of clinical and experimental studies has demonstrated that Al overload reduces circulating PTH levels (7). Al suppresses PTH either indirectly by increasing serum calcium levels or directly influences PTH synthesis, degradation or release. Earlier reported studies suggested that direct effect is more frequent and significant as compared to indirect mechanism of PTH inhibition (as shown in fig.1). Some researchers agreed on the toxic effect of aluminium in bones which is multi factorial, altering not only the mineralization, but also the cellular activity of parathyroid and bone cells (8).Aluminum toxicity generally leads to an accelerated cell death due to chronic disruption of cell metabolism(9, 10,11).

The relationship between Al, PTH, and Calcium was well defined, but not a single study was related to Bauxite dust exposed mine workers in India. Therefore this is the first study emphasizing on estimation of parathyroid hormone in three major Bauxite ore producing Indian mines.

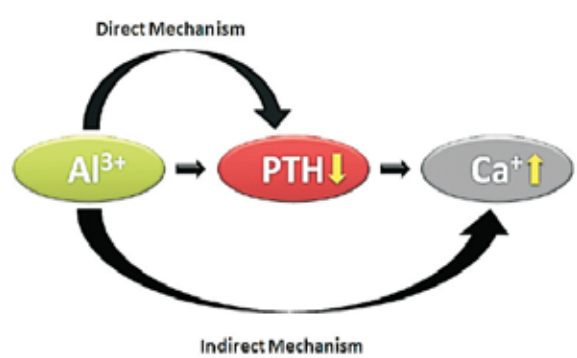

Figure.1: Mechanism of PTH

Methods

The current study is based on Exploratory and Stratified Randomized design which was carried out in three different major Bauxite producing mines i.e. HINDALCO (n= 78), BALCO (n= 88), and NALCO (n= 87). Total 273 mine workers and control subjects were selected. Workers, who were directly exposed to bauxite dust were categorized

Volume : 4 | Issue : 12 | Dec 2014 | ISSN - 2249-555X

into experimental group (n=150) for comparison. Workers, who were age and sex matched and residing at same geographical region but not directly exposed to Bauxite dust were selected as experimental controls (n=73). Healthy individuals were considered as a control group (n=50). All subjects of control group had no history of Al containing Bauxite dust exposure. Workers having exposure period of more than 1 year were included and those who were occupationally exposed to any known chemical agents, history of chronic diseases and female workers were excluded from the study. A standard questionnaire was used to record information on base line characteristics. Informed consent was obtained from all study subjects. The study was approved by Institutional Ethics Committee (IEC) of National Institute of Miners' Health (NIMH), Nagpur.

Blood collection:
Blood samples were collected from mine workers prior to shifting them in dust free environment. Collected blood samples were allowed to clot and centrifuged at 1000 rpm for 5min. Separated serum samples were allowed to freeze immediately and stored at -40ºC in accordance with accepted procedures. Whole blood samples (2ml) were used for Aluminium metal analysis by ICP-AES method while serum samples were used for Parathyroid Hormone (PTH) and calcium analysis.

Determination of Parathyroid Hormone (PTH) by ELISA:
PTH level was evaluated in the sera by using Streptavidin Coated Strips (Kit-DIA source Belgium Cat log No. KAP1481). 25µl of serum samples were added into the mapped well and added 50µl of Biotinylated antibody followed by addition of 50µl of Enzyme Labeled into each of the same wells which already contain the sample and incubated the plate for 3 hours on an orbital shaker (170 rpm). After incubation, wells were washed five times with the wash buffer and added 150µl of TMB Substrate into each of the wells and incubated at 37°C for 10 min. The reaction was stopped with addition of 150µl TMB Stop solution and the absorbance of colour in each well was read at 450 nm. Each sample was tested in duplicate.

Determination of Calcium:
Calcium level was estimated in the sera by using commercially available kit (BEACON - Cat log No. Z08). Its absorbance was read at 530nm by Semi autoanalyser and each sample was tested in duplicate.

Determination of Aluminium by ICP-AES method:
A set of experiment was prepared by using 2 ml blood sample with 1 ml triton x-100, 2ml of concentrated Perchloric acid, 5ml ultrapure concentrated HCl and 8.5 to 10ml ultrapure concentrated Nitric acid. This mixture was digested on hot plate at 150^0C for 30 minutes and filtered through whatman filter paper no. 40 and filtrate was diluted with nitric acid (5%) and made up volume up to 10 ml. Instead of blood sample, ultrapure water was used in another set of experiment conducted with same procedure. This set of experiment was used as blank. Then final solution was aspirated in Inductive Coupled Plasma Atomic Emission Spectrometry (ICP-AES) for further analysis. Each sample was tested in duplicate

Statistical analysis
All the statistical analysis was performed using R-2.15.1 programming language with pre-validated programs. Descriptive statistics of basic characteristics of subjects in three study groups were done by using *one-way analysis of variance, t-test of independent sample, and Chi-square test* followed by *Tukey's post-hoc* for comparison. *Pearson's correlation coefficient* Graphs of respective data were prepared using Prism (version 5) software (Graph Pad Software, Inc. San Diego, CA). *p* value of <0.05 was considered statistically significant for all the analysis.

Results
Table-1 provides the descriptive statistics of basic characteristics of subjects in three study groups. As regards age, the difference in mean age across study groups was statistically significant with *P*-value < 0.0001 using *one-way analysis of variance*. The mean age of subjects in control group (37.9 ± 8.61 yrs) was significantly lower than the other two groups. The mean duration of exposure for subjects in experimental control group (20.71 ± 9.36 yrs) was insignificantly different than that of experimental group (19.63 ± 9.45 yrs) as indicated by a *P*-value of 0.422 as per *t-test of independent samples*. Further, the mean body mass index (BMI) of

subjects across study groups differed significantly as revealed by a *P*-value of 0.001 (*P*< 0.05) using *one-way analysis of variance*. The mean BMI in experimental control group (26.11 ± 4.38 kg/m2) was significantly higher than the control (24.66 ± 4.38 kg/m2) and experimental groups (24.05 ± 3.58 kg/m2). The dietary habits of subjects showed insignificant association with the study groups as indicated by a *P*-value of 0.1463 using *Chi-square test.* The proportion of subjects with smoking habit in experimental group (40.6%) was significantly higher than that of experimental control (24.6%) and control (14%) group as revealed by *P*-value of 0.0007 (*P*< 0.05) using *Chi-square test*. As regards tobacco consumption, the proportion of subjects in control (38%) and experimental control (36.9%) groups was nearly same and differed insignificantly with that of experimental group (50.6%) as indicated by *P*-value of 0.089 (*P*> 0.05) using *Chi-square test*. The proportion of subjects consuming alcohol in experimental group (57.3%) was significantly higher than that of experimental control (35.6%) and control (46%) groups as revealed by *P*-value of 0.008 (*P*< 0.05).

Table-2 provides the mean and standard deviation of the biomarker according to behavioral habits of subjects. For PTH, the mean levels for alcoholic group (44.70 ± 26.17 pg/ml) was significantly lower as compared to that of non-alcoholic group (55.67 ± 34.05 pg/ml) with a *P*-value of 0.003 (*P*< 0.05). The mean level of PTH for smoker and tobacco chewer group was lower as compare to nonsmoker and nontobacco chewer group but it was not statistically significant.

Table-3 provides the mean and standard deviation of Aluminium, Calcium and PTH biomarker according to study groups. The estimates were obtained for each mine as well as after pooling over the three mines. However, considering that *age*, *BMI* and behavioral habits i.e. *smoking*, *tobacco* and *alcohol* consumption could have a possible confounding effect on the levels of these parameters; *analysis of covariance* (ANCOVA) was carried out for each parameter independently to adjust for these confounders and to determine the true effect of exposure. As a result, the adjusted parametric levels were obtained for each subject and were summarized in terms of adjusted mean and standard deviation as shown in Table 4. The statistical significance of difference in the overall mean adjusted values of parameters across study groups was evaluated using *one-way analysis of variance* (ANOVA). The parameters violating the assumption of normality were log-trans-

Volume : 4 | Issue : 12 | Dec 2014 | ISSN - 2249-555X

formed and then the significance testing was carried out. One-way ANOVA revealed that all the parameters differed significantly across three groups. The significance was contributed by the mean levels in control group as confirmed through *Tukey's post-hoc* comparison. The experimental control and experimental groups showed statistically significant difference of mean of PTH, (*P*-value < 0.0001). There was significant (*P*-value < 0.0001) difference in the level of Calcium in experimental and experimental control group as compared to control group. It was also observed that there was slight increase in level of aluminum in experimental group as compared to both groups but it was not statistically significant and lies within normal range.

The percent change in overall mean levels of parameters in three groups after adjusting for confounders is shown in Table-5. Considering a thumb rule of 10% change as noticeable, in experimental group, the adjusted mean PTH levels showed an increase of ~13% over unadjusted mean. For remaining parameters, the percent change was less than 10% suggesting that confounders had a very negligible role on parametric levels in statistical sense.

Table-6 shows the mean and standard deviation of each parameter of each mine and three groups. The significance of difference in mean levels of each parameter across group was evaluated separately for each mine. All parameters showed statistically significant differences in mean levels of groups. The significance was mainly contributed by the control group for all the three mines.

Figure-2 shows the scatter plot of relationship between PTH and Aluminium levels for subjects in three groups. Pearson's correlation coefficient for the two parameters was - 0.52 with a *P*-value < 0.0001 indicating statistically significant negative relationship between the two parameters. In this comparison also, the negative relationship was contributed by the control group.

Figure-3 provides the scatter plot of adjusted PTH and Calcium levels for subjects in three groups. Pearson's correlation coefficient as a measure of relationship between the two parameters was obtained as - 0.20 with a *P*-value of 0.001 (*P*< 0.05). It suggests that the two parameters have inverse relationship, which is statistically significant. The negative relationship was mainly due to Control group, which showed high PTH levels and low Calcium levels. In experimental control and experimental groups, the PTH levels were low while Calcium levels were higher than that of control group.

Figure-4 shows bar plots for mean duration of exposure and mean PTH levels for experimental control and experimental groups. The difference in the mean duration of exposure in these two groups was statistically insignificant (*P*-value: 0.422). However, mean PTH level in the experimental control group was significantly higher than the experimental group with *P*-value < 0.0001. In other words, even though mean duration of exposure in these groups was nearly same, the mean PTH level in experimental control group was 1.11 times higher than experimental group. This implies that some other factors like exposure concentration, type of activity etc. could be fundamental in affecting the PTH levels.

Discussion

Aluminum (Al) is abundantly present in the environment and its exposure to individuals is inescapable task. Previously Al was not included in the list of hazardous substance, but later on it was included in the priority list of hazardous substances identified by Agency for Toxic Substances and Disease Registry (ATSDR) (12).

Toxicity of aluminium is reported to be diverse and not well documented; therefore a cohesive pattern of its cellular mechanism fails to emerge after reviewing the literature (7). Earlier reported studies on interaction between Al and PTH were generally carried out in heamodialysis patients, healthy subjects who consumed Al containing food products, preterm infants with parental nutrition and also in experimental animals (13). However, there is no single study which reported on toxicity of Aluminium in Bauxite dust exposed mine workers of India.

The thrust of the present study was on evaluation of Al, PTH and calcium in Bauxite dust exposed mine workers and try to find out the impact of Al containing Bauxite dust and behavioral habits of exposed workers on serum PTH level.

The effect of behavioral habits such as smoking, alcohol and tobacco consumption on the level of PTH in bauxite dust exposed workers was also studied. It was observed that mean level of PTH was lower in smokers than non-smokers. Similar trends were also observed in alcohol and tobacco consuming workers. Several scientists, N. Faroug *et. al.* (14), R Jorde *et. al.* (15) and D. Kapoor *et. al* (16)., reported the relationship between smoking and low serum PTH level, however the actual mechanism remains to be clarified. It was believed that tobacco smoking may be associated with decreased bone density and calcium absorption and therefore abnormalities in PTH level expected in smokers. Aluminium is one of the major constituents in tobacco smoking and its direct toxic effect on parathyroid cells cannot be ruled out. In addition, there might be substances in smoke that could interact directly with the calcium receptor; smoking could enhance degradation of PTH in blood samples and cause low PTH levels.

The result of the current study indicated that PTH levels among all the three groups were significantly different. The mean level of PTH was significantly decreased (p <0.0001) in experimental group as compared to control and experimental control groups (table no.6), which may also be due to exposure to bauxite dust. The lower levels of serum PTH among exposed group may be explained by presence of high level of aluminum, which inhibits PTH by different mechanisms, such as aluminum accumulation in parathyroid glands, which can reduce parathyroid response to hypocalcaemia and prevents release of PTH, interferes with synthesis of PTH and has an inhibitory effect on parathyroid cell proliferation. The PTH level was also decreased in experimental control group as compared to control group, although levels were within the normal range. Results of present study shows that there was significant (p= <0.0001) negative correlation between PTH level and blood Al (r = -0.52), indicating that as Al level increases, PTH level decreases (Fig.2). Similarly, inverse correlation was also observed between PTH and calcium (Fig.3). It was noted that the degree of PTH and calcium suppression was proportional to the degree of Al overload among the bauxite dust exposed mine workers. The lower levels of serum PTH among exposed group may be explained by the presence of high level of aluminium which inhibits PTH by different mechanisms, such as aluminium accumulation in parathyroid glands can reduce parathyroid response to hypocalcaemia and prevents release of PTH. A number of studies have demonstrated that aluminium overload reduc-

Volume : 4 | Issue : 12 | Dec 2014 | ISSN - 2249-555X

es circulating parathyroid hormone level and Ca in circulating system (15).

Metwally and Mazhar (17) reported that serum calcium level was significantly lower in Al exposed group than the control group and same consistent was found in the present study. Similar results were obtained by Ahmad et.al(18). Studied on workers exposed to aluminum dusts had higher levels of aluminum in blood compared to controlsThis findings support the direct and indirect regulatory mechanism of PTH as depicted in (Fig no.1). There is evidence that aluminium interferes mainly with the secretion and release of PTH rather than its synthesis.

Results in this study explained that long duration exposure to aluminum and its accumulation in blood decreases the serum PTH t level. This is in conformity with the results obtained by Díaz-Corte *et. al.* (7) who studied the effect of aluminum load on parathyroid hormone synthesis. They found that percentage fall in PTH level was due to increased exposure period of aluminium.

On the basis of the findings of present study, it was concluded that PTH along with panel of biomarkers can be used as a reliable biomarker for the early detection of bauxite dust toxicity among exposed workers which may help for the early diagnosis of occupational diseases. A further study on larger numbers of aluminum exposed workers is necessary to support the presence of an association between aluminum exposure, parathyroid disorders and calcium metabolism. Although the level of aluminium measures was within the recommended range, still there is a health problem among exposed workers. So these threshold limit values should be further investigated.

Acknowledgement
All Authors would like to thank Ministry of Mines (S&T) for funding the study. Authors would also like to acknowledge the Director of National Institute of Miners' Health for their constant support and encouragement.

Table 1: Descriptive statistics for demographic and behavioral parameters according to study groups

Parameter	Study groups (n=273)											
	Control (n=50)				Experimental control (n=73)			Overall	Experimental (n=150)			
Mines	Phase I (n=10)	Phase II (n=20)	Phase III (n=20)	Overall	Hindalco (n=17)	Balco (n=20)	Nalco (n=36)		Hindalco (n=51)	Balco (n=49)	Nalco (n=50)	Overall
Age (yrs.) [M ± SD]	28.2 ± 4.44	42.5 ± 5.58	38.15 ± 8.89	37.9 ± 8.61	48.24 ± 9.30	41.25 ± 12.15	48.31 ± 7.79	46.36 ± 9.88	45.88 ± 9.90	41.92 ± 10.12	45.98 ± 9.99	44.62 ± 10.11
Exposure (yrs.) [M ± SD]	-	-	-	-	22.65 ± 10.58	15.35 ± 10.46	22.78 ± 6.87	20.71 ± 9.36	21.06 ± 9.97	15.67 ± 9.66	22.06 ± 7.38	19.63 ± 9.45
BMI (kg/m2) [M ± SD]	20.95 ± 2.59	26.78 ± 4.43	24.40 ± 3.84	24.66 ± 4.38	26.65 ± 5.04	22.80 ± 3.92	27.70 ± 3.27	26.11 ± 4.38	23.90 ± 3.46	23.09 ± 3.37	25.14 ± 3.65	24.05 ± 3.58
Diet												
Vegetarian	4 (40)	5 (25)	6 (30)	15 (30)	7 (41.18)	2 (10)	8 (22.22)	17 (23)	2 (3.92)	12 (24.49)	12 (24)	26 (17)
Both	6 (60)	15 (75)	14 (70)	35 (70)	10 (58.82)	18 (90)	28 (77.78)	56 (77)	49 (96.08)	37 (75.51)	38 (76)	124 (83)
Smoking (Yes)	3 (30)	4 (20)	0	7 (14)	3 (17.65)	8 (40)	7 (19.44)	18 (25)	20 (39.22)	23 (46.94)	18 (36)	61 (41)
Tobacco (Yes)	0	10 (50)	9 (45)	19 (38)	5 (29.41)	12 (60)	10 (27.78)	27 (37)	23 (45.10)	29 (59.18)	24 (48)	76 (51)
Alcohol (Yes)	4 (40)	11 (55)	8 (40)	23 (46)	10 (58.82)	10 (50)	6 (16.68)	26 (36)	33 (64.71)	33 (67.35)	20 (40)	86 (57)

Note: n= Data are presented as n=number of cases, ( )= Percentage for categorical data, Abbreviations: BMI;body mass index

Table 2: Comparison of selected biomarker according to behavioral habits

Parameter	Smokers (n=86)	Non-smokers (n=187)	Alcoholic (n=135)	Non-alcoholic (n=138)	Tobacco (n=122)	No tobacco (n=151)
PTH (pg/ml)	45.91 ± 29.56	52.24 ± 31.29	44.70 ± 26.17	55.67 ± 34.05	48.00 ± 30.36	52.06 ± 31.21
P-value	0.109		0.003		0.279	

Volume : 4 | Issue : 12 | Dec 2014 | ISSN - 2249-555X

Table 3: Unadjusted mean and standard deviation of Aluminium, Calcium and PTH biomarker to study groups and mine

Parameter	Study groups / Mine											
	Control (n=50)			Overall	Experimental control (n=73)			Overall	Experimental (n=150)			
Mines	Phase I (n=10)	Phase II (n=20)	Phase III (n=20)		Hin-dalco (n=17)	Balco (n=20)	Nalco (n=36)		Hin-dalco (n=51)	Balco (n=49)	Nalco (n=50)	Overall
Calcium (9.0-10.6 mg/dl)	6.34 ± 1.24	10.56 ± 1.10	8.26 ± 2.41	8.79 ± 2.37	8.59 ± 2.82	10.81 ± 2.22	10.98 ± 4.02	10.38 ± 3.45	8.62 ± 1.61	10.64 ± 0.89	11.11 ± 5.61	10.11 ± 3.56
PTH (9-94 pg/ml)	35.26 ± 15.77	55.33 ± 28.22	70.12 ± 13.92	57.23 ± 24.44	34.57 ± 10.56	46.80 ± 31.16	70.41 ± 37.46	55.60 ± 34.62	36.69 ± 17.96	29.70 ± 19.23	69.41 ± 33.92	45.31 ± 30.10
Aluminium (upto 17 µg/dl)	0.71 ± 0.34	0.56 ± 0.33	0.44 ± 0.33	0.54 ± 0.34	0.72 ± 0.38	0.75 ± 0.32	0.94 ± 0.57	0.84 ± 0.49	0.82 ± 0.39	0.98 ± 0.53	0.90 ± 0.47	0.90 ± 0.47

Table 4: Adjusted mean and standard deviation for Aluminium, Calcium and PTH biomarker according to study groups and mines*

Parameter	Study groups / Mine											
	Control (n=50)			Overall	Experimental control (n=73)			Overall	Experimental (n=150)			Overall
Mines	Phase I (n=10)	Phase II (n=20)	Phase III (n=20)		Hin-dalco (n=17)	Balco (n=20)	Nalco (n=36)		Hin-dalco (n=51)	Balco (n=49)	Nalco (n=50)	
Calcium (9.0-10.6 mg/dl)†	8.77 ± 0.40	8.77 ± 0.47	8.69 ± 0.50	8.74 ± 0.46	10.71 ± 0.64	10.52 ± 0.49	10.32 ± 0.41	10.46 ± 0.51	10.53 ± 0.50	10.39 ± 0.48	10.24 ± 0.49	10.39 ± 0.50
PTH (9-94 pg/ml)†‼	69.66 ± 4.75	60.67 ± 6.24	62.05 ± 5.88	63.02 ± 6.65	58.07 ± 5.850	62.54 ± 8.81	53.37 ± 6.31	56.98 ± 7.93	51.58 ± 5.97	53.65 ± 5.73	48.11 ± 6.06	51.10 ± 6.31
Aluminium (upto 17 µg/dl)†	0.48 ± 0.09	0.49 ± 0.08	0.53 ± 0.05	0.50 ± 0.07	0.81 ± 0.09	0.79 ± 0.08	0.80 ± 0.08	0.8 ± 0.08	0.85 ± 0.08	0.84 ± 0.09	0.85 ± 0.07	0.85 ± 0.08

***Adjusted for** *age*, **BMI,** *smoking*, *alcohol* **and** *tobacco* **using logistic regression model; ‡*P*-value < 0.05 (S) for overall data from each group; † *P*-value < 0.0001 (HS) for overall data from each group; ‼ Statistical significance evaluated using log-transformed data**

Table 5: Percent change in the mean levels of each parameter after adjusting with the confounders

Parameter	Percentage change		
	Control	Experimental control	Experimental
Calcium (9.0-10.6 mg/dl)	0.57	0.76	2.77
PTH (9-94 pg/ml)	10.12	2.42	12.78
Aluminium (upto 17 µg/dl)	7.41	5	5.56

Volume : 4 | Issue : 12 | Dec 2014 | ISSN - 2249-555X

Table 6: Comparative study on three mine wise distribution of data, adjusted mean and standard deviation for Aluminium, Calcium and PTH biomarkers according to study groups.

Parameter	Hindalco (n=78)				Balco(n=89)				Nalco(n=106)			
	Control (n=10)	Experimental control(n=17)	Experimental (n=51)	P-value	Control (n=20)	Experimental control (n=20)	Experimental (n=49)	P-value	Control (n=20)	Experimental control (n=36)	Experimental (n=50)	P-value
Calcium (9.0-10.6 mg/dl)	8.77 ± 0.40	10.71 ± 0.64	10.53 ± 0.50	< 0.0001	8.77 ± 0.47	10.52 ± 0.49	10.39 ± 0.48	< 0.0001	8.69 ± 0.50	10.32 ± 0.41	10.24 ± 0.49	< 0.0001
PTH (9-94 pg/ml)	69.66 ± 4.75	58.07 ± 5.850	51.58 ± 5.97	< 0.0001	60.67 ± 6.24	62.54 ± 8.81	53.65 ± 5.73	< 0.0001	62.05 ± 5.88	53.37 ± 6.31	48.11 ± 6.06	< 0.0001
Aluminium (upto 17 µg/dl)	0.48 ± 0.09	0.81 ± 0.09	0.85 ± 0.08	< 0.0001	0.49 ± 0.08	0.79 ± 0.08	0.84 ± 0.09	< 0.0001	0.53 ± 0.05	0.80 ± 0.08	0.85 ± 0.07	< 0.0001

*Adjusted for *age*, *bmi*, *smoking*, *alcohol* and *tobacco* using logistic regression model

Correlation analysis

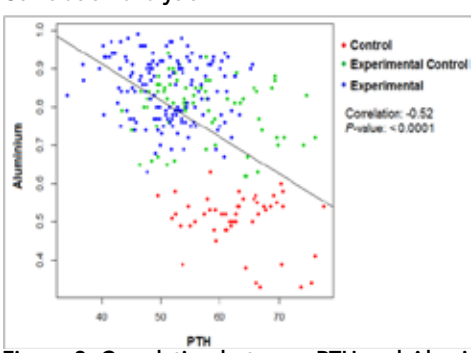

Figure 2: Correlation between PTH and Aluminium

Figure 3: Correlation between PTH and Calcium

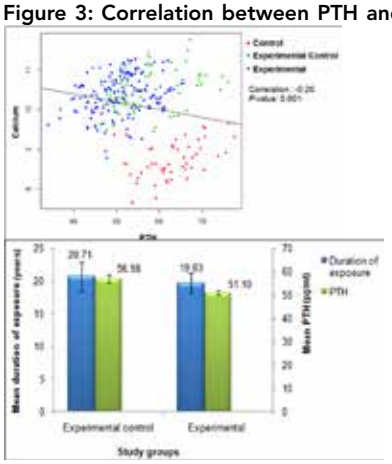

Figure 4: Bar chart with error bars showing mean duration of exposure and PTH

REFERENCE

1. Jamal K., David O.C. & Irina B. Cytotoxicity of environmentally relevant concentrations of Aluminum in Murine Thymocytes and Lymphocytes. J Toxicology 2011; 796719, 1-7. | 2. ATSDR, 2009 Priority data needs for aluminum. Agency for Toxic Substances and Disease Registry.http://www.atsdr.cdc.gov | 3. Nieboer E., Gibson B.L., Oxman A.D., et al. Health effects of aluminum: A critical review with emphasis on aluminum in drinking water. Environ Rev 3, 1995; 29-81. | 4. Greger J.L., Sutherland J.E. Aluminum exposure and metabolism. Crit Rev Clin Lab Sci. 1997; 439-74. Review. PubMed PMID: 9405895. | 5. Jeffery EH., Abreo K., Burgess E., et al. Systemic aluminum toxicity: Effects on bone, hematopoietic tissue, and kidney. J Toxicol Environ Health 1996, 649-665. | 6. Cannata Andia J. B., Aluminium toxicity: its relationship with bone and iron metabolism. Nephrol Dial Transplant. 1996; 69-73. | 7. Carmen D. C., Jose L. F., Barreto S. et al. Effect on aluminium load on parathyroid hormone synthesis. Nephrol Dial Transplant. 2001; 742-745. | 8. Cournot W. G., Plachot J. J., Bordeau A. Effect of aluminium on bone and cell localization. Kidney Int 1986; 37-40. | 9. Sua´rez-Ferna´ndez M.B., Soldado A.B., Sanz-Medel A,. et al. Aluminum-induced degeneration of astrocytes occurs via apoptosis and results in neuronal death. Brain Res. 1999; 125–136. | 10. Pan J.W., Zhu M.Y., Chen H. Aluminum-induced cell death in root-tip cells of barley. Environ Exp Bot. 2001; 71–79 | 11. Aremu D.A., Meshitsuka S. Accumulation of aluminum by primary cultured astrocytes from aluminum amino acid complex and its apoptotic effect. Brain Res 2005; 284–296 | 12. ATSDR, 2007. Notice of the revised priority list of hazardous substances that will be the subject of toxicological profiles. Agency for Toxic Substances and Disease Registry. Fed Regist.73:12178-9. | 13. De Kom J.F.M., Dissels H.M.H., Van Der Voet G.B., et al. Serum aluminum levels of workers in the bauxite mines. Clin Toxicol. 1997; 645-51. | 14. Noora F, Elhashimi E. Hassan, et al. ,The effect of smoking in parathyroid hormone (pth) and alkaline phosphtase (alp). world journal of pharmacy and pharmaceutical sciences, 2014; 1491-1499 | 15. Jorde R., Saleh F., Figenschau Y. , et al. Serum parathyroid hormone (PTH) levels in smokers and non-smokers. The fifth Tromsø study, European Journal of Endocrinology. 2005; 39–45 | 16. Kapoor D., Jones T. H. Smoking and hormones in health and endocrine disorders, European Journal of Endocrinology. 2005; 491–499 | 17. Metwally F.M., Mazhar M.S., Al effects on essential elements in humans. Arh Hig Rada Toksikol. 2007; 305-11. | 18. Boran A.M., Al-Khatib A.J., Alanazi B.S., et al. Investigation of aluminum toxicity among workers in aluminum industry sector. European Scientific Journal. 2013; 24 |