Advances in Bioresearch
Adv. Biores., Vol 8 (2) March 2017: 208-217
©2017 Society of Education, India
Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.8.2.208217

Advances in Bioresearch

ORIGINAL ARTICLE

Analysis of Rheumatoid Arthritis Factor and Haematological Parameters among stone quarry Dusts exposed Workers and Establishing its correlation with years of exposure to stone Quarry Dust

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ABSTRACT
Exposure to stone quarry dusts is a major menace to the workers exposed to it. These deadly dust particles are so harmful that it may be responsible for the development of joint pain and arthritis. The present study is a step towards searching a link between the developments of Rheumatoid Arthritis (RA) and silica exposed workers. Total 209 subjects were selected and grouped as Experimental (N=201) and Control (N=208). Blood samples were collected and used for haematological analysis and RA factor determination. The value of RA was found to be higher in exposed subjects compared to Control. Significant alteration was observed among haematological profile of exposed workers. Insignificant positive correlation was noted between years of exposure to stone quarry dust and Haemoglobin (Hb%) among Experimental subject (r= 0.061, p =0.540 i.e. P value >0.05) while negative correlation was observed for exposure with platelet & total leukocyte count however exposure & RBCs didn't show any correlation. The correlation between RA factor and years of exposure to stone quarry dust was found to be negative among Experimental subjects (r= -0.052, p=0.598). Also, Hb% was negatively correlated with RA factor in case of both the subjects. RBCs showed no correlation with RA factor in case of both the subjects. Exposure to stone quarry dusts enhances immunological response and levels of RA.

Keywords: *Exposure, Haemoglobin, Platelet, Rheumatoid Arthritis, Stone quarry.*

Received 31/11/2016 Revised 10/01/2017 Accepted 19/02/2017

How to cite this article:
Mehere B.A, Pingle S.K, Patil M.B, Thakkar L.R, Tumane R.G, Jawade A.A. Analysis of Rheumatoid Arthritis Factor and Haematological Parameters among stone quarry Dusts exposed Workers and Establishing its correlation with years of exposure to stone Quarry Dust. Adv. Biores., Vol 8 [2] March 2017: 208-217

INTRODUCTION

India is one of the largest processor of various kinds of stones that provide the construction needs globally, hence lots of stone quarries are operated to evacuate stones, marbles, granite and other materials required for various kinds of industrial activities. Stones of stone quarry units in India are broadly comprised of Silica, Lead, Iron and other trace metal ores with impurities, among these; silica mineral is present in bulk quantities (47%) [1]. Silica is one of the most notorious workplace contaminants It is the second most common mineral in the earth's crust and is a major component of sand, rock, and mineral ores [2]. Considering the deposits of silica, 3.150 million tons deposit of quartz is found only in Vidharbh region of Maharashtra [3]. Occupations such as mining, tunnelling, sandstone industry, stone quarrying, drilling and working in foundries are closely associated with hazardous exposure to silica [4].

Workers in the stone cutting units, and stone industry are continuously exposed to respirable crystalline silica dust particles. When workers cut/drill objects having crystalline silica, it could enter through breathing and possibly cause health hazards [5]. Since majority of stone quarries are non mechanised especially small unorganized factories; the collection of ground quartz is still done manually which is

more dangerous for workers [6]. It is surprising to note that, approximately 83% of stone quarry workers including sandblasters, miners, millers, tunnelers, and potters are exposed to the respirable crystalline silica particles causing many irreversible occupational health effects and hence these workers are at risk of development of occupational diseases [7]. Remarkably, the incidence of silicosis is more among previous workers than the existing workers. Singh MP [6], documented that ex-quartz factory workers has higher morbidity levels than existing workers in West past of India. These dangerous dust particles affect haematological parameters. Thus, haematological parameters may help the scientist to understand the mechanism of disease [8]. It has been reported that exposure to crystalline silica initiates several immune responses, but conflicts are there in the level of Rheumatoid Arthritis Factor (RF) following silica exposure. The present study was focused to measure RF levels and haematological parameters among silica exposed workers and its comparison with control subjects.

MATERIALS AND METHODS

Selection of area and subjects:

Stone quarries from Central India were selected for the study. A standard questionnaire was used to record information on base line characteristics such as age, sex; habits like smoking, tobacco chewing, alcohol consumption, duration of exposure to stone quarry dust, health history and medication etc. The study was explained to each volunteer and all subjects enrolled in the study signed a statement agreeing to the use of their medical information for research purposes. The study was approved by local Research Advisory Committee (RAC) and local Ethics Committee.

Inclusion and Exclusion criteria:

Workers having exposure period more than 10 years were included in this study and those who were occupationally exposed to any known chemical agents, cardiovascular diseases, inflammatory disease, diabetes, anaemia etc were excluded from the study. Total 209 subjects were selected for this study. These were further categorized as Experimental (Exp) and Control (Con). Subjects who were directly exposed to stone quarry dust were categorized into Experimental group (n=101), for comparison, age matched healthy subjects, residing at the same geographical region but not exposed to stone quarry dust were selected as Control population (n=108).

Blood collection

Blood samples were collected from subjects in the medical room under dust free condition. To minimize the possibility of sample contamination, workers were instructed to report for the collection before the start of the shift. Total 5mL blood was collected among which 1mL blood was collected in Heparinized tube for haematological analysis. Remaining blood sample was allowed to clot and centrifuged at 1000 rpm for 5min. The resulting serum sample was transferred to sterile tubes. Three to four aliquots of serum samples were prepared and allowed to freeze. Samples were stored at -40ºC in accordance with accepted procedures. Serum samples were used for further analysis.

Determination of Haematological parameters:

Automatic digital machine-Care cell counter (Beckman Coulter, model no. ACTDIFF-02) was used for haematological examination. Test was performed according to the protocol. Each sample was tested in duplicate.

Determination of RF levels by Enzyme Linked Immunosorbent Assay (ELISA) (Kit Method):

Serum RF was determined by standard protocol by indirect ELISA method using commercially available kit (DRG International, Inc., USA Catalogue No. EIA-3585). Assay was performed as per the instruction manual of the kit. The absorbance was measured at 450 nm. Each sample was tested in duplicate.

Statistical Analysis:

Statistical analysis was performed using MedCalc Software *Version 10.1.2*. t-test of independent samples were used to evaluate the results, years of exposure, RF, haematological parameters. Pearson's correlation coefficient graph of respective data was prepared using MedCalc software *Version 10.1.2*.

RESULTS AND DISCUSSION

The present study is concerned with determination of RF and haematological parameters to search possible link between inflammation and haematological abnormalities among stone quarry exposed miners. Exposure to silica and other related compounds have the ability to recruit cellular responses such as, inflammasome activation, cytokine production, or ROS release in case of autoimmune diseases (especially in RA), as divulged by experimental and epidemiological corroboration [9, 10]. The mechanism of enhanced level of RA can be cited from the study of Cesar A. Speck-Hernandez and GladisMontoya-Ortiz [10], who reported that silica is responsible for generation of molecular and

immunological modifications that may elicit autoimmune responses in RA. Also, silica is involved in pathogenesis of RA by functioning as super-antigens and activates polyclonal activation of T cells.

Table 1 gives information about the years of exposure among Experimental subjects. From the table, it is clear that males had higher duration of exposure than females; however duration of exposure of the overall population falls amid males and females.

Table 2, 3 and 4 provides the mean and standard deviation of haematological parameters and RF values. It was evident from the table that for overall population, except eosoniphils and basophils, all other parameters were statistically significant (all had *p value* <0.05). However male subjects showed insignificant difference in polymorphs, eosinophils and basophils, while in case of females, differential count was insignificant, except monocyte, rest of the parameters were statistically significant. Statistically significant higher level of serum RF was reported among Experimental group as compared to Control however, the value of RF lies within normal range.

Table 1 showing Mean and standard deviation of Exposure to dust among Exp subjects

S.N	Parameters	Con	Exp	p Value
	Exposure to dust (Yrs)			
1	Overall population	-	17.77 ±5.61	-
2	Males	-	19.02±5.56	
3	Females	-	15.43±4.96	0.0019**

** = P value <0.0001 were considered as highly significant. Yrs=Years

Table 2 showing Mean and standard deviation of haematological parameters and RA values of both the groups

S.N	Parameters	Con	Exp	p Value
	Haematological parameters			
1	Haemoglobin (gm/dl)	12.38 ±1.27	11.87 ± 0.69	0.0004**
2	Haematocrit (%)	37.13 ±3.81	35.65±2.02	0.0005**
3	TLC (per µL)	6873.14 ±935.05	8236.43 ±700.88	0.0001**
4	Polymorphs (%)	60.02 ±6.62	62.07 ±6.10	0.021*
5	Lymphocyte (%)	35.74 ±7.00	33.48 ±5.75	0.011*
6	Eosinophil (%)	2.72 ±1.60	3.09 ±1.36	0.07
7	Monocytes (%)	1.23 ±0.65	1.61 ±0.84	0.0004**
8	Basophils (%)	0.12 ±0.33	0.14 ±0.35	0.694
9	Platelet count (Lacks/cu.mm)	2.46 ±0.67	2.90 ±0.85	0.0001**
10	RBC Count (Cells/cumm)	4.24 ±0.60	3.60 ±0.78	0.0001**
	Biochemical parameter			
11	RF (IU/mL)	13.27 ±2.22	18.03 ±2.63	0.0001**

* =P value <0.05 were considered as significant, ** = P value <0.0001 were considered as highly significant. N= Number

Table 3 showing Mean and standard deviation of haematological parameters and RA values among males of both the groups

S.N	Parameters	Con Males	Exp Males	p Value
	Haematological parameters			
1	Haemoglobin (gm/dl)	13.11± 0.89	12.11 ±0.63	0.0001**
2	Haematocrit (%)	39.34 ±2.66	36.33 ±1.85	0.0001**
3	TLC (per µL)	6970.00 ±971.23	8157.27±780.60	0.0001**
4	Polymorphs (%)	61.17 ±6.11	63.18 ±6.24	0.06
5	Lymphocyte (%)	34.57 ±6.60	32.31 ±5.86	0.037
6	Eosinophil (%)	2.78 ±1.70	3.04 ±1.46	0.342
7	Monocytes (%)	1.11 ±0.64	1.43± 0.86	0.014*
8	Basophils (%)	0.11 ±0.32	0.16 ±0.37	0.382
9	Platelet count (Lacks/cu.mm)	2.50 ±0.72	2.99 ±0.94	0.0008**
10	RBC Count (Cells/cumm)	4.31 ±0.62	3.64 ±0.82	0.0001**
	Biochemical parameter			
11	RF (IU/mL)	12.95± 2.34	17.96 ±2.94	0.0001**

* =P value <0.05 were considered as significant, ** = P value <0.0001 were considered as highly significant. N= Number

Table 4 showing Mean and standard deviation of haematological parameters and RA values among females of both the groups

S.N	Parameters	Con Females	Exp Females	p Value
	Haematological parameters			
1	Haemoglobin (gm/dL)	11.03± 0.56	11.43 ±0.58	0.004*
2	Haematocrit (%)	33.07± 1.65	34.37 ±1.68	0.001*
3	TLC (per µL)	6694.73 ±847.87	8385.71±494.76	0.0001**
4	Polymorphs (%)	57.92±7.08	60.0 ±5.30	0.163
5	Lymphocyte (%)	37.89 ±7.28	35.68±4.89	0.13
6	Eosinophil (%)	2.60 ±1.42	3.20 ±1.18	0.057
7	Monocytes (%)	1.44± 0.60	1.94 ±0.72	0.002*
8	Basophils (%)	0.15 ±0.36	0.11 ±0.32	0.594
9	Platelet count (Lacks/cu.mm)	2.39± 0.56	2.72 ±0.62	0.018*
10	RBC Count (Cells/cumm)	4.13±0.55	3.54 ±0.72	0.0002**
	Biochemical parameter			
11	RF (IU/mL)	13.86 ±1.87	18.17 ±1.94	0.0001**

* =P value <0.05 were considered as significant, ** = P value <0.0001 were considered as highly significant. N= Number

Correlation between RF and years of exposure is depicted in fig 1. It is evident from the graph that the correlation between the two was negative among Experimental subjects (r=-0.052, p=0.598). Fig 2 shows the Pearson's Correlation Coefficient between years of exposure and Hb% among Experimental, in this positive correlation (r= 0.061, p =0.540 i.e. *P valu*e >0.05) was observed. While in case of correlation between platelet count with years of exposure, negative correlation (r= -0.156, p = 0.117) was observed. Similarly, TLC showed negative correlation with years of exposure (r= -0.177, p= 0.076) but no correlation was observed for exposure & RBCs (r= 0.006, p= 0.946) as depicted in fig 3, 4 and 5 respectively.

Fig 6 shows the Pearson's Correlation Coefficient between serum RF levels and Hb% of both the subjects. From the fig, it is evident that Hb% was negatively correlated with RF levels in case of both the subjects (r= -0.023, p= 0.814 and r= -0.206, p= 0.032 for Experimental and Control respectively). On the other hand, platelet count showed negative correlation with RF levels among Experimental although it was not significant (r= -0.089, p= 0.371) (fig. 7). RBCs showed no correlation with RF in case of both the subjects (r= 0.011, p=0.117 for Experimental and r= -0.005, p=0.957 for Control) (fig. 8). However, TLC was positively correlated with RA factor levels among both the subjects (r=0.041, p=0.677 Experimental and r= 0.074, p= 0.443 Control) (fig 9).

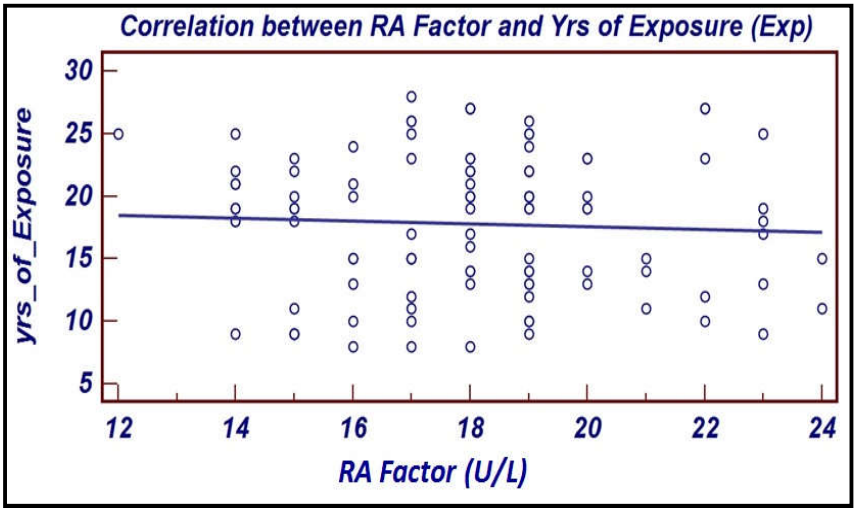


Figure 1: Correlation analysis between RF and Yrs of Exposure (r=-0.052, p= 0.598)

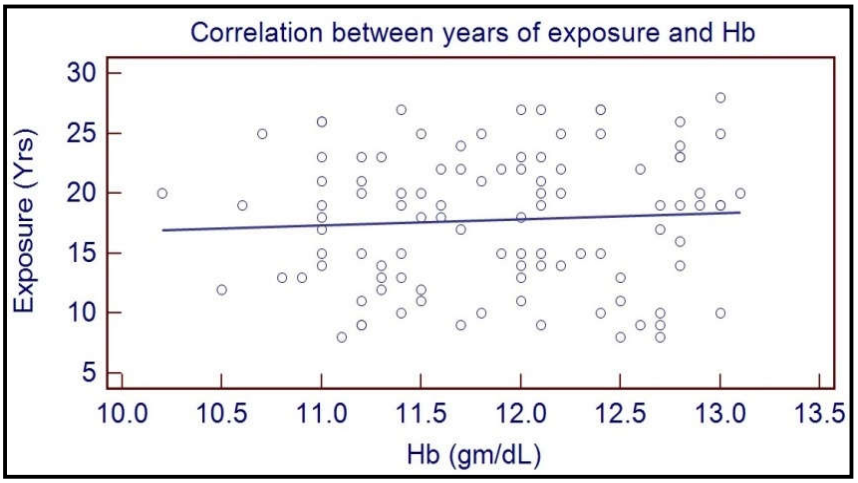


Figure 2: Correlation analysis between Yrs of Exposure and Hb% (r= 0.061, p= 0.540)

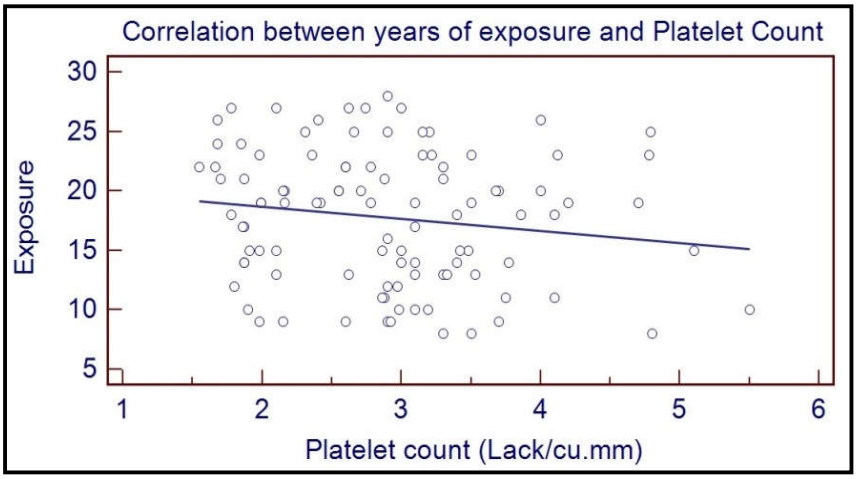


Figure 3: Correlation analysis between Yrs of Exposure and Platelet Count (r= -0.156, p= 0.117)

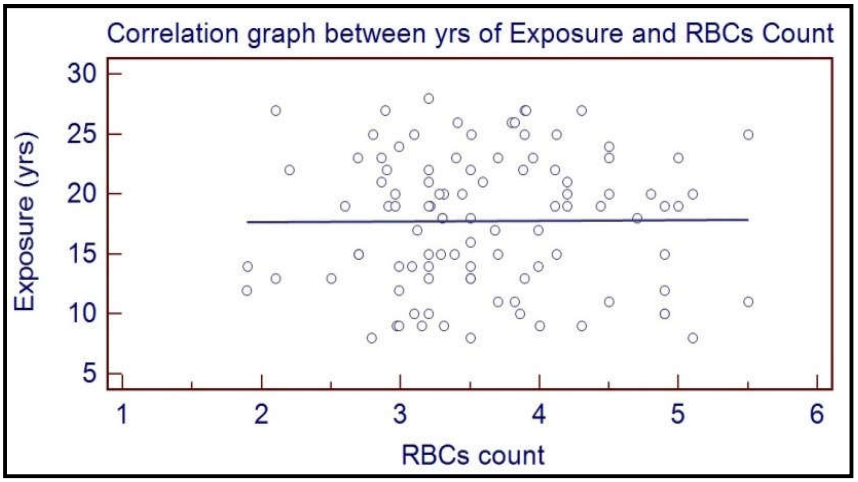
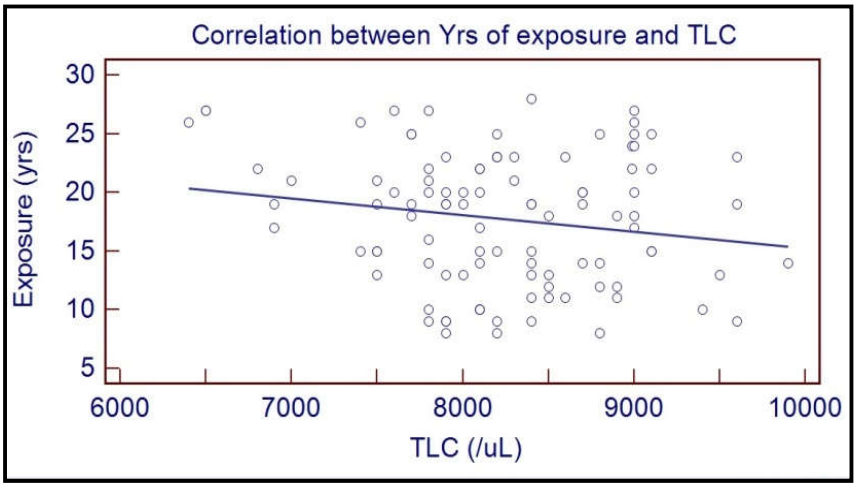
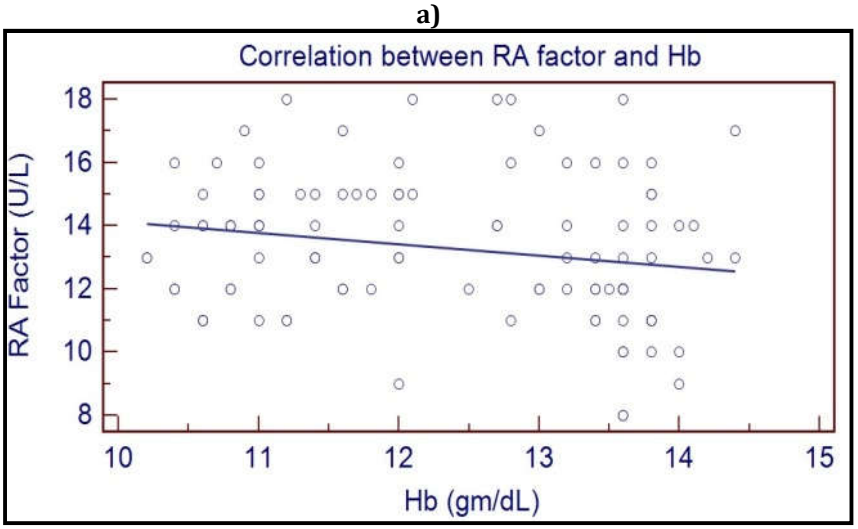


Figure 4: Correlation analysis between Yrs of Exposure and RBCs Count (r= 0.006, p=0.946)



a)



b)

Figure 5: (a, b) Correlation analysis between Yrs of Exposure and TLC (r= -0.177, p= 0.076)

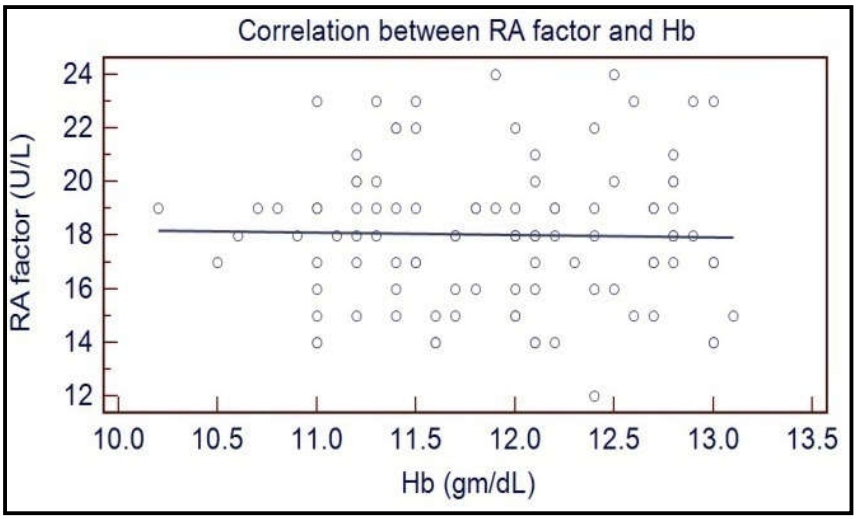


Figure 6: Correlation analysis between RF and Hb% among Exp and Con (r= -0.023, p= R.814 Exp, r= -0.206, p= 0.032 Con)

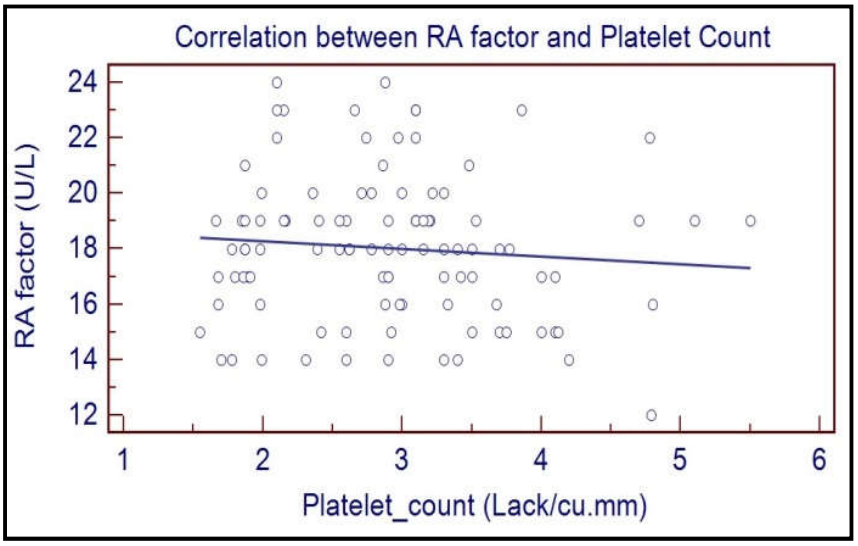
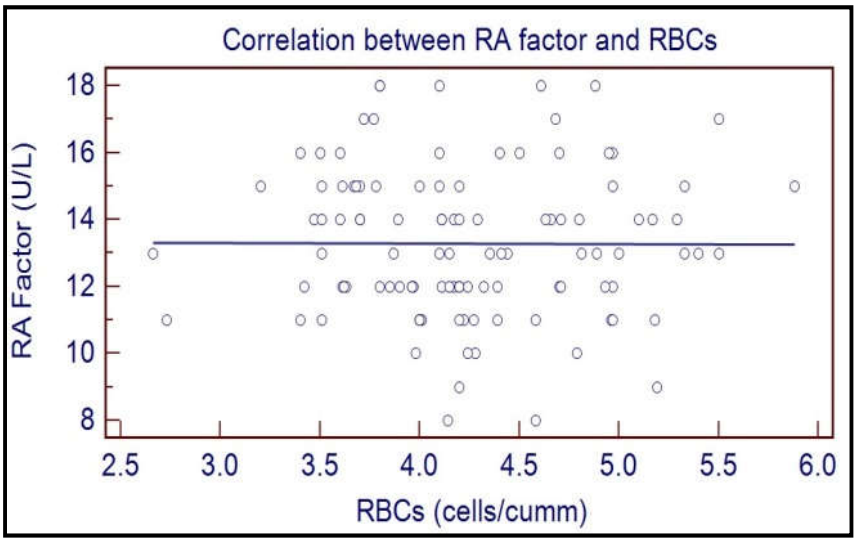
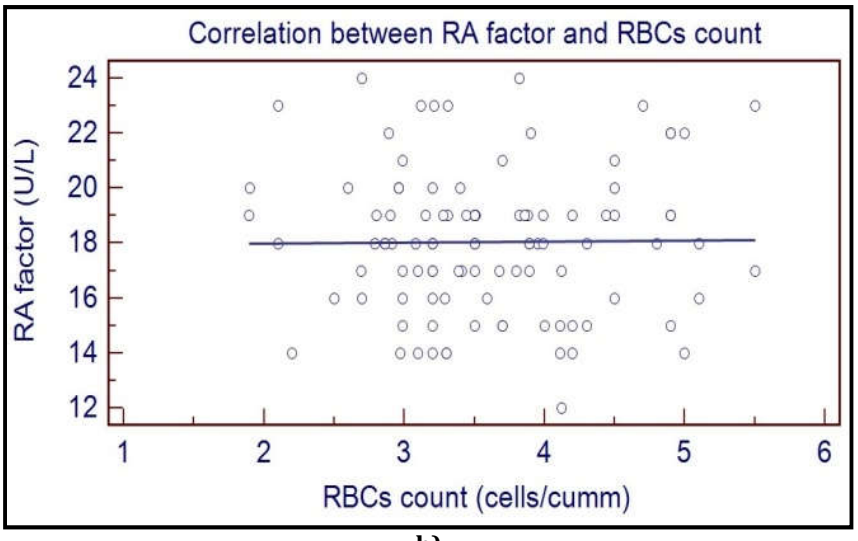


Figure 7: Correlation analysis between RF and Platelet Count among Exp (r= -0.089, p=0.371 Exp)

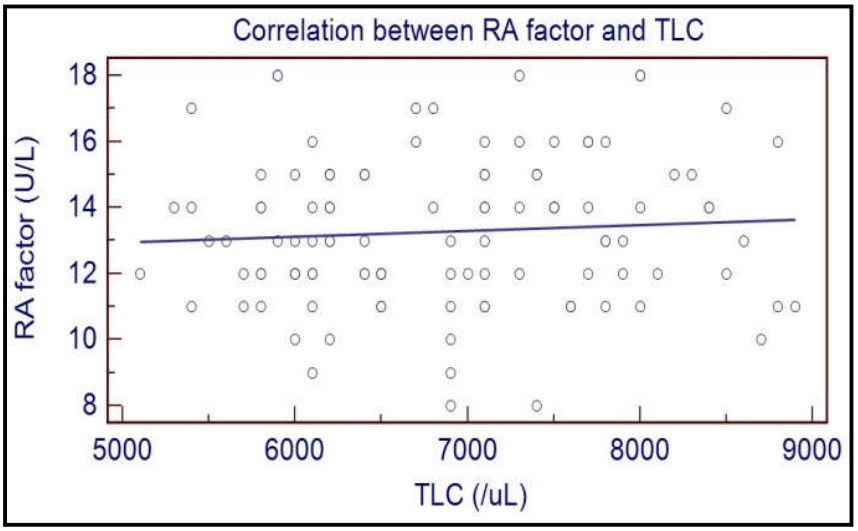


a)

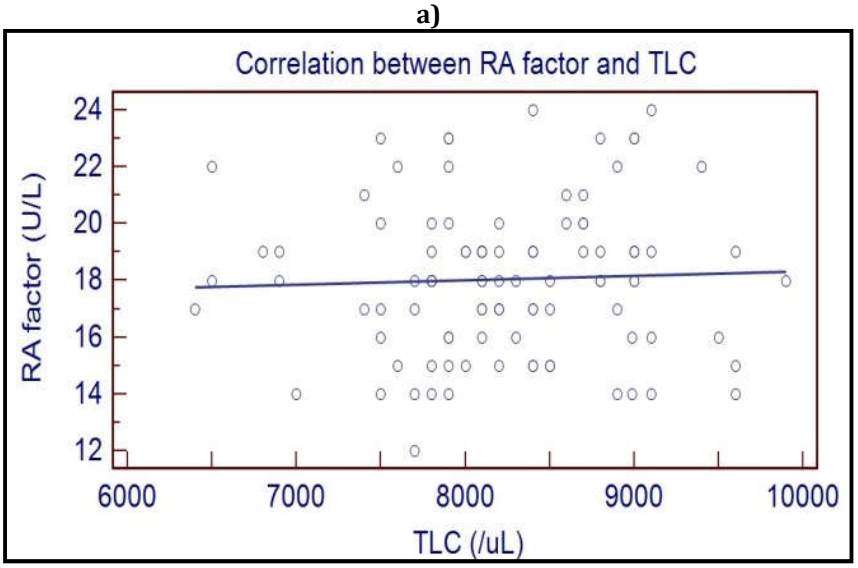


b)

Figure 8 (a, b): Correlation analysis between RF and RBCs among Exp and Con (r= 0.011, p=0.117 Exp, r= -0.005, p=0.957 Con)



a)



b)

Figure 9: Correlation analysis between RF and TLC among Exp and Con (r=0.041, p=0.677 Exp), (r= 0.074, p= 0.443 Con)

Considering the Haematological parameters, it was noted that these parameters revealed significant differences in both the groups. The reduced Hb% and Heamatocrit value and increased WBCs count (except lymphocyte) among Experimental as compared to Control suggest enhanced immunological response caused due to inhalation of silica dusts. Additionally, significant rise in platelet count and reduced RBCs value was also observed in case of Experimental subjects. This is in line with Mandal and Suva [8] who observed decrease in Hb% and increased eosinophil count in construction workers exposed to cement dust in West Bengal (India). According to them, the decrease in Hb% may be due to enhanced response of body in stress condition to keep the total RBCs count normal which leads to elevate immature erythrocytes in circulation. The increased WBCs count suggests enhanced allergic response after exposure to silica dust. The high platelet count levels is in positive association with Mojiminiyi *et al.* [11] who found the same among Nigerian cement factory exposed workers.

RA factor is a significant marker of Rheumatoid Arthritis (RA) and hence the values were determined to find out association between exposure to silica dust and alteration in values of RF along with haematological parameters. Significantly higher RF values were noted among Experimental subjects than Control. However the values were in normal range. Since, silicosis is also an auto immune disease; the mechanism of auto immunity may impede the biochemical pathway of development of RA. Further, it was also noted that, no individual was found to be suffering from RF among all the population, hence it can be said that the alteration in haematological parameters and enhanced RF values was only due to exposure to stone quarry dust containing silica. P Stolt, H Ka¨llberg *et. al*. [12] reported higher risk of RF among

men working in stone cutting and rock drilling. However, our finding is paradoxical to the above reported study as far as male population is concerned. However, Susan Turner S *et. al* [13] didn't find any positive association of occurrence of RF among occupationally silica exposed workers in United Kingdom. Aminian O *et. al* [14] also noted the same observation in his study in which he reported that exposure to silica dust didn't increase the level of RF. The above reported studies are in positive agreement of the current findings.

The mechanism of enhanced levels of RF can be explained by the work done by P Stolt, H Ka¨llberg *et. al*. (2005) who reported that exposure to silica dusts increases the inflammatory mediators from alveolar macrophages which may enhance the production of Matrix Metalloproteinases (MMP)—enzymes. Silica exposures influence the activity of Transcription Factor, Nuclear Factor κB that regulates the synthesis of MMP as well as of inflammatory factors (Tumour Necrosis Factor α and interleukin 1β) [12]. Yazici S, Yazici M *et. al.* (2010) reported significantly higher WBCs and platelet count among RA patients [15]. Further, Milovanovic M, Nilsson E *et. al.* (2004) also found the same in their study on active RA patients [16]. In the present study, higher levels of platelet and TLC were also observed among Experimental subjects who have higher RF values. Considering the correlation between the duo, TLC was positively correlated with RF levels among both the subjects. On the other hand, platelet count showed negative correlation with RF among Experimental. The enhanced platelet count among Experimental subjects may be linked with immunological responses in RA occurred due to exposure to silica dust causing inflammation.

In the present study Hb% was negatively correlated with RA factor in case of both the subjects. Smyrnova G (2014), reported statistically significant negative correlation between haemoglobin level and RF levels which is in positive agreement with the current findings [17]. Moreover, RBCs showed no correlation with RF in case of both the subjects. Olumuyiwa Akeredolu OO, Pretorius E (2015) reported positive correlation between RBC counts and RA which is incongruous with the present findings [18]. RBCs are associated with development of RA is well known. Also, the reticulocyte count and immature erythrocytes are the key factor in RA pathology [19]. But in the present study, exposure to silica dusts reduces the level of RBCs among Experimental subjects which may be an indicator of development of RA among Experimental subjects.

The correlation between RF and years of exposure to stone quarry dust was insignificantly negative among Experimental subjects indicating duration of exposure is not directly linked with development of RA. P Stolt, H Ka¨llberg *et. al.* (2005), postulated the possible mechanism behind the biological effects of silica on RA. According to them, the inflammatory mediators from alveolar macrophages which engulfed the silica particles may stimulate macrophages and lymphocytes in the rheumatoid synovium causing development of RA [12].

Positive correlation was noted between years of exposure to stone quarry dust and Hb% among Experimental, while negative correlation was observed for exposure Vs platelet and exposure Vs TLC however exposure Vs RBCs didn't show any correlation. Very few literatures are available with respect to exposure to silica dust and its correlation with exposure and haematological parameters. Mojiminiyi *et al.* (2007) found positive correlation between years of exposure to cement dust with platelet count and WBC counts which is paradoxical to the present study [11]. Although the higher value of platelet and TLC in our study can't be excluded.

Males and females of Experimental subjects showed significantly higher RF than Control. Also, males and females of Experimental showed decrease in Hb%, heamatocrit and RBCs value while enhanced WBCs and platelet count as compared to Control. But it is also interesting to note that Experimental females had slightly high Hb% compared to Control. Further, female subjects among Experimental group showed high TLC count as compared to Experimental males. Additionally, RF value was also higher among females compared to males. Although males have higher exposure to stone quarry dusts than females, this finding suggests that females of the present study were highly prone to menace caused to exposure to stone quarry dusts.

From the present study, it can be concluded that exposure to stone quarry dust enhances the levels of RF and significantly affects the haematological parameters causing enhanced immunological reaction among exposed subjects and possibly play role in enhancing inflammation. No individual was found to be suffering from RF among all the population, hence it can be assumed that the alteration in haematological parameters and enhanced RF values was only due to exposure to stone quarry dust containing silica. Males and females are at greater risk of immunological alteration caused due to exposure of stone quarry dusts. Further investigation with large population size is therefore warranted to support the findings of the present study.

SOURCE OF FUNDING
This study was funded by University Grant Commission, Govt. of India with Grant No. (F. No. 33-219).

ACKNOWLEDGEMENT
The authors would like to thank to UGC for funding the study. Authors are grateful to Principal, Dr. Ambedkar College for constant support and encouragement throughout the study. Authors are indebted to all volunteers who participated in this study.

COMPETING INTERESTS
The authors have declared that no competing interest exists.

REFERENCES
1. Silicastone, (2016). The Editor, Encyclopedia Britannica, Last accessed on 20th April, 2016: Available on: http://www.britannica.com/science/silicastone.
2. Slivka, J. (2005). Silica: The Next Environmental Issue, Expert Commentary, International Risk Management Institute Inc. April 2005, Available on: https://www.irmi.com/articles/expert-commentary/silica-the-next-environmental-issue
3. Mineral Resources of Maharashtra, (2014). Directorate of Geology and Mining, Govt of Maharashtra, Nagpur. Available on: http://www.mahadgm.gov.in/InternalPage.aspx?Antispam
4. Sivanmani, K. & Rajathinakar, V. (2013). Silicosis in Coimbatore district of Tamil Nadu: A passive surveillance study. Ind. J. Occup. Environ. Med.,17:25-28
5. Occupational Safety and Health Administration. (2010). Occupational Exposure to Respirable Crystalline Silica-Review of Health Effects Literature and Preliminary Quantitative Risk Assessment Occupational Safety and Health Administration Docket OSHA-2010-0034, Available on: https://www.osha.gov/OshDoc /data_ General_Facts/crystalline-factsheet.pdf
6. Singh, MP. (2011). Quartz factories spewing silicosis in Gujarat. In: One World South Asia, 5th May, 2011. Available on: http://southasia.oneworld.ne t/news/india quartz factories spewing silicosis in gujarat#.
7. National Institute for Occupational Safety and Health. (2016). Silica, Last updated on 28th June, 2016, Available on: www.cdc.gov/niosh/topics/silica/ National Institute for Occupational Safety and Health Respiratory, Health Division (RHD)
8. Mandal (Majee), A. & Suva, P. (2014). Haematological changes among construction workers exposed to cement dust in West Bengal, India. Prog. Health. Sci., 4(1): 88-94
9. Harijith, A. Ebenezer, DL. & Natarajan,V. (2014). Reactive oxygen species at the crossroads of inflammasome and inflammation. Front. Physiol. 5(352):1-11.
10. Speck-Hernandez. & Ortiz, GM. (2012). Silicon, a Possible Link between Environmental Exposure and Autoimmune Diseases: The Case of Rheumatoid Arthritis. Arthritis., 2012:1-11
11. Mojiminiyi, FBO. Merenu, IA. Ibrahim, MTO. Nioku, CH. and Ibrahim, MTO. (2007). Regression Formulae for predicting Hematologic and liver functions from years of exposure to cement dust in cement Factory Workers in Sokoto, Nigeria. Afr. J. Biomed. Res.,10:235 - 40.
12. Stolt, P. Ka¨llberg, H. Lundberg, I. Sjo¨gren, B. Klareskog, L. & Alfredsson, L. (2005). Silica exposure is associated with increased risk of developing rheumatoid arthritis: results from the Swedish EIRA study, Ann. Rheum. Dis., 64:582–586.
13. Turner, S. & Cherry, N. (2000). Rheumatoid arthritis in workers exposed to silica in the pottery industry. Occup. Environ. Med., 57: 443–447
14. Aminian, O. Sharifian, SA. Mehrdad, R. Haghighi, KS. & Mazaheri, M. (2009). Antinuclear antibody and rheumatoid factor in silica-exposed workers. Arh. Hig. Rada. Toksikol., 60:185-190
15. Yazici, S. Yazici, M. Erer, B. Erer, B. Calik, Y. Ozhan, H. Ataoglu, S. (2010). The platelet indices in patients with rheumatoid arthritis: mean platelet volume reflects disease activity. Platelets., 21(2):122-5.
16. Milovanovic, M. Nilsson, E. Järemo, P. (2004). Relationships between platelets and inflammatory markers in rheumatoid arthritis. Clin Chim Acta., 343(12): 237-40.
17. Smyrnova, G. (2014). The relationship between hemoglobin level and disease activity in patients with rheumatoid arthritis. Rev Bras Reumatol., 54(6):437-40.
18. Olumuyiwa Akeredolu, OO. (2015). Pretorius E, Platelet and red blood cell interactions and their role in rheumatoid arthritis, Rheumatol Int., 35(12):1955-64.
19. Eustice, C. (2016). Platelet Counts in Rheumatoid Arthritis, Elevated Platelet Not Uncommon With Inflammatory Conditions, Artheritis., Updated November 22, 2015, last accessed on June 06, 2016, Available on, https://www. verywell.com /plateletcountsinrheumatoidarthritis18961.